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April 23, 2021

PROFESSOR VICKI GRASSIAN, Chair
Department of Chemistry and Biochemistry

SUBJECT: Proposed PhD in Biochemistry and Molecular Biophysics

At its April 12, 2021 meeting, the Graduate Council approved the proposal to establish a new degree program of study leading to a PhD in Biochemistry and Molecular Biophysics, with an MS degree option. The proposal was also endorsed by the Committee on Planning and Budget. The Graduate Council will forward the proposal for placement on an upcoming Representative Assembly agenda.

Please note that proposers may not accept applications to the program or admit students until systemwide review of the proposal is complete and the UC Office of the President has issued a final outcome.

Sincerely,

Lynn Russell, Chair
Graduate Council

cc: M. Allen
J. Antony
S. Boggs
S. Constable
B. Cowan
T. Javidi
E. Komives
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February 21, 2021

Dear Graduate Council,

On behalf of the Department of Chemistry and Biochemistry, I am submitting a proposal for a new graduate program in Biochemistry and Molecular Biophysics.

Currently, the Department offers a PhD and MS in Chemistry, and students are associated with one of seven tracks within Chemistry. One of these tracks, Biochemistry and Biophysics, will award this new PhD in Biochemistry and Molecular Biophysics to appropriately recognize the research and academic focus of this track. An MS in Biochemistry and Molecular Biophysics will be offered en route to the PhD.

This new program will be administered by the Department of Chemistry and Biochemistry. The structure of the track, including academic requirements, rotations, admissions process, funding policy, will be unchanged from the current practices of the Chemistry Program. Thus, this new degree requires minimal modification to our existing structure. The primary modification is to establish a Steering Committee for the new degree program.

We hope you agree that these new degree programs (PhD and MS in Biochemistry and Molecular Biophysics) will be beneficial to UC San Diego. As department chair, I am most enthusiastic about this new degree program and opportunities for our graduate students who receive a PhD degree in this important area.

We look forward to your favorable response.

Sincerely yours,

Vicki H. Grassian

Vicki Grassian
Distinguished Professor and Chair

Proposal for Ph.D. Degree in Biochemistry and Molecular Biophysics and M.S. Degree in Biochemistry and Molecular Biophysics (M.S. degree to be awarded to continuing or separating students)

Executive Summary

The Chemistry & Biochemistry department currently awards PhD degrees only in Chemistry despite having a large cohort of faculty and PhD students pursuing research in Biochemistry, Structural Biology & Biophysics. Currently, all PhD students in the Chemistry & Biochemistry Department receive a Chemistry PhD degree. Since 2015, the Department of Chemistry & Biochemistry has had different graduate program Tracks and those PhD students interested in Biochemistry, Structural Biology & Biophysics choose the Biochemistry & Biophysics track when they apply. We wish to offer these PhD students the degree that is appropriate for what they are actually studying. Detailed in this document are reasons why students in the Biochemistry & Biophysics track should be receiving a degree in Biochemistry & Molecular Biophysics. These reasons include: 1) The Department is home to a large NIH-funded T32 Molecular Biophysics Training Program. 2) The students take different coursework that is appropriate for their Biochemistry & Biophysics Track. 3) This coursework does not include training in traditional Chemistry disciplines such as Organic, Inorganic or Physical Chemistry. 4) The Biochemistry & Biophysics Track currently comprises 30% of the graduate students in Chemistry and Biochemistry, yet they are subject to traditional Chemistry program requirements 5) The separate degree program would allow the participating faculty to have more flexibility in the educational program that is currently not possible within the uniform standards required for a degree in Chemistry. For example, the new degree could require longer rotations and yearly thesis committee meetings as is standard for most Biochemistry PhD programs. 6) Some faculty who participate in the Biochemistry and Biophysics Track are interdisciplinary and come from other departments and from Health Sciences.

The offering of two degrees (PhD in Biochemistry and Molecular Biophysics as well as PhD in Chemistry) from a single department is not uncommon. Of note, the Department of Chemistry & Biochemistry at UCLA offers two different PhD degrees, one in Chemistry and the other in Biochemistry, Molecular & Structural Biology. Similarly, the Department of Chemistry & Biochemistry at UC Santa Cruz offers both a Chemistry PhD and a Biomedical Sciences PhD. As at these other UC schools, the new degree program would remain within the UCSD Department of Chemistry & Biochemistry and very little would have to change, except the name of the degree that the students are receiving. A modest increase in administrative effort would be needed to administer this new graduate program, but no other additional support would be required because the students under the new degree would still enter through the Chemistry & Biochemistry Department and would still be supported during their first year by TAships within the Department of Chemistry & Biochemistry as they are now. In subsequent years 2-5, student support would be unchanged from the current practice. There is strong support for this change from the leadership in the Chemistry & Biochemistry Department and Division of Physical Sciences.

Section 1. Introduction

1. ***Aims and objectives of the program.*** We aim to grant a degree in Biochemistry and Molecular Biophysics to those students who are doing their graduate studies in this field instead of the current degree in Chemistry. We hope to accomplish two main objectives by addition of this degree program: 1) To raise the awareness of the strong research in Biochemistry, Structural Biology & Biophysics on the UCSD campus (Biochemistry is

currently ranked 10th in the nation, Biophysics is not currently ranked because no program carries this name, however we have one of the strongest NIH-funded T32 Molecular Biophysics Training Programs in the country. There is no structural biology PhD at UCSD despite our strength in this area.) In this era of heightened competition for strong graduate students, particularly those from underrepresented backgrounds, it has become imperative that our strength in Biochemistry & Molecular Biophysics be recognized with an appropriate degree program. 2) We hope to align the graduate educational experience of the PhD students working in the fields of Biochemistry, Structural Biology & Biophysics with that of other graduate programs in similar fields. 3) A third motivating factor is that students will be able to document their training more appropriately on their resumes making them more competitive for life sciences industry jobs that are a strength in the San Diego area.

Although the degree would be in Biochemistry and Molecular Biophysics, the graduate program would remain in the Department of Chemistry & Biochemistry. The students would continue to TA Chemistry & Biochemistry courses in their first year, and they would continue to take the graduate courses that are currently offered to them through the Biochemistry & Biophysics Track (note the current Track name does not include the word "Molecular" because there was a desire to keep a shorter name such that it would fit on the website tab). The target audience would be those PhD students who enter the Chemistry & Biochemistry graduate program in the Biochemistry & Biophysics track. The vast majority constitute a very strong pool of applicants, which is growing each year.

TABLE 1. Applicants to the Biochemistry & Biophysics PhD Track in the Chemistry Graduate Program

YEAR	Applicants			
	in state	out of state	international	TOTAL
2020	50	42	47	139
2019	38	43	40	140
2018	36	33	18	121
	Matriculants			
2020	6	4	1	11
2019	5	2	0	7
2018	14	13	2	29

2. ***Historical development of the field and historical development of departmental strength in the field.*** The Department of Chemistry & Biochemistry has always had a strong component of faculty working in the areas of Biochemistry, Structural Biology & Biophysics. In fact, leading faculty who were and are members of the National Academy of Sciences such as Bruno Zimm (Biophysics), Martin Kamen (Molecular Biophysics), Nathan Kaplan (Biochemistry), Joe Kraut (Structural Biology), Russell Doolittle (Biochemistry and Structural Biology), Andy McCammon (Computational Biochemistry), and Susan Taylor (Biochemistry and Structural Biology) represent these fields. In 1995, the Chemistry Department recognized the presence of this strong area of research by changing its name to the Department of Chemistry & Biochemistry but neglected to follow this name change with a request to grant a graduate degree in Biochemistry, Structural Biology & Biophysics. Since 1995, the culture of Biochemical Graduate programs has diverged from the culture of Chemistry Graduate programs. For example, most Chemistry graduate programs do not interview the students prior to admission, they require entrance exams and/or cumulative exams, the thesis committees typically do not meet yearly, and students rely more heavily

on TAships for support. In general, Biochemistry graduate programs interview students prior to admission, they require more focused exams such as a research proposal defense, the thesis committees are chosen by the student and their advisor in consultation with the program Steering Committee, students meet yearly with their thesis committee, and students are supported on training grants and research grants.

3. Aside from these logistical differences in the program itself, the Biochemistry, & Molecular Biophysics graduate programs tend to attract students who were undergraduate majors in Biochemistry or a related field. In the last two most recent years, of the students who were admitted to the Biochemistry & Biophysics Track within the Chemistry graduate program, over 60% were undergraduates in Biochemistry or a related Biological field and only 20% were undergraduate majors in Chemistry. Another 20% did double majors in Chemistry and Biochemistry and 4% were Physics majors. These students expect to continue to build on their Biochemistry expertise, and do not expect to have to prove themselves as Chemists nor do they expect to receive their PhD degree in Chemistry.

4. The faculty members of the Biochemistry & Biophysics Track are expected to form the nucleus for the training faculty in the new graduate program (CVs for key faculty are provided in the Appendix). The faculty number 30 total of which 12 are women including one NAS member, and three are from underrepresented groups. Of these founding faculty, 19 have their primary appointment in Chemistry & Biochemistry, 1 has his primary appointment in Cell and Molecular Medicine, 2 have their primary appointment in Pharmacology, and 2 have their primary appointment in SSPPS. Two additional new faculty have 50% appointments in Chemistry & Biochemistry and Health Sciences.

5. The Chemistry and Biochemistry Department currently has seven graduate program tracks. In most years, the Biochemistry & Biophysics (BB) track and the Chemical Biology track are the two largest tracks (see Table 2 below). Of the PhD students currently enrolled, 30% are in the BB Track. These students in the students in the Biochemistry & Biophysics Track who would receive the Biochemistry and Molecular Biophysics PhD degree, while students in the other tracks would continue to receive the Chemistry PhD.

TABLE 2. PhD students in the Chemistry Graduate Program by Track. The tracks include Biochemistry & Biophysics (BB), Chemical Biology (CB), Analytical (A), Physical (P), Theoretical (T), Inorganic (I), Organic (O).

entered	BB	CB	A	P	T	I	O	TOTAL
2020	11	4	4	3	9	9	7	47
2019	7	7	6	5	1	5	4	35
2018	25	6	7	2	5	5	4	54
2017	11	10	3	5	1	9	13	52
2016	10	8	5	1	3	5	2	34
2015	19	4	1	2	7	7	7	47
2014	7	7	3	2	1	10	6	36
2013	2	2	1	4			2	11
TOTAL:	81	44	26	21	18	41	38	269

6. ***Timetable for development of the program, including enrollment projects.*** This request is a bit different from a typical degree proposal because the program is already developed, and the students are already enrolled. There are currently 81 students in the Biochemistry & Biophysics track within the Chemistry & Biochemistry Department. They are already following the graduate program developed for this cohort within the department and

working in the labs of a very strong group of faculty researchers. Whereas students in the other six tracks take coursework in Organic, Inorganic, and Physical Chemistry, coursework for students in the Biochemistry & Biophysics track focuses on structure and function of biological macromolecules. We are hoping that the new degree program would be fully approved by FA21 so current students can transfer to the new program in FA21 and the first cohort can be admitted in FA21 (for matriculation in FA22). If FA21 is not possible, of course we would be grateful for a FA22 start.

Relation of the proposed program to existing programs on campus and to the Campus Academic Plan. The Biochemistry & Biophysics Track within the Chemistry & Biochemistry Department is highly interdisciplinary with faculty participants from several different departments in both the Health Sciences and the main campus. The interdisciplinary nature of the program could be much better supported if it were a separate graduate program. Formation of the Graduate Program in Biochemistry and Molecular Biophysics will foster and expand research collaboration across different disciplines, in line with the Campus Strategic Plan. It is not expected that any negative effects on existing graduate and undergraduate programs will result. In fact, with the newly modified undergraduate degree in Biochemistry combined with the recently eliminated Biochemistry major offered by Biological Sciences,it is imperative that we attract the best and the brightest PhD students as TAs and research mentors for what is already a growing number of undergraduate majors in Biochemistry.

Contributions to diversity: The percentage of underrepresented PhD students that matriculate in the Biochemistry & Biophysics track has been 38% (3 out of 8), 22% (2 out of 9), 18% (5 out of 28), and 14% (1 out of 7) in 2016, 2017, 2018, and 2019, respectively. We envision that with the increased visibility of the new graduate program in Biochemistry and Molecular Biophysics, we will be able to recruit even more students from underrepresented backgrounds who are currently attracted to other institutions that are offering a Biochemistry PhD degree. Biochemistry is ranked 10th by US News and World Report, while the rankings of the Chemistry & Biochemistry Department have been lower. Students from underrepresented backgrounds may not be aware of the high ranking of Biochemistry at UCSD or where to find the Biochemistry PhD degree since it is hidden within Chemistry. We hope to raise the visibility of the program, which has a diverse faculty (50% female and 13% from underrepresented groups), because we feel that a more diverse student population will be highly attracted to our top-ranked and diverse graduate program.

Table 3. Applicants to the Biochemistry & Biophysics Track, past four years.

	2019					2018					2017					2016				
	All	F	URM	DOM	INTL	All	F	URM	DOM	INTL	All	F	URM	DOM	INTL	All	F	URM	DOM	INTL
BIOCHEMISTRY & BIOPHYSICS																				
Apps	123	60	28	82	41	110	49	16	79	31	89	36	12	56	33	83	35	13	54	28
Target	15					16					10					11				
Dept Invite	36	19	7	30	6	52	24	9	48	4	36	16	5	29	7	36	11	6	31	5
Dept Admit	26	17	6	29	5	48	21	9	44	4	26	16	5	21	5	31	11	6	27	4
Student Visited	26	11	5	22	4	45	17	9	44	1	22	13	2	20	3	26	9	6	25	2
Student Accept	7	4	1	6	1	28	13	5	24	3	9	5	2	6	3	8	2	3	8	0
Student Accepted and Visited	5	2	1	5	0	25	11	5	24	1	7	3	2	6	1	8	2	3	8	0
Percentage of Accepted to Admitted	27%	24%	17%	21%	20%	58%	62%	56%	55%	75%	35%	31%	40%	29%	60%	26%	18%	50%	30%	0%
Percentage of Accepted to Target	47%					175%					90%					73%				

Here we include a list of specific steps the degree program will take in its first five years in conjunction with its home department to move it toward the identification, recruitment, and retention of underrepresented minority students and faculty. We will engage in both student- and faculty-driven efforts to enhance diversity. Susan Taylor, a Biochemistry professor, recently chaired the EDI committee and is engaged in all topics that pertain to EDI. For example, this committee is taking the lead in writing the first EDI Strategic Plan for the

Division of Physical Sciences and provides feedback on the constitution of department committees to ensure balance and equitable distribution of workload. The Department EDI Committee also partners closely with the Dean of the Division of Physical Sciences, which has its own Division-wide EDI Committee, to help implement broader goals to increase diversity within the Division of Physical Sciences. One program that has been particularly effective in increasing faculty diversity is the Dean's Excellence Searches, which is a mechanism to hire faculty with strong track records and demonstrated commitment to enhancing diversity. Through a combination of Excellence Searches and proactive emphasis on diversity, 61% (11 out of 18) of the Assistant Professors in the Department are female, underrepresented, and/or members of the LGBTQ+ community or first in their family to obtain a college degree. Seven of these are Biochemists. Since 2015, Chemistry & Biochemistry has used a holistic review process for admissions. We use a specific rubric that de-emphasizes metrics like the GRE scores and emphasizes research experience and resilience. As can be seen from Table 3, this process has dramatically increased the percentage of URM students we admit. Application fee waivers for students in need are offered by the Graduate Division.

Many Biochemistry faculty members mentor URM undergraduates through two undergraduate-graduate transition programs that also support diversity: The Summer Training Academy for Research Success (STARS) Graduate Fellowship, and the UC Leadership Excellence through Advanced Degrees Program (UC LEADS). Biochemistry faculty also frequently give seminars at Hispanic Serving Institutions (HSIs) and Historically Black Colleges. Several of the Cal State schools such as San Diego State University are designated HSIs and at least one Biochemistry faculty is invited each year to speak there. Two African American students from SDSU are currently graduate students in the Chemistry and Biochemistry program.

The Department and Graduate Division supports students, faculty, and staff to attend conferences such as SACNAS, NOBCChE, ABRCMS, and recruiting efforts at the conferences. Biochemistry faculty participate actively in these efforts and represent the Department at SACNAS, ABRCMS, the Northern and Southern Cal Diversity Forum, and the Biophysical Society meeting. We also have representatives who participate in the American Society of Biochemistry and Molecular Biology (ASBMB) meeting which in the past few years has offered scholarships for students from underrepresented groups to attend. Track faculty attend both of these meetings and are active in recruiting graduate students.

Many of our PhD students in the Chemistry & Biochemistry Department are committed to increasing diversity, and UC San Diego offers them many opportunities to mentor and engage in outreach activities. Biochemistry PhD students are strongly encouraged to recruit one or more undergraduate researchers with whom they can work on their PhD research, and for whom they can serve as a mentor. At UCSD some 20% of these undergraduates are from underrepresented groups and another 20% are economically disadvantaged. A large percentage of UC San Diego undergraduates go on to top graduate schools, and the mentorship they receive working with graduate student mentors in the labs of top researchers is a critical component of their success in the graduate program of their choice. Our graduate students have many different opportunities to mentor other underrepresented students. For example, the Preuss school is a high school on the UCSD campus that enrolls 450 students per year with a demographic mix that is 67% Hispanic, 19% Asian and Pacific Islander, 10% African American, and 4% White and 95% disadvantaged. Many Biochemistry graduate students become tutors at Preuss including several of our current MBTG trainees. We also have lots of opportunities for mentoring over the summer including Rommie Amaro's BioChemCOR and Elizabeth Komives' Research Scholars program besides our campus-wide SURF program and the new Meyerhoff program that began here

last year. We find that engaging students from underrepresented groups in mentoring is one of the best ways to help them grow in the skills they will need to be successful professionals. Importantly, the Chemistry & Biochemistry graduate program involves students on the Admissions and Graduate Affairs committees. Care is taken that these students represent the diversity of the graduate student population so that all voices are heard when changes in policies are proposed. The students who serve on the Admissions committee play a critical role in helping to recruit students from underrepresented groups to choose UCSD. Encouraging our students from diverse groups to be involved in such activities provides leadership opportunities that solidify their desire to complete their degree and to become scientific leaders in the future.

Biochemistry PhD students participate in the Chemistry Graduate Student Council (CGSC) as well as the campus-wide student governance organization, the Graduate and Professional Student Association (GPSA), which is comprised of representatives from each graduate program/department. Community-building organizations are also essential to creating a positive climate for all students, including Bridge Fellows. One of the most active student organizations in the Department is the Society for Women in Graduate Studies in Chemistry & Biochemistry (SWIGS), a nine-year old graduate student organization that aims to build a community and raise awareness of issues related to gender equity in STEM. SWIGS organizes workshops/seminars on topics such as negotiation and non-academic jobs, hosts social events, and participates in outreach activities that are open to the student Chemistry & Biochemistry community. They receive financial support from the Department of Chemistry & Biochemistry to host events and bring awareness to topics that help enrich the graduate student experience.

7. ***Collaboration and/or competition with other programs within the University.*** It is not anticipated that there will be any competition with other programs within the University. Instead, the development of a separate graduate program in Biochemistry and Molecular Biophysics will strengthen the advancement of structural biology, particularly cryo-electron microscopy that is currently underway in both the Division of Biological Sciences and in the hiring of new faculty in Chemistry & Biochemistry who are part of the training faculty for this new program. Because this new PhD program remains in the Chemistry & Biochemistry Department, we do not anticipate that it will reduce the applications to other graduate programs in Biology or Biomedical Sciences which get a much larger number of applicants than the Biochemistry & Biophysics Track in the Chemistry & Biochemistry Department. We realize that there is a specialization in Biophysics within the Physics Department, but this program requires the same requirements as the Physics PhD, and we do not believe it Il compete for students with Biochemistry backgrounds interested in our new program. We are not aware of any other similar proposals at other campuses. A survey of the other UC Campuses shows that UCSB is the only other Chemistry & Biochemistry department that only offers a Chemistry PhD. The Department Chemistry & Biochemistry at UCLA and UC Santa Cruz already have separate graduate programs for Biochemistry students. UC Berkeley, UC Davis, and UC Irvine have a Chemistry Department that is separate from the Biochemistry Department.

8. ***Department or group which will administer the program.*** The Chemistry & Biochemistry Department will be home to the new Biochemistry and Molecular Biophysics graduate degree program.

9. ***Plan for evaluation of the program within the offering departments(s), by the Academic Senate and campus-wide.*** The new Biochemistry and Molecular Biophysics degree program will be reviewed every 7-8 years at the same time as the review of the Chemistry degree program.

Section 2. Program

1. ***Undergraduate preparation for admission.*** Applicants to the new Biochemistry, & Molecular Biophysics graduate program are expected to have obtained at least a 3.0 GPA and at least a BS or BA degree from an accredited four-year college or university. Applicants are expected to have a substantial amount of research experience as undergraduates. The rubric used for admission to the Chemistry & Biochemistry Department is attached in the Appendix.

2. ***Foreign language.*** International applicants must demonstrate English Language proficiency according to the one of the following test policies:

   The Test of English as a Foreign Language (TOEFL): The minimum TOEFL score for admission is 85 for the Internet Based Test and 64 for the Paper Based Test. Please note the Paper Based Test does not have a speaking component. TOEFL information and forms are available at the TOEFL website.

   The International English Language Testing System (IELTS) Academic Training exam: The minimum IELTS score is Band 7.0. IELTS registration information is available on the IELTS website.

   The Pearson Test of English Academic (PTE Academic). The minimum PTE academic score required for graduate admission is overall score 65. Registration and test information is available on the Pearson website.

3. Program of study:

   a. ***Specific fields of emphasis:*** Biochemistry and Molecular Biophysics.

   b. Plan(s): PhD students in Biochemistry and Molecular Biophysics will be expected to meet specific milestones, but some aspects of their training will be customized to reflect individual preferences, educational background, and research interests. The first year is unchanged from the current activities and timelines of the Biochemistry & Biophysics Track. Students take courses, begin their teaching apprenticeships, participate in rotations to choose research advisors, and eventually embark on their dissertation research. Three main differences between the PhD program in Chemistry and the new degree program are anticipated: 1) Prospective students will be interviewed prior to admission to UCSD. 2) Should the Chemistry & Biochemistry Department decide to shorten the length of the rotations, the PhD students in Biochemistry and Molecular Biophysics would continue to have two rotations in the fall quarter, and their third rotation in the first half of the winter quarter. The length of each rotation for the PhD students in Biochemistry and Molecular Biophysics could only be changed by the program Steering Committee in consultation with the program faculty. The PhD students in Biochemistry and Molecular Biophysics will be required to have yearly thesis committee meetings as is standard for most Biochemistry PhD programs.

      During their first year, students are advised by an assigned first-year advisor who provides guidance on coursework, selection of rotations, and any other issues related to first-year milestones prior to students joining a research group. Students consult with the first-year advisor to arrange for lab rotations with faculty members whose research program interests them. Typically, students will have identified their thesis advisor by mutual agreement by end of Winter Quarter. By the end of the first year, all students will be expected to have joined a research group. Students may join research groups outside of the department; in these cases, a departmental co-advisor will be required, and the non-departmental advisor will sign a form acknowledging and agreeing to the academic and financial policies of our program.

      In the first Summer, the emphasis is on research. Students will have typically completed their course requirement by the end of their first year, but other courses

of special interest may be taken throughout a student's graduate career. At the beginning of the second year, students will work with their advisor to write a preliminary dissertation proposal. By the end of Fall quarter, the student, in consultation with their advisor and the program Steering Committee, will choose three in-departmental members of their departmental committee who will evaluate their written proposal. By end of Winter quarter, they will take an oral departmental exam in which they will defend their dissertation proposal to their three committee members. This departmental exam does not require preliminary data nor an anticipated timeline. Before the end of Winter quarter of their third year, students will form their complete dissertation committee, including a tenured member from outside the department. They will advance to candidacy for the doctorate by presenting both a written and oral defense of their proposed dissertation including preliminary findings, and future research plans, as well as a concise timeline for their dissertation. Subsequent years will focus on dissertation research and writing. Most students are expected to graduate during their fifth year.

c. ***Unit requirements***: Students pursuing a PhD degree in Biochemistry and Molecular Biophysics will have the same unit requirements as for the Chemistry PhD. Students will be required to maintain a 3.0 GPA and to take 36 units of graduate coursework of which 12 units can be upper division undergraduate courses. These units will allow the students to earn an MS degree in Biochemistry and Molecular Biophysics en route to the PhD and/or if they decide to leave the program before completing the Ph.D.

First-year students will typically take graduate-level courses (see list in section 5). However, upper-division undergraduate coursework as well as classes in other departments (e.g., Biology, Pharmacology, Biomedical Sciences, Mathematics, Physics, Materials Science, and Scripps Institute of Oceanography) will be allowed by exception if appropriate. Coursework will be chosen in consultation with the first-year and research advisors, taking into consideration the student's background, and research interests. The only courses required of all graduate students will be CHEM 250, CHEM 500 and CHEM 509. CHEM 250 primarily covers scientific ethics (Responsible Conduct of Research). This class will ensure that all of our doctoral students will be in compliance with funding agency (e.g. NIH and NSF) requirements for ethics training. CHEM 500 and CHEM 509 are courses related to teaching apprenticeship. By the second year, the emphasis will on research, and further courses will typically not be taken unless appropriate for the student's thesis research. A typical schedule for a first-year student in the new Biochemistry and Molecular Biophysics degree program, and which would also satisfy the requirements for the MS degree will be as follows:

YEAR 1 FALL - Required: CHEM 219A, CHEM 509, CHEM 298 - rotations
Electives: CHEM 209 or CHEM 214.

YEAR 1 WINTER - Required: CHEM 500, CHEM 298 - rotations
Electives: CHEM 204, CHEM 210, CHEM 213A, CHEM 215, CHEM 221, CHEM 265, CHEM 280

YEAR 1 SPRING - Required: CHEM 250, CHEM 500, CHEM 299 Research
Electives CHEM 207, CHEM 213B, CHEM 217, CHEM 283, CHEM 286

These courses primarily deal with structure and function of biological macromolecules in contrast to the coursework taken by students in the other graduate tracks which deal with Organic, Inorganic, and Physical Chemistry. Teaching apprenticeships will be an integral part of graduate student training. Four

quarters of teaching will be required unless the student receives funding beginning in their second year in which case only three quarters of teaching will be required. Students will complete three TAships in their first year, and the fourth may be completed in any subsequent quarter. Students will be expected to TA both discussion and laboratory sections. During the first quarter in which they teach, students will enroll in CHEM 509, an in-depth TA training seminar designed to provide literature-based knowledge and skills related to teaching. This seminar will serve as a valuable resource in terms of building a TA community, learning practical techniques for being an effective TA, and understanding basic theories of science education. TAs will be also encouraged to use the resources of the UCSD Teaching and Learning Commons, which offers courses and seminars on topics related to teaching, and also provides individual guidance for TAs requesting it. Students will earn academic credit for TAships in the form of CHEM 500, "Apprentice Teaching". Their performance will be evaluated by the students in the class as well as by the course instructor to ensure that they perform at a satisfactory level. Students who perform poorly may earn a grade of 'U' for CHEM 500. TAs who excel at teaching may be nominated by faculty for a TA award, which comes with a $200 award as well as congratulatory announcements throughout the Department.

d. ***Field examinations – written and oral.*** At the beginning of the second year, students work with their advisor to write their preliminary dissertation/Research proposal. The Research Proposal is a grant-writing exercise that takes place during the Fall of the 2nd year. The purposes of the written Research Proposal component are 1) to encourage the student and their thesis advisor to work together at an early stage to develop the student's Thesis research project, 2) to train the student in developing testable hypotheses and developing strategies to test their hypotheses. 3) to have the student become familiar with the background literature relevant to their project and to see how their project fits into the bigger picture, 4) to teach the student writing skills, and 5) to provide the basis for fellowship applications. The written proposal should be 6 pages in length and must include specific aims, background, approach, expected outcomes, and references. The student and their thesis advisor choose three in-departmental members of the thesis committee who will review the written proposal. Students should work with their advisor and committee members during the fall quarter. The advisor and committee members should ensure that the proposed research project focuses on a significant problem, the methods are appropriate and rigorous, the research has been thoroughly and carefully designed, pitfalls and alternatives are considered, that the research can be accomplished in a reasonable amount of time, and that completion of the proposed research will lead to the Ph.D, degree. By the end of Fall quarter of the 2nd year, students must submit a copy of their final research proposal with electronic signatures of their thesis advisor as well as the 3-member committee indicating their final approval of the document. Committee members will also provide an assessment of the project according to the proposal assessment rubric (Appendix).

   In the Winter quarter, students take an oral exam in which they defend their proposal to their three thesis committee members. The committee members assess the oral performance according to the assessment rubric (Appendix). Students who complete the necessary coursework and pass this proposal exam qualify for the MS degree in Biochemistry and Molecular Biophysics.

4. ***Qualifying examinations – written and/or oral.*** Before the end of Winter quarter of their third year, each student in consultation with their thesis advisor and the program Steering Committee forms their complete dissertation committee including a tenured member from outside the department. Students advance to candidacy for the doctorate by presenting both a written (3-5-page summary) and oral defense of their proposed dissertation work including

preliminary findings, and future research plans, as well as a concise timeline for their dissertation.

5. ***Thesis and/or dissertation.*** Students in the Biochemistry and Molecular Biophysics PhD program will meet in person yearly with their dissertation committee. At least four of the five committee members must be present for this meeting. Typically, students complete their research in 5-6 years and are then ready to defend their PhD dissertation. The student, in consultation with their advisor decides the timing of the defense. Students are strongly encouraged to have at least one first-author publication prior to defending their dissertation.
6. ***Normative time from matriculation to degree.*** The normative time to degree for students in the Chemistry PhD program is currently 5.33 years. We expect that the normative time to degree for students in the Biochemistry & Molecular Biophysics PhD program will be the same. The pre-candidacy, support, and total-registered time limits (PCTL, SUTL, and TRTL, respectively) will be identical to the current program in Chemistry. Students are expected to meet the milestones prior to these time limits, e.g. students will advance to candidacy in 2.5 years, which is shorter than the current PCTL of 4 years. The possibility of obtaining T32 training grant support and/or other fellowship support is a strong *incentive to support expeditious times-to-degree* because this funding alleviates the need to TA for financial support, which is typical for students pursuing the Chemistry PhD.

Section 3. Projected need

1. ***Student demand for the program.*** Applications to the Biochemistry and Biophysics Track within the Chemistry PhD program have steadily increased over the past few years from 85 in 2018 to 140 in 2020. We are anticipating that applications will increase even more when our program is visible as a separate graduate program. Also, we are anticipating continued growth of TA support for PhD students with Biochemistry undergraduate degrees as we roll-out the modified Biochemistry undergraduate major.
2. ***Opportunities for placement of graduates.*** Most of the graduates from the Biochemistry & Biophysics Track in the Chemistry & Biochemistry Department continue in research intensive careers by choosing to do Postdoctoral research. Eventually 27% of them obtain tenure track academic positions, another 20% obtain research positions in Research Institutes or at universities, and 45% obtain research positions in industry. We are not aware that any of our graduates have difficulty obtaining gainful employment after graduating. Our graduates are in high demand by the local Biotech and Pharmaceutical companies on the La Jolla Mesa, but many also find positions in the San Francisco Bay area or in the Boston area, the other two meccas for cutting-edge biochemical research. We have not tracked the small number of foreign graduates to see how many remain in the US or return to their countries.
3. ***Importance to the discipline.*** UCSD has never had a separate department of Biochemistry despite the fact that faculty members in Chemistry have been National Academy Members in Biochemistry and related fields. Bruno Zimm and Russell Doolittle developed fundamental understanding of polymeric biomolecules and of how macromolecular sequences evolved. Susan Taylor solved the first structure of a kinase. J Andrew McCammon pioneered computational simulations of macromolecules now known as Molecular Dynamics. Faculty in Biochemistry have received numerous awards including the Searle Scholars Award, Barany Award from the Biophysical Society, and the Blavatnik National Laureate Award. Despite the strength of the faculty, their research programs have been hidden under the Chemistry PhD program. Students wishing to pursue a PhD degree with nationally ranked faculty in Biochemistry don't know where to find the appropriate graduate program at UCSD because it currently doesn't exist. Thus, the establishment of this separate degree program will undoubtedly raise the profile of the disciplines of Biochemistry, Structural Biology and Biophysics at UCSD.

4. ***Ways in which the program will meet the needs of society.*** The Biotechnology revolution continues to improve human health with advancements that increasingly include macromolecules as treatments for disease. Understanding how macromolecules function in human biology is still in its infancy as we now realize that genomics only reveals basic sequences whereas macromolecule diversity is hundreds of times more complex. Not only do we need to understand how macromolecules function in human health, we need to understand how to create them and replace them in disease. Biochemistry & Molecular Biophysics are the disciplines that are revolutionizing our understanding of macromolecule diversity. On the La Jolla Mesa, new biotechnology and pharmaceutical companies are burgeoning with San Diego now ranking close behind San Francisco and Boston. These industries are in dire need of well-trained PhD scientists who will be graduates of the Biochemistry & Molecular Biophysics graduate program.

5. ***Relationship of the program to research and/or professional interests of the faculty.*** The 23 faculty who have self-identified as members of the Biochemistry & Biophysics graduate track in the Chemistry PhD program have done so because of their research interests in Biochemistry & Molecular Biophysics. Many of these faculty also participate in the Molecular Biophysics Training Grant, a strong T32 training program funded by the NIH. These faculty are currently training 81 PhD students (cf. Table 2).

6. ***Program Differentiation.*** Biochemistry & Molecular Biophysics are interdisciplinary fields that are based in different departments at different institutions. At UCSD, these fields have traditionally been based in Physical Sciences, but have been buried within the Chemistry & Biochemistry Department which only offers Chemistry PhD degrees. Despite this deficiency, UCSD has one of the strongest NIH-funded training programs in Molecular Biophysics, which is based in the Chemistry & Biochemistry Department and is currently in its 30th year. A survey of other UC campuses reveals that UCLA offers a degree in Biochemistry and Molecular Biology from within the Chemistry & Biochemistry Department, but UCLA does not have a funded Molecular Biophysics Training grant. Similarly, UC Santa Cruz offers degrees in Chemistry and in Biomedical Science and Engineering from within their Chemistry & Biochemistry Department, but they also do not have an NIH-funded Molecular Biophysics Training grant. Others have separate departments on Biochemistry and/or Molecular Biology and Biophysics but these are not based in the Physical Sciences. It is a unique strength of UCSD that Biochemistry & Biophysics research has traditionally been based within the Division of Physical Sciences with strong ties to the Health Sciences. Indeed, three of the 23 participating faculty are based in Health Sciences but affiliated with the Chemistry & Biochemistry Department and active participants in the Biochemistry & Biophysics Graduate program track. It is anticipated that those students who are interested in molecular and physically-based graduate work will apply to the Biochemistry & (Molecular) Biophysics degree within the Chemistry & Biochemistry Department, and that they will have differentiated themselves from students interested in Biology and/or Physics (Biophysics). There is some overlap between students who apply to the Biomedical Sciences (BMS) Graduate Program, and several faculty members from Chemistry & Biochemistry participate in the BMS program. We hope to continue to collaborate during the admissions process, as we have in years past, so as to admit as many of the qualified students as possible into both programs. In general, fewer students interested in quantitative and molecular biochemistry are admitted to the BMS program and they have many more applicants than the Biochemistry & Biophysics Track within Chemistry & Biochemistry so we do not anticipate there will be any negative effects of the new degree on the BMS program.

Section 4. Faculty

The faculty who will participate in the new Biochemistry & Molecular Biophysics graduate program are expected to be those faculty currently participating in the Biochemistry & Biophysics graduate track in the Chemistry PhD program: Rommie Amaro, Itay Budin, Michael

Burkart, Kevin Corbett (primary appt Cell and Molecular Medicine), Galia Debelouchina, Lalit Deshmukh, Neal Devaraj, Daniel Donoghue, Fleur Ferguson (50/50 Chem/SOM), Gourisankar Ghosh, Michael Gilson (primary appt SSPPS), Partho Ghosh, Mark Herzik, Patricia Jennings, Simpson Joseph, Judy Kim, Elizabeth Komives, Alexis Komor, Colleen McHugh, Tatiana Mishanina, Ulrich Muller, Johannes Schoeneberg (50/50 Chem/SOM), Susan Taylor (primary appt Pharmacology), F. Akif Tezcan, Navtej Toor, Dong Wang (primary appt SSPPS), Wei Wang, Jerry Yang, Jin Zhang (primary appt Pharmacology), Brian Zid. Those faculty members whose primary appointment is not in Chemistry & Biochemistry have been granted Affiliate status in the Chemistry & Biochemistry Department in order to participate in the graduate program. The 30 active faculty members are 12 are women and 3 from underrepresented groups. There are currently ten assistant professors, five Associate professors and the rest full professors. Additional faculty will continue to be hired in future years according to departmental needs. Complete CVs of the principal faculty administering and teaching in the new program are included in a separate PDF supporting document to be submitted simultaneously with the proposal.

Section 5. Courses

No new courses will need to be created for the new Biochemistry and Molecular Biophysics graduate program. The course offerings are (and will continue to be) as follows:

CHEM 204 X-ray Crystallography (W) (4) Instructor: Partho Ghosh. Analysis of macromolecular structures by X-ray diffraction. Topics include symmetry, geometry of diffraction, detection of diffraction, intensity of diffracted waves, phase problem and its solution, heavy atom method, isomorphous replacement, anomalous dispersion phasing methods (MAD), direct methods, molecular replacement.

CHEM 207 Protein NMR (S) (4) Instructor: Stanley Opella. A broad introduction to the uses of nuclear magnetic resonance to characterize and understand proteins. Not highly mathematical, this course should be accessible to chemistry graduate students working with proteins.

CHEM 209 Macromolecular Recognition (F) (4) Instructor: Navtej Toor. Structures and functions of nucleic acids, folding and catalysis of nucleic acids, motifs and domains of proteins, principles of protein-protein interactions, chemistry of protein/DNA and protein/RNA interfaces, conformational changes in macromolecular recognition.

CHEM 210 Lipid Cell Signaling Genomics, Proteomics, and Metabolomics (W) (2) Instructor: Edward Dennis. Overview of new systems biology “-omics” approached to lipid metabolism and cell signaling, including interrogating gene and lipid databases, techniques for lipidomics, and implications for profiling and biomarker discovery in blood and tissues relevant to inflammatory and other human diseases. Cross-listed with BIOM 209 and PHAR 208. Recommended preparation: one quarter of undergraduate biochemistry.

CHEM 212 Biochemistry & Biophysics of Cell Membranes (S) (4) Instructor: Itay Budin. Structure and function of biological membranes and their lipid building blocks. Topics include lipid metabolism, membrane dynamics, protein-lipid interactions, lipid signaling, and cellular trafficking. Lectures covering fundamentals will be combined with literature-based discussions and presentations.

CHEM 213A Structure of Biomolecules and Biomolecular Assemblies (W) (4) Instructors: Kevin Corbett and Mark Herzik. A discussion of structures of nucleic acids and proteins and their larger assemblies. The theoretical basis for nucleic acid and protein structure, as well as methods of structure determination including X-ray crystallography, cryoEM, and computational modeling approaches will be covered. Letter grades only.

CHEM 213B Physical Chemistry of Biological Macromolecules (S) (4) Instructor: Galia Debelouchina. Discussion of the physical principles governing biomolecular structure and

function. Experimental and theoretical approaches to understand protein dynamics, enzyme kinetics, and mechanisms will be covered.

CHEM 214 Molecular and Cellular Biochemistry (F) (4) Instructor: Gourisankar Ghosh. This is an introductory course for graduate students and covers topics in molecular and cellular biochemistry. Emphasis will be placed on contemporary approaches to the isolation and characterization of mammalian genes and proteins, and molecular genetic approaches to understanding eukaryotic development and human disease.

CHEM 215 Genome, Epigenome, and Transcriptome Editing (W) (4) Instructor: Alexis Komor. A discussion of current topics involving nucleic acid modification, including systems derived from zinc fingers, TALEs, and CRISPR-Cas9. Topics of particular emphasis include delivery of genome editing agents, gene drives, and high-throughput genetic screens.

CHEM 216 Chemical Biology (W) (4) Instructor: Neal Devaraj. A discussion of current topics in chemical biology including mechanistic aspects of enzymes and cofactors, use of modified enzymes to alter biochemical pathways, chemical intervention in cellular processes, and natural product discovery.

CHEM 217 RNA Structure, Function, and Biology (S) (4) Instructor: Simpson Joseph. Selected topics in RNA structure and function, such as the ribosome, ribozyme, antibiotics, splicing and RNA interference, as they relate to the RNA role in gene expression and regulation. Emphasis on techniques to study the dynamics of macromolecular complexes and the mechanism of RNA catalysis.

CHEM 219A Special Topics in Biochemistry (F) (4) Instructor: Brian Zid. This special-topics course is designed for first-year graduate students in biochemistry. Topics presented in recent years have included protein processing, the chemical modification of proteins, the biosynthesis and function of glycoproteins, lipid biochemistry and membrane structure, and bioenergetics.

CHEM 219C Special Topics in Biochemistry (W) Instructor: Patricia Jennings. This course is designed to help first year students to successfully write grant proposals. Generation of hypotheses, experimental design and effective communication are covered in an open discussion format with each student receiving feedback from peers.

CHEM 220 Regulatory Circuits in Cells (W, not currently offered) (4) Modulation cellular activity and influencing viral fate involve regulatory circuits. Emergent properties include dose response, cross regulation, dynamic, and stochastic behaviors. This course reviews underlying mechanisms and involves mathematical modeling using personal computer tools. Recommended: some background in biochemistry and/or cellular biology. Mathematical competence at the level of lower-division college courses.

CHEM 221 Signal Transduction (S, not currently offered) (4) The aim of this course is to develop an appreciation for a variety of topics in signal transduction. We will discuss several historical developments while the focus will be on current issues. Both experimental approaches and results will be included in our discussions. Topics may vary from year to year.

CHEM 225 Bioinorganic Chemistry (W) (4) Instructor: Akif Tezcan. The role of metal ions in biological systems, with emphasis on transition metal ions in enzymes that transfer electrons, bind oxygen, and fix nitrogen. Also included are metal complexes in medicine, toxicity, and metal ion storage and transport.

CHEM 250 Research Survival Skills (S) (2) Instructor: Susan Taylor. Course offers training in responsible conduct of research in chemistry and biochemistry, as well as presentation skills, teamwork, and other survival skills for a career in research. Objectives include learning rules, issues, and resources for research ethics; understanding the value of ethical decision-making; and creating a positive disposition toward learning about research ethics. The course is designed to meet federal grant requirements for training in the responsible conduct of

research.

CHEM 264 Structural Biology of Viruses (S) (4) Instructor: Colleen McHugh. An introduction of virus structures, how they are determined, and how they facilitate the various stages of the viral life cycle from host recognition and entry to replication, assembly, release, and transmission to uninfected host cells. Students will be required to complete a term paper. (May not be offered every year.) (Cross-listed with BGGN 264.)

CHEM 265 3D Electron Microscopy of Macromolecules (W) (4) Instructors: Mark Herzik and Elizabeth Villa. The resolution revolution in cryo-electron microscopy has made this a key technology for the high-resolution determination of structures of macromolecular complexes, organelles, and cells. The basic principles of transmission electron microscopy, modern cryo-electron microscopy, image acquisition, and 3D reconstruction will be discussed. Examples from the research literature using this state-of-the-art technology will also be discussed. (May not be offered every year.) (Cross-listed with BGGN 262.)

CHEM 280 Applied Bioinformatics(W) (4) Instructor: Wei Wang. Publicly available databases and bioinformatics tools are now an indispensable component of biomedical research. This course offers an introductory survey of selected tools and databases; the underlying concepts, the software, and advice on using them. Practical exercises will be included.

CHEM 283 Supramolecular Structure Determination Laboratory (S) (4) Instructors: Majid Ghassemian and Elizabeth Komives. A laboratory course combining hands-on mass spectrometry and bioinformatics tools to explore the relationship between structure and function in macromolecules. Tools for peptide sequencing, analysis of post-translational modification, and fragmentation analysis by mass spectrometry are examples of experiments students will run.

CHEM 286 Molecular Simulations Lab (S) (4) Course in computational methods, with focus on molecular simulations. The course content is built on a background in mathematics and physical chemistry and provides an introduction to computational theory and molecular mechanics. The emphasis is on applications and reliability.

CHEM 295 Biochemistry Seminar (F) (2) Formal seminars or informal puzzle sessions on topics of current interest in biochemistry, as presented by visiting lecturers, local researchers, or students. (S/U grades only.)

CHEM 298 Special Study in Chemistry (Rotations) Reading and laboratory study of special topics for first-year graduate students under the direction of a faculty member. Exact subject matter to be arranged in individual cases. (S/U grades only.) This course will be changed to Special Study in Biochemistry, Structural Biology, and Biophysics.

CHEM299 Research in Chemistry (1-12) This course will be changed to Research in Biochemistry, Structural Biology, and Biophysics.

CHEM 500 Apprentice Teaching (4) Under the supervision and mentorship of a course instructor, MS and PhD students serve as teaching assistants to undergraduate laboratory and lecture courses. To support teaching competency, regular meetings with the instructor and attendance at lectures are required. S/U grades only.

CHEM 509 Teaching Methods in Chemistry and Biochemistry (2) This course explores teaching strategies specific to chemistry at the college level, and promotes the development of skills for facilitating active, student-centered learning in both lecture and laboratory settings. It is required for first-time teaching assistants. S/U grades only.

Section 6. Resource requirements[6]

We have estimated for the first 5 years the additional cost of the program, by year, for each of the following categories:

1. FTE faculty: Growth will be determined by the Chemistry & Biochemistry Departmental research and teaching needs
2. Library acquisition: None
3. Computing costs: None
4. Equipment: None
5. Space and other capital facilities: None
6. Other operating costs: Because the number of students in our graduate program in Chemistry and Biochemistry is not expected to increase, Staff in the Chemistry & Biochemistry Department Student Affairs Office will be able to cover any additional costs by internal reallocation of workload assignments at least for the time being. The department will continue to evaluate staffing needs as the number of undergraduate Biochemistry majors increases and this may eventually result also in an increase in the TA resources to support the Biochemistry courses.

State Resources to Support New Programs. We expect that based on campus enrollment plans and resource plans, the Chemistry & Biochemistry Department faculty numbers will continue to grow. In addition, three years ago, the Division of Biology changed their undergraduate major offerings so that Biochemistry is no longer included as an undergraduate major. The Department of Chemistry & Biochemistry has been approved to offer a revised Biochemistry major within the Chemistry & Biochemistry Department that will be effective FA20. Once that undergraduate major is effective, we expect that the number of Biochemistry research faculty will need to further increase. Thus, faculty resources for the graduate program in Biochemistry and Molecular Biophysics will come from the normal faculty allocations based on undergraduate enrollment. Graduate enrollment growth is also tied to number of faculty, and we expect this to also grow with the revised Biochemistry major.

Section 7. Graduate Student Support

Graduate student support will continue to come primarily from TAships and departmental Block Grant allocations in the first year and a combination of NIH T32 training grant funding and faculty research funding in subsequent years. The Chemistry & Biochemistry Department receives sufficient TA funding to cover the enrolled PhD students based on the large number of undergraduates taking Freshman Chemistry, Organic Chemistry, and Chemistry laboratory courses that are required for many STEM majors at UCSD. NIH T32 training grant funding supports 12 trainees per year from the Molecular Biophysics Training Grant (PIs Komives and Corbett) and up to an additional six trainees per year from the Growth Regulation and Oncogenesis training grant (PIs Yang and Donoghue). Faculty within the Biochemistry & Biophysics Track are well-funded with an average of $650,000 in direct costs per year.

Section 8. Governance

The new graduate program in Biochemistry and Molecular Biophysics is being offered by the Department of Chemistry & Biochemistry which currently offers a PhD degree in Chemistry. Governance will remain within this department. Faculty currently affiliated with the Biochemistry & Biophysics Graduate Track will be primarily responsible for the governance of the program. Faculty will meet regularly (monthly at the beginning and at least quarterly after procedures are established). Decisions regarding substantive changes to the program will be discussed openly and decided by vote of all program faculty. The Program Faculty will also choose a Program Steering Committee which will be primarily responsible for overseeing the progress of the students. The five-member Program Steering Committee will have both junior and senior faculty members who will be responsible for Admissions (3) and First year Advising (1) and for overall guidance of the program (1). One of the faculty responsible for Admissions will coordinate with the Chemistry & Biochemistry Department Admissions committee. The

Chair of the Steering Committee will represent the Program on the Chemistry & Biochemistry Department Graduate Affairs Committee. They will work closely with the Student Affairs staff from the Chemistry & Biochemistry Department to oversee graduate student funding and tracking of progress and outcomes.

Section 9. Changes in Senate regulations

No changes in Senate Regulations at the Divisional level or in the Assembly of the Academic Senate will be required.

Optional Appendices

Complete CVs of the principal faculty administering and teaching in the new program are included in a separate PDF supporting document to be submitted simultaneously with the proposal.

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Elizabeth Komives
Professor of Chemistry and Biochemistry
UC San Diego
9500 Gilman Dr.
La Jolla, CA 92093-0378

December 10, 2020

Dear Professor Komives,

The Graduate Committee of the Division of Biological Sciences at UCSD is pleased to support the proposed PhD in Biochemistry and Molecular Biophysics run by the Department of Chemistry and Biochemistry. Your proposal has articulated very effectively the wider benefits of a PhD degree program in this area, for research, and for increased competitiveness and visibility in PhD recruitment. The proposed program will benefit the overall research environment and doctoral training at UCSD. Given the interests of many Biological Sciences faculty and students in research areas such as structural biology, protein-protein interactions, and in vitro reconstitution, the proposed PhD program should strongly synergize with existing research and doctoral training in the Division of Biological Sciences. We wish you success in setting up this program.

Best regards,

Andrew Chisholm
Professor and Associate Dean, Division of Biological Sciences
Chair, Biological Sciences Graduate Committee

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LA JOLLA, CA 92093-0751
Phone: (858) 822-5569
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Nov. 17, 2020

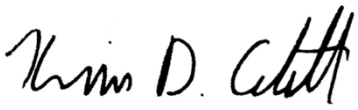
Dear Professor Komives,

We are writing today in strong support of your proposal for a new Ph.D. degree program in Biochemistry and Molecular Biophysics, to be administered by the Department of Chemistry and Biochemistry. The Biomedical Sciences (BMS) Graduate Program is an umbrella Ph.D. program based in the UCSD Health Sciences, and over the last several years our program has worked closely with the existing Biochemistry and Biophysics Track within the Chemistry and Biochemistry Ph.D. Program. Several faculty based in Health Sciences departments including Cellular & Molecular Medicine and Pharmacology are also affiliated with the Biochemistry and Biophysics Track, and several more have mentored Biochemistry and Biophysics Track Ph.D. students. We also work closely on the Molecular Biophysics Training Grant, with BMS faculty member Jin Zhang co-chairing the training grant and two other BMS faculty, Kevin Corbett and Geoffrey Chang, serving on the grant's steering committee. Finally, in creating our own Molecular and Structural Biology Research Area within BMS, we recruited several faculty from the Biochemistry and Biophysics Track to officially join our graduate program.

We agree with you that while UCSD has tremendous strength in the areas of Biophysics and Structural Biology, students interested in obtaining an advanced degree in this area are not well-served by existing graduate programs. Establishing a separate Ph.D. degree program in Biochemistry and Molecular Biophysics promises to better serve these students in many ways, and contribute to both international recognition and improved student and faculty recruitment for this area. Given the successful history of the Molecular Biophysics Training Grant and the dedication of its faculty, we are confident that the academic and scientific rigor of this new program will be high, and that the graduates will be well-prepared for modern academic and industrial research careers.

Sincerely,

Åsa Gustafsson
Professor, School of Pharmacy and Pharmaceutical Science
Chair, Biomedical Sciences Graduate Program



Kevin D. Corbett
Associate Professor, Department of Cellular & Molecular Medicine
Vice-Chair, Biomedical Sciences Graduate Program

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M. Brian Maple
Chair, Department of Physics
Distinguished Professor of Physics
Bernd T. Matthias Endowed Chair

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USA
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December 21, 2020

Dear Professor Komives,

I have asked the members of our Biophysics group and our Committee on Graduate Education and Policy members to review your proposal for the new degree program in Biochemistry and Molecular Biophysics. The feedback we have received has been quite positive. We support the program as has been described in the proposal. Best of luck.

Sincerely,

M. Brian Maple

M. Brian Maple
Chair, Department of Physics

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: CORBETT, Kevin D.

eRA COMMONS USER NAME (credential, e.g., agency login): corbettkd

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE	END DATE	FIELD OF STUDY
University of Virginia, Charlottesville, VA	BS	05/2000	Chemistry
University of California Berkeley, Berkeley, CA	PHD	12/2005	Molecular Cell Biology
University of California Berkeley, Berkeley, CA	Postdoctoral Fellow	11/2006	Structural Biology of prokaryotic DNA topoisomerases
Harvard Medical School, Boston, MA	Postdoctoral Fellow	07/2011	Structural Biology of the eukaryotic kinetochore

A. Personal Statement

I am an experienced biochemist and structural biologist, with twenty years' experience in the purification and structure/function analysis of chromosome-associated proteins and multi-protein complexes. I am an expert in a variety of structural techniques, chiefly x-ray crystallography (over 75 x-ray crystal structures determined) and increasingly cryo-electron microscopy. As such, my research program is highly relevant to the goals of the UCSD Molecular Biophysics Training Program.

I am committed to graduate education and training, and in particular have worked to improve inclusiveness within the UCSD Biomedical Sciences (BMS) Graduate Program in my nine years at UCSD. As **Chair of the BMS Graduate Admissions Committee in 2017 and 2018**, I overhauled admissions policies to reduce reliance on biased metrics like GRE scores and encourage holistic applicant review, resulting in dramatically improved recruitment of students from underrepresented backgrounds. I currently serve as the **Vice-Chair of of the BMS Graduate Program (2019-2022)**, and in this capacity I have instituted the program's first Diversity Committee. I will serve as Chair of the BMS Graduate Program from 2022-2025. To improve my training and mentoring skills, in 2018 I attended two mentorship workshops: the UCSD Health Sciences Faculty Mentor Training Program (8 class hours), and the Associate Professor Leadership Development Seminar "Emotional Intelligence & Collaborative Intelligence" (8 class hours).

I have trained five graduate students (two graduated, three current) including two from underrepresented backgrounds, including MBTG alumnus Sarah Ur. I have additionally trained four post-baccalaureate scholars (three went on to PhD programs), 12 undergraduate students (five went on to PhD or MD/PhD programs), and have served on 12 graduate thesis committees. I hold regular one-on-one meetings with all of my trainees, with a major topic of discussion being the trainee's career goals and our shared plans for achieving these goals. I support professional development of trainees, with each student completing an IDP each year and attending at least one national meeting in their field every two years. For graduate trainees considering careers outside the traditional academic path, I encourage attendance at meetings like the American Society for Cell Biology Annual Meeting, which Sarah Ur attended in Washington D.C. in 2019, and attended sessions focused on scientific careers within the government. I work closely with graduate students to ensure that each publishes at least one first-author or co-first author paper prior to graduation. The papers shown below are first-author papers by three different graduate student trainees from 2014-2020 (graduate student authors shown in bold type). In 2018, I was recognized for excellence in graduate mentorship with the **UCSD Graduate Student Association Faculty Mentorship Award**, which is awarded to one UCSD faculty member per year.

a. **Lau RK**, Ye Q., Birkholz E.A., Berg K.R., Patel L., Mathews I.T., Watrous J.D., Ego K., Whiteley A.T., Lowey B., Mekalanos J.J., Kranzusch P.J., Jain M., Pogliano J., Corbett K.D. Structure and mechanism of a cyclic trinucleotide-activated bacterial endonuclease mediating bacteriophage immunity. *Molecular Cell*. 2020 Feb 20; 77:723-733. Pubmed PMID 31932164; Pubmed Central PMCID PMC7065454.

b. **West AMV***, **Rosenberg SC***, **Ur SN**, Lehmer MK, Ye Q, Hagemann G, Caballero I, Uson I, MacQueen AJ, Herzog F, Corbett KD. A conserved filamentous assembly underlies the structure of the meiotic chromosome axis. *Elife*. 2019 Jan 18; 8:e40372. (*co-first author) PubMed PMID: 30657449; Pubmed Central PMCID PMC6349405.

c. **West AMV**, Komives EA, Corbett KD. Conformational dynamics of the Hop1 HORMA domain reveal a common mechanism with the spindle checkpoint protein Mad2. *Nucleic Acids Research.* 2018 Jan 9; 46(1):279-292. PubMed PMID: 29186573; PubMed Central PMCID: PMC5758881.

d. Kim Y*, **Rosenberg SC***, Kugel CL, Kostow N, Rog O, Davydov V, Su TY, Dernburg AF, Corbett KD. The chromosome axis controls meiotic events through a hierarchical assembly of HORMA domain proteins. *Developmental Cell.* 2014 Nov 24; 31(4):487-502. (*co-first author) PubMed PMID: 25446517; PubMed Central PMCID: PMC4254552.

B. Positions and Honors

Positions and Employment

2000 - 2005	Graduate Student, University of California, Berkeley, Berkeley, CA
2006	Postdoctoral Fellow, University of California, Berkeley, Berkeley, CA
2006 - 2011	Postdoctoral Fellow, Harvard Medical School, Boston, MA
2011 - 2018	Assistant Member, Ludwig Institute for Cancer Research, San Diego, CA
2018 -	Visiting Scientist, Ludwig Institute for Cancer Research, San Diego, CA
2011 - 2017	Assistant Professor, University of California, San Diego, San Diego, CA
2017 -	Associate Professor, University of California, San Diego, San Diego, CA

Other Experience and Professional Memberships

2009 -	Member, American Society for Cell Biology

Honors

2001	Graduate Research Fellowship, National Science Foundation
2004	Outstanding Graduate Student Instructor, UC Berkeley
2005	Alan Bearden Memorial Award for Outstanding Ph.D. Thesis Research in Biophysics, UC Berkeley
2007	Postdoctoral Research Fellow, Helen Hay Whitney Foundation
2010	Postdoctoral Research Fellow, Charles A. King Trust
2012	Scholar Award, Sidney Kimmel Foundation for Cancer Research
2012	Recognition Award, Ray Thomas Edwards Foundation
2018	UCSD Graduate Student Association Faculty Mentorship Award

C. Contribution to Science

1. **Mechanistic basis for bacteriophage immunity by bacterial CD-NTases and associated HORMA domain proteins.** Recent bioinformatics surveys have identified thousands of bacterial CD-NTases in putative defense operons throughout bacteria, including important human pathogens. We have shown that in a subset of these operons, HORMA domain proteins regulate second messenger synthesis by their cognate CD-NTases, and that signaling is likely triggered by detection of foreign proteins. Cyclic tri-AMP synthesized by these CD-NTases activates a new nuclease family, NucC. We showed that one CD-NTase operon from a patient-derived *E. coli* strain confers immunity to bacteriophage λ when expressed in non-pathogenic *E. coli*.

   a. Ye Q., Lau R.K., Mathews I.T., Birkholz E.A., Watrous J.D., Azimi C.S., Pogliano J., Jain M., Corbett K.D. HORMA domain proteins and a Trip13-like ATPase regulate bacterial cGAS-like enzymes to

mediate bacteriophage immunity. Molecular Cell. 2020 Feb.20;77(4)709-722. Pubmed PMID 31932165; Pubmed Central PMCID PMC7037143.

b. Lau R.K., Ye Q., Birkholz E.A., Berg K.R., Patel L., Mathews I.T., Watrous J.D., Ego K., Whiteley A.T., Lowey B., Mekalanos J.J., Kranzusch P.J., Jain M., Pogliano J., Corbett K.D. Structure and mechanism of a cyclic trinucleotide-activated bacterial endonuclease mediating bacteriophage immunity. Molecular Cell. 2020 Feb 20;77(4)723-733. Pubmed PMID 31932164; Pubmed Central PMCID PMC7065454.

2. **Structural basis for self-assembly and function of the meiotic chromosome axis.** The chromosome axis is crucial for organization of meiotic chromosomes, and for their recombination and segregation in meiosis I. My laboratory has outlined the molecular interactions of meiotic HORMA domain proteins in *C. elegans*, fungi, plants, and mammals, revealing that they are recruited to the axis and undergo self-assembly through HORMA domain-closure motif interactions. More recently, we have identified a filamentous protein "core" of the chromosome axis, and showed that this structure is highly conserved. Finally, through related work on the HORMA domain protein regulator Pch2/TRIP13, we have determined how meiotic HORMA domain proteins are depleted from the axis in a feedback pathway regulating meiotic recombination.

   a. Patel L, Kang R, Rosenberg SC, Qiu Y, Raviram R, Chee S, Hu R, Ren B, Cole F, Corbett KD. Dynamic reorganization of the genome shapes the recombination landscape in meiotic prophase. Nat Struct Mol Biol. 2019 Mar;26(3):164-174. PubMed PMID: 30778236; PubMed Central PMCID: PMC6403010.

   b. West AM, Rosenberg SC, Ur SN, Lehmer MK, Ye Q, Hagemann G, Caballero I, Usón I, MacQueen AJ, Herzog F, Corbett KD. A conserved filamentous assembly underlies the structure of the meiotic chromosome axis. Elife. 2019 Jan 18;8. PubMed PMID: 30657449; PubMed Central PMCID: PMC6349405.

   c. Rosenberg SC, Corbett KD. The multifaceted roles of the HORMA domain in cellular signaling. J Cell Biol. 2015 Nov 23;211(4):745-55. PubMed PMID: 26598612; PubMed Central PMCID: PMC4657174.

   d. Kim Y, Rosenberg SC, Kugel CL, Kostow N, Rog O, Davydov V, Su TY, Dernburg AF, Corbett KD. The chromosome axis controls meiotic events through a hierarchical assembly of HORMA domain proteins. Dev Cell. 2014 Nov 24;31(4):487-502. PubMed PMID: 25446517; PubMed Central PMCID: PMC4254552.

3. **Regulation of Mad2 and meiotic HORMAD proteins by Pch2/TRIP13.** My laboratory determined the 3D structure of the conserved AAA+ ATPase Pch2/TRIP13, showing that it is a protein remodeler/unfoldase and revealing the mechanistic basis for ATP-driven conformational changes in this enzyme. We showed that this enzyme, aided by $p31^{comet}$, can recognize the HORMA-domain protein Mad2 in its active "closed" state and convert it to its inactive "open" state through partial unfolding of Mad2's N-terminal region, thus explaining how Pch2/TRIP13 and $p31^{comet}$ contribute to silencing of the spindle assembly checkpoint. We later showed that this partial-unfolding mechanism also applies to the regulation of meiotic HORMAD protein complexes on meiotic chromosomes. This work, along with current work detailing TRIP13's detailed role in spindle assembly checkpoint dynamics, has helped explain how either loss of TRIP13 or its overexpression can contribute to cancer onset.

   a. Ye Q, Kim DH, Dereli I, Rosenberg SC, Hagemann G, Herzog F, Tóth A, Cleveland DW, Corbett KD. The AAA+ ATPase TRIP13 remodels HORMA domains through N-terminal engagement and unfolding. EMBO J. 2017 Aug 15;36(16):2419-2434. PubMed PMID: 28659378; PubMed Central PMCID: PMC5556265.

   b. Ye Q, Rosenberg SC, Moeller A, Speir JA, Su TY, Corbett KD. TRIP13 is a protein-remodeling AAA+ ATPase that catalyzes MAD2 conformation switching. Elife. 2015 Apr 28;4PubMed PMID: 25918846; PubMed Central PMCID: PMC4439613.

4. **Structural basis for *S. cerevisiae* monopolin complex function in mitosis and meiosis.** As a post-doctoral fellow and in my own lab, I determined structures of all four subunits of the budding-yeast monopolin complex, which mediates sister kinetochore co-orientation in meiosis I. My structural work on the Csm1:Lrs4 subcomplex suggested a direct kinetochore cross-linking mechanism for the complex, which I supported using targeted structure-based mutations in yeast genetic assays. We later proved this

model in vitro using purified kinetochore particles and purified recombinant protein, in collaboration with Charles Asbury and Adele Marston. Later work on Mam1 and Hrr25 has suggested that these proteins modulate the Csm1-kinetochore interface through Hrr25-mediated phosphorylation, thereby enforcing the specificity for sister kinetochore cross linking. More recent work has revealed a new role for Csm1:Lrs4 in nucleolar rDNA silencing, and revealed a wider conservation of monopolin within eukaryotes than previously thought.

a. Plowman R[#], Singh N[#], Tromer EC, Payan A, Duro E, Spanos C, Rappsilber J, Snel B, Kops GJPL, Corbett KD*, Marston AL*. The molecular basis of monopolin recruitment to the kinetochore. Chromosoma 2019 Apr 30; doi: 10.1007/s00412-019-00700-0. ([#]co-first author; *co-corresponding author) PubMed PMID: 31037469.
b. Ye Q, Ur SN, Su TY, Corbett KD. Structure of the *Saccharomyces cerevisiae* Hrr25:Mam1 monopolin subcomplex reveals a novel kinase regulator. EMBO J. 2016 Oct 4;35(19):2139-2151. PubMed PMID: 27491543; PubMed Central PMCID: PMC5048352.
c. Sarangapani KK, Duro E, Deng Y, Alves Fde L, Ye Q, Opoku KN, Ceto S, Rappsilber J, Corbett KD, Biggins S, Marston AL, Asbury CL. Sister kinetochores are mechanically fused during meiosis I in yeast. Science. 2014 Oct 10;346(6206):248-51. PubMed PMID: 25213378; PubMed Central PMCID: PMC4226495.
d. Corbett KD, Yip CK, Ee LS, Walz T, Amon A, Harrison SC. The monopolin complex crosslinks kinetochore components to regulate chromosome-microtubule attachments. Cell. 2010 Aug 20;142(4):556-67. PubMed PMID: 20723757; PubMed Central PMCID: PMC2955198.

5. **Structure and mechanisms of prokaryotic type IIA and IIB topoisomerases.** As a graduate student, I outlined the ATP binding and hydrolysis cycle of the ATP-hydrolyzing B-subunit of topoisomerase VI (topoVI), a type II topoisomerase from archaea. I later determined the 3D structure of the topo VI A_2B_2 holoenzyme, the first intact type II topoisomerase structure, which showed how conformational changes driven by ATP hydrolysis are coupled to strand passage. The structure and mechanism of type IIB topoisomerases informs the mechanisms of eukaryotic Spo11, a key factor for meiotic recombination. I also determined the mechanistic basis for DNA supercoiling and topology control by the bacterial type IIA topoisomerases DNA gyrase and topoisomerase IV. I showed that a specialized accessory domain in these enzymes adopts a novel “β-pinwheel” fold that binds and significantly bends DNA. This domain is used by both DNA gyrase and topoisomerase IV to enable these enzymes' specific activities - DNA supercoiling for gyrase, and specific relaxation of positive supercoils for topoisomerase IV.

a. Corbett KD, Benedetti P, Berger JM. Holoenzyme assembly and ATP-mediated conformational dynamics of topoisomerase VI. Nat Struct Mol Biol. 2007 Jul;14(7):611-9. PubMed PMID: 17603498.
b. Corbett KD, Schoeffler AJ, Thomsen ND, Berger JM. The structural basis for substrate specificity in DNA topoisomerase IV. J Mol Biol. 2005 Aug 19;351(3):545-61. PubMed PMID: 16023670.
c. Corbett KD, Shultzaberger RK, Berger JM. The C-terminal domain of DNA gyrase A adopts a DNA-bending beta-pinwheel fold. Proc Natl Acad Sci U S A. 2004 May 11;101(19):7293-8. PubMed PMID: 15123801; PubMed Central PMCID: PMC409912.
d. Corbett KD, Berger JM. Structure of the topoisomerase VI-B subunit: implications for type II topoisomerase mechanism and evolution. EMBO J. 2003 Jan 2;22(1):151-63. PubMed PMID: 12505993; PubMed Central PMCID: PMC140052.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/kevin.corbett.1/bibliography/40379156/public/

D. Research Support

Ongoing Research Support

R01 GM104141 Corbett (PI) 12/10/2012-1/31/2022
A Molecular View of Chromosome Recombination & Segregation in Eukaryotic Meiosis
This grant supports structural and biochemical work on budding-yeast and mammalian meiotic chromosome-associated protein complexes.
Role: PI

R01 GM128464 Corbett (PI) 5/21/2018-3/31/2022
Expanding the CRISPR/Cas toolbox for RNA modulation
This grant supports the development of optimized genome-editing tools geared specifically for the editing and/or destruction of mRNAs in cells, with potential impacts in both basic research and human health.
Role: PI

R21 AI148814 Corbett (PI) 1/17/2020-12/31/2021
Molecular mechanisms of the first-identified bacterial HORMA and Pch2-like proteins in a novel second-messenger signaling pathway
This grant supports research into the molecular mechanisms of the CBASS bacterial immunity pathway in *E. coli* strain MS115-1, including identification of the activating peptide signal and the mechanism of the Trip13 ATPase in HORMA:CdnC regulation.
Role: PI

Completed Research Support

Laboratory of Structural Biology, Ludwig Institute for Cancer Research Corbett (PI) 07/01/11-08/31/18
General Laboratory
The Ludwig Institute supports Dr. Corbett's salary and the purchase of basic lab supplies and equipment not covered by specific grants.
Role: PI

FY13-1352 , March of Dimes Foundation Corbett(PI) 06/01/14-05/31/17
Mechanistic studies of the chromosome axis, a conserved structure central to recombination and chromosome segregation in meiosis
This grant supports work on the physical mechanisms of protein complexes that regulate chromosome structure and recombination in *C. elegans* meiosis, including the chromosome axis, the synaptonemal complex, and the ATPase PCH-2.
Role: PI

RGP0008/2015, Human Frontiers Science Program Toth; Corbett; Herzog (PI) 11/01/15-10/31/19
Molecular mechanisms of meiotic feedback regulation by the conserved chromosome axis
This is a collaborative grant, submitted with Drs. Attila Toth (TU Dresden) and Franz Herzog (U Munich), to study the structure and signaling mechanism of the meiotic chromosome axis in the mouse. The role of the Corbett lab is to reconstitute and study the structure and biochemical activities of protein complexes identified by genetic and mass spectrometry studies.
Role: PI

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Debelouchina, Galia

eRA COMMONS USER NAME (credential, e.g., agency login): galiad

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Colby College, Waterville, MA	BA	05/2005	Chemistry, Mathematics
Massachusetts Institute of Technology, Cambridge, MA	PHD	09/2011	Physical Chemistry
Princeton University, Princeton, NJ	Postdoc	06/2017	Chemical Biology

A. Personal Statement

I am currently starting my fourth year as an assistant professor in the Department of Chemistry and Biochemistry at UCSD. My research program is focused on the development of chemical and spectroscopic tools for structural biology in the cellular environment. In particular, we develop sensitivity-enhanced nuclear magnetic resonance (NMR) methodologies that allow us to study the atomic resolution structure, dynamics and interactions of endogenous proteins in the cellular milieu.

Currently, I have nine group members, six graduate students, one postdoctoral researcher and two undergraduate students. In my role as a mentor for my relatively young group and for the MBTG program, I am committed to training researchers who are rigorous experimentalists and analytical thinkers, who can effectively communicate their work, and who are not afraid to learn new skills and tackle new scientific challenges.

1. Due to the multidisciplinary nature of our work, all lab members receive training in relevant chemical and biological techniques including small molecule synthesis, advanced NMR spectroscopy, cell biology and imaging, protein chemistry and biochemistry, structural biology techniques, instrumentation upkeep and repair. I interact with my students on a daily basis and often train them in lab myself. We hold weekly group meetings where we discuss the scientific progress of each student and all group members actively participate in providing feedback and new ideas. We also hold weekly journal club meetings where we discuss relevant scientific literature and organize classes where lab members teach each other NMR spectroscopy and chemical synthesis. Each lab member contributes to the mentoring of undergraduate researchers and we actively participate in programs aimed at providing research opportunities to underrepresented students such as the Summer Training Academy for Research Success (STARS) at UCSD. To improve my mentoring skills, I have also attended workshops such as the Cottrell Scholars Collaborative New Faculty Workshop in Washington, DC.
2. Each lab member keeps an online lab notebook and we discuss appropriate record keeping, control experiments and data analysis once a week. The third-year students in the lab have already gone through the process of writing and successfully publishing manuscripts where they worked independently under my guidance. The second-year students are getting close to this stage as well. All students also participate in peer review where they evaluate submitted manuscripts under my guidance and we emphasize rigorous experimental design and unbiased data interpretation. I also teach CHEM 213a (Macromolecular structure) and CHEM 213b (Biophysics), two graduate courses

that are recommended for the MBTG program. As part of the courses, the students work with "real-life" NMR protein structural data and evaluate the significance of NMR chemical shift changes using statistical methods. The students also write NIH-style proposals and we hold mock review panels where the students serve as reviewers.

3. I encourage each lab member to attend career development workshops and symposia offered through UCSD or the large number of biotechnology and pharmaceutical companies in the San Diego area. Each student also participates in at least one national or international conference a year where they can network with scientists both from academia and industry. My lab also has close connections with Bruker Biospin, a manufacturer of NMR technology. Once a year, my students visit the company in Billerica, MA and participate in a week-long training on NMR instrumentation, which also gives them the opportunity to network and to experience life in industry. Once a year, I meet with my students to specifically discuss their IDPs and to devise a long-term plan regarding their professional development training and future goals.
4. I am committed to the well-being and success of my students and their timely graduation from the Ph.D. program. I interact with them daily and teach them strategies to be productive in lab and at the same time maintain a good work-life balance. The students also interact regularly with their thesis committee faculty members to ensure that they are on track for a successful and timely graduation.

a. Ackermann BE, Debelouchina GT. Heterochromatin Protein HP1α Gelation Dynamics Revealed by Solid-State NMR Spectroscopy. Angew Chem Int Ed Engl. 2019 May 6;58(19):6300-6305. PubMed PMID: 30845353; PubMed Central PMCID: PMC6482055.

b. Debelouchina GT, Muir TW. A molecular engineering toolbox for the structural biologist. Q Rev Biophys. 2017 Jan;50:e7. PubMed PMID: 29233219; PubMed Central PMCID: PMC5978726.

c. Debelouchina GT, Gerecht K, Muir TW. Ubiquitin utilizes an acidic surface patch to alter chromatin structure. Nat Chem Biol. 2017 Jan;13(1):105-110. PubMed PMID: 27870837; PubMed Central PMCID: PMC5161692.

B. Positions and Honors

Positions and Employment

2017 -	Assistant Professor, University of California, San Diego

Other Experience and Professional Memberships

2014 -	Member, American Chemical Society
2014 - 2015	Co-chair and chair, NMR Topical Group, North Jersey Section, American Chemical Society
2018 –	Member, Biophysical Society
2019 –	Member, Protein Society
2019 –	Member, International Society for Magnetic Resonance
2019 –	Co-chair, Southern California Users of Magnets Meeting
2019 –	MBTG, Executive Committee member
2019	Reviewer, Swiss National Science Foundation
2020	Early career reviewer, MSFC study section, NIH
2021	MagLab User Advisory Committee member

Honors

2012	Raymond Andrew Prize for outstanding PhD thesis in the field of magnetic resonance, Ampere Society
2016	Salutes to Excellence Award, American Chemical Society, North Jersey Section
2020	Hellman Fellowship

C. Contributions to Science

1. Chromatin is the functional form of the genome and its main building block is a protein-DNA complex known as the nucleosome. The nucleosomes are active hubs of post-translational modifications that control access to DNA and are at the heart of all chromatin-related biological processes such as transcription, replication and DNA repair. As a postdoctoral researcher, I focused on ubiquitin as a chromatin post-translational modification and designed biophysical and biochemical experiments, including solution NMR, to understand its effects on chromatin higher order structural organization (first author). I also used state-of-the-art chemical biology tools to build a synthetic chromosome and to study the impact of DNA methylation on gene regulation (second author). As an independent investigator, my group has used solid-state NMR spectroscopy to characterize the molecular basis of heterochromatin protein 1α (HP1α) phase separation and its impact on chromatin dynamics (corresponding author).

    a. Beh LY, Debelouchina GT, Clay DM, Thompson RE, Lindblad KA, Hutton ER, Bracht JR, Sebra RP, Muir TW, Landweber LF. Identification of a DNA N6-Adenine Methyltransferase Complex and Its Impact on Chromatin Organization. Cell. 2019 Jun 13;177(7):1781-1796.e25. PubMed PMID: 31104845; PubMed Central PMCID: PMC6570567.
    b. Ackermann BE, Debelouchina GT. Heterochromatin Protein HP1α Gelation Dynamics Revealed by Solid-State NMR Spectroscopy. Angew Chem Int Ed Engl. 2019 May 6;58(19):6300-6305. PubMed PMID: 30845353; PubMed Central PMCID: PMC6482055.
    c. Debelouchina GT, Gerecht K, Muir TW. Ubiquitin utilizes an acidic surface patch to alter chromatin structure. Nat Chem Biol. 2017 Jan;13(1):105-110. PubMed PMID: 27870837; PubMed Central PMCID: PMC5161692.

2. My PhD thesis focused on the development of sensitivity enhancement methodologies for solid-state nuclear magnetic resonance (NMR) spectroscopy. These methodologies, known as dynamic nuclear polarization (DNP), can increase NMR signals 10^2-10^4 fold and allow unprecedented savings in data acquisition times (from months to days), thus enabling the structural investigations of large and complex biological assemblies or materials. My work contributed to the development of polarization agents for DNP (supporting author), the theoretical understanding of DNP polarization mechanisms (supporting author), and the application of DNP to the structural characterization of biological samples such as amyloid fibrils (first author). As an independent investigator, my group is developing unique DNP polarization agents that can be targeted to specific proteins in cells and that can be used for in-cell structural biology applications (corresponding author).

    a. Lim BJ, Ackermann BE, Debelouchina GT. Targetable Tetrazine-Based Dynamic Nuclear Polarization Agents for Biological Systems. Chembiochem. 2020 May 4; 21(9):1315-1319. PubMed PMID: 31746101.
    b. Debelouchina GT, Bayro MJ, Fitzpatrick AW, Ladizhansky V, Colvin MT, Caporini MA, Jaroniec CP, Bajaj VS, Rosay M, Macphee CE, Vendruscolo M, Maas WE, Dobson CM, Griffin RG. Higher order amyloid fibril structure by MAS NMR and DNP spectroscopy. J Am Chem Soc. 2013 Dec 26;135(51):19237-47. PubMed PMID: 24304221; PubMed Central PMCID: PMC3909659.
    c. Hu KN, Debelouchina GT, Smith AA, Griffin RG. Quantum mechanical theory of dynamic nuclear polarization in solid dielectrics. J Chem Phys. 2011 Mar 28;134(12):125105. PubMed PMID: 21456705; PubMed Central PMCID: PMC3078165.
    d. Debelouchina GT, Bayro MJ, van der Wel PC, Caporini MA, Barnes AB, Rosay M, Maas WE, Griffin RG. Dynamic nuclear polarization-enhanced solid-state NMR spectroscopy of GNNQQNY nanocrystals and amyloid fibrils. Phys Chem Chem Phys. 2010 Jun 14;12(22):5911-9. PubMed PMID: 20454733; PubMed Central PMCID: PMC4440577.

3. Amyloid fibrils are non-soluble, non-crystalline protein assemblies associated with neurodegenerative disease and amyloidosis. Due to the lack of suitable structural methods, for a long time the structure of amyloid fibrils remained a mystery. Solid-state NMR (often in combination with cryo-electron microscopy) has now made significant contributions to these investigations, and my graduate work contributed structural information for several amyloid systems: β_2-microglobulin fibrils, associated with dialysis-related amyloidosis (first author); the fibrils formed by a small segment of transthyretin, a protein associated with senile systemic amyloidosis (supporting author); and the functional amyloid formed by the yeast prion

protein Sup35 (supporting author). As an independent investigator, my group is developing new NMR and chemical biology tools to characterize the origin of amyloidogenesis and the connections to protein phase separation both *in vitro* and in cells (corresponding author, manuscript in preparation).

a. Frederick KK, Debelouchina GT, Kayatekin C, Dorminy T, Jacavone AC, Griffin RG, Lindquist S. Distinct prion strains are defined by amyloid core structure and chaperone binding site dynamics. Chem Biol. 2014 Feb 20;21(2):295-305. PubMed PMID: 24485763; PubMed Central PMCID: PMC4030713.
b. Fitzpatrick AW, Debelouchina GT, Bayro MJ, Clare DK, Caporini MA, Bajaj VS, Jaroniec CP, Wang L, Ladizhansky V, Müller SA, MacPhee CE, Waudby CA, Mott HR, De Simone A, Knowles TP, Saibil HR, Vendruscolo M, Orlova EV, Griffin RG, Dobson CM. Atomic structure and hierarchical assembly of a cross-β amyloid fibril. Proc Natl Acad Sci U S A. 2013 Apr 2;110(14):5468-73. PubMed PMID: 23513222; PubMed Central PMCID: PMC3619355.
c. Debelouchina GT, Platt GW, Bayro MJ, Radford SE, Griffin RG. Intermolecular alignment in β2-microglobulin amyloid fibrils. J Am Chem Soc. 2010 Dec 8;132(48):17077-9. PubMed PMID: 21077676; PubMed Central PMCID: PMC2996106.
d. Debelouchina GT, Platt GW, Bayro MJ, Radford SE, Griffin RG. Magic angle spinning NMR analysis of beta2-microglobulin amyloid fibrils in two distinct morphologies. J Am Chem Soc. 2010 Aug 4;132(30):10414-23. PubMed PMID: 20662519; PubMed Central PMCID: PMC2919207.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/galia.debelouchina.1/bibliography/40190681/public/

D. Research Support

Ongoing Research Support

R35GM138382 Debelouchina (PI) 07/01/20 – 06/30/25
NIGMS
Title: Structural biology of chromatin in vitro and in cells
The goal of this project is to develop solid-state NMR methodology for the structural studies of chromatin in vitro and in cells.
Role: PI

Hellman Fellowship Debelouchina (PI) 07/01/2020 – 06/30/21
UCSD Hellman Fellows Program
Title: Development of targetable polarization agents for structural biology in cells
This project focuses on the synthesis of polarization agents for dynamic nuclear polarization (DNP) NMR spectroscopy.
Role: PI

P30G062429-02 Brewer, James (PI) 04/01/20 – 03/31/21
NIA and Shiley-Marcos Alzheimer's Disease Research Center at UCSD
Title: Research Education Component
The goals of this project are to receive training in AD research from local experts in the field; to learn how to effectively utilize the infrastructure and resources of the Shiley-Marcos ADRC to advance my research and to obtain pilot data for future R01 submissions.
Role: Trainee

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Mark Anthony Herzik Jr.

eRA COMMONS USER NAME (credential, e.g., agency login): mherzik

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Houston (Houston, TX)	B.S	05/2007	Biochemistry/Chemistry
University of California, Berkeley (Berkeley, CA)	Ph.D.	05/2014	Molecular and Cell Biology
The Scripps Research Institute (La Jolla, CA)	Post-doc	12/2018	Structural Biology

A. Personal Statement

One of my true passions in science is using complementary structure-function approaches to reverse-engineer the molecular machines that are critical to human physiology. I am particularly interested in the three-dimensional (3D) conformational landscapes endowing proteins with specific functions and how these structures are dynamically related during signal transduction. My research career thus far has entailed using structural methods to obtain mechanistic insights into signal transduction pathways contributing to a variety of disorders, ranging from cardiovascular disease to neurodegeneration and chronic pain.

For the last decade I have been developing targeted biochemical and structural approaches directed towards elucidating transiently populated conformational states of key biomedically relevant protein complexes. As a *Helen Hay Whitney Foundation postdoctoral fellow* at in the laboratory of Dr. Gabriel Lander at the Scripps Research Institute, I obtained extensive expertise in the development of novel high-resolution, high-throughput single-particle cryogenic electron microscopy (cryoEM) methodologies to push the technology closer to the theoretical size and resolution limits and have become a world-recognized leader in the field. These studies have endowed me with substantial expertise in the expression, purification, characterization, and structure determination of various biological specimens of various sizes (~4.5 kDa to ~700 kDa) and complexities (monomer to 28-mer, etc.). From these works, I have established myself as an expert in structural biology and a key member of the global cryoEM community. My body of work includes a Thermo Fisher Scientific-sponsored webinar for cryoEM methods developments, an invited book chapter in Methods and Molecular Biology focused on high-throughput and high-resolution single-particle cryoEM data collection, and have served as an invited speaker at several national workshops and conferences dedicated to cryoEM.

My extensive background in structural biology, has provided me with the necessary skills to probe important transient pathways in a targeted manner and elucidate the key conformational switches with atomistic precision. My current group uses the latest cutting-edge cryo-EM instrumentation together with novel sample preparation, data collection and processing algorithms to determine the molecular basis for a variety of age-related and neurodegenerative diseases, focusing primarily on mitochondrial biogenesis and molecular transport mechanisms. Building upon my prior research experience, my group develops novel strategies for specimen preparation, imaging, and processing to enable high-resolution structural determination of these critical protein complexes. To further explore the conformational landscape these complexes sample to perform their functions my group also develops novel strategies for quantifying local and global conformational dynamics within cryo-EM data to better understand the molecular-level transitions necessary for protein function. As a result of these efforts, I was awarded the *Searle Scholars Award* for my innovative approaches to structure determination and its application to mitochondrial protein biogenesis.

My long-term career goal has always been to conduct cutting edge interdisciplinary biomedical research in a stimulating and collaborative environment that prioritizes the education of students from disadvantaged backgrounds, like myself. As a first-generation college student, I take great pride in the education and mentorship of our next generation of scientists and strive to develop engaging and innovative curriculum and learning resources to ensure their success. I specifically chose a position at The University of California, San Diego because of the supportive scientific environment, the breadth of science being performed, the long-term commitment of UCSD to becoming a pioneer in cryo-EM, as well as the extensive supportive training programs and educational resources for training and mentoring students. My lab is ideally suited to train innovative and transformative young scientists. I currently am training two PhD students, one of whom is from an underrepresented group, and the other is a first-generation immigrant. I also have already trained three undergraduate students, two of whom are first-generation college students.

1. Wu M, Lander GC[#], **Herzik MA Jr**[#]. *Sub-2 Å Resolution Structure Determination Using Single-Particle Cryo-EM at 200 keV*. JSB X. 2020 Feb 27; 4(100020). doi: 10.1016/j.yjsbx.2020.100020. eCollection 2020. PMID: 32647824
   [#]corresponding author
2. **Herzik MA Jr.*,** Wu M*, Lander GC. *High-resolution structure determination of sub-100 kDa complexes using conventional cryo-EM.* Nature Communications. 2019 Mar 4;10(1):1032
3. Hirschi M*, **Herzik MA Jr***, Wie J, Suo Y, Borschel WF, Ren D, Lander GC, Lee SY. *Cryo-electron microscopy structure of the lysosomal calcium-permeable channel TRPML3*. Nature. 2017 Oct;550(7676):411-414. Doi: 10.1038/nature24055. PMID: 29019979
4. **Herzik MA Jr**, Fraser JF, Lander GC. Fraser JF, Lander GC. *A multi-model approach to assessing local and global cryo-EM map quality.* Structure. 2019 Feb 5;27(2):344-358.e3. doi: 10.1016/j.str.2018.10.003. Epub 2018 Nov 15. PMID: 30449687

B. Positions and Honors

ACTIVITY/ OCCUPATION	START DATE (mm/yy)	ENDING DATE (mm/yy)	FIELD	INSTITUTION/ COMPANY	SUPERVISOR/ EMPLOYER
Undergraduate Researcher	01/06	05/07	Structural Biology	University of Houston	Dr. Glen B. Legge
Research Technician	05/07	08/08	Structural Biology	University of Houston	Dr. Glen B. Legge
Graduate Student	08/08	05/14	Structural Biology/ Biochemistry	University of California, Berkeley	Dr. Michael A. Marletta
Research Associate	05/14	10/14	Chemistry	The Scripps Research Institute	Dr. Michael A. Marletta
Post-doctoral Research Associate	10/14	12/18	Structural Biology	The Scripps Research Institute	Dr. Gabriel C. Lander
Assistant Professor	01/19	Current	Biochemistry/ Biophysics	University of California, San Diego	University of California, San Diego

Academic and Professional Honors

University of California, San Diego:
Searle Scholar Award — July 2020 – Present
Southern California Society for Microscopy and Microanalysis — April 2019 – Present
Board Member – Executive Council in Biology

The Scripps Research Institute:
The Scripps Research Institute Society of Fellows Research Travel Award — Spring 2017
Helen Hay Whitney Postdoctoral Fellowship — April 2016 – January 2019

University of California, Berkeley:
American Heart Association Predoctoral Fellowship (Award# 11PRE7370086) — July 2011 – June 2013
NIH Biophysics Training Grant (Award #T32GM008295-24) — July 2010 – June 2011

C. Contributions to Science

My contributions to science are organized into three categories: I. Cryogenic Electron Microscopy (cryo-EM) Method Development, II. Protein Dynamics, and III. Structural Studies of Integral Membrane Proteins. I have deposited 40 Protein Data Bank Entries (1 unpublished), 18 Electron Microscopy Data Bank (EMDB) entries (2 unpublished) and authored/co-authored 21 publications/book chapters. A full list of my current publications can be found at the following location: https://www.ncbi.nlm.nih.gov/myncbi/1v1UFrlamy-At/bibliography/public/

I. Cryogenic Electron Microscopy (cryo-EM) Method Development:

From the outset of my introduction to single-particle cryo-EM I have dedicated significant efforts toward furthering the technology beyond the currently perceived limits (1,2,3). Working at the forefront of the field, I have spearheaded the development of novel cryo-EM sample preparation, data collection, and image processing strategies that have advanced the known lower molecular size limit to obtain high-resolution reconstructions of macromolecular protein complexes that had traditionally been deemed too small to image by cryo-EM (2,3). The smallest of these complexes, ~42 kDa (2), held the world-record for the smallest complex that had been imaged to sub-nanometer resolution at the time of publication. Furthermore, these studies demonstrated not only that such small macromolecular complexes could be imaged by single-particle approaches, but that distinct conformational states of a protein could be resolved for complexes as small as ~64 kDa (2). In addition, I have furthered the attainable resolution limits of single-particle cryo-EM closer to the theoretical limits, obtaining 3D reconstructions of well-behaved mammalian macromolecular complexes to as high as ~1.7 Å resolution (1). These structures are of sufficient quality to resolve ordered water molecules, alternative rotameric conformations, as well as holes in the EM density for aromatic side chains and proline residues (1). Each of these works represent key milestones in the field of EM and have revolutionized the perceived capabilities of current instrumentation. The raw data from each of these works have been uploaded to the Electron Microscopy Publix Image Archive Repository (EMPIAR) and have served as important datasets for the development of new data processing algorithms. Additionally, the methodologies critical to the success of these works is also the focus of a chapter in Methods in Molecular Biology entitled “Setting up parallel illumination on the Talos Arctica for high-resolution data collection”, 2020 *in press*, MA Herzik Jr.

Research Papers:

1. Wu M, Lander GC*, **Herzik MA Jr***. *Sub-2 Å Resolution Structure Determination Using Single-Particle Cryo-EM at 200 keV*. JSB X. 2020 Feb 27; 4(100020). https://doi.org/10.1016/j.yjsbx.2020.100020
   **Denotes equal contribution*
2. **Herzik MA Jr.*,** Wu M*, Lander GC. *High-resolution structure determination of sub-100 kDa complexes using conventional cryo-EM.* Nature Communications. 2019 Mar 4;10(1):1032
   **Denotes equal contribution*
   ***Recommended by Faculty of 1000*
3. **Herzik MA Jr***, Wu M*, Lander GC. *Achieving better Than 3 Å resolution by single particle cryo-EM at 200 keV*. Nature Methods. 2017 Nov;14(11):1075-1078. doi: 10.1038/nmeth.4461. PMID: 28991891
   **Denotes equal contribution*

Symposia

4. **Herzik MA Jr** and DeRosier D. 3rd Annual Southern California Cryo-EM Symposium 2018. Organizer.

II. Protein Dynamics:

A longstanding goal of my research has been the development of new strategies directed towards obtaining a molecular-level understanding of the conformational landscape proteins must traverse to perform their functions. During my undergraduate and graduate careers, I developed targeted biochemical and structural methodologies to visualize transiently populated states during signaling cascades (4) and obtain molecular ensembles of these critically important complexes. To glean more information into conformational dynamics present within cryo-EM data I developed a novel, user-independent multi-model pipeline that provided critical insights into the function of the 26S proteasome lid (2) and resulted in the first molecular ensemble derived from cryo-EM data deposited to the PDB (PDB ID: 3JCK). I then applied these methodologies to all high-resolution cryo-EM structures in the EMDB to obtain a molecular ensemble that represented the EM data

and provided a quantitative and qualitative means to assess the local and global quality of a cryo-EM reconstruction (1). Using these approaches, in collaboration with the lab of Dr. Seok-Yong Lee (Duke), together with novel sample preparation and data processing methodologies I was able to show for the first time that the transient receptor potential (TRP) channel family of ion channels undergo significant conformational changes during sensitization and activation (3). These studies are evidence of my capable dedication to developing novel approaches to directly visualizing local and global conformational dynamics.

Research Papers:

1. **Herzik MA Jr**, Fraser JF, Lander GC. *A multi-model approach to assessing local and global cryo-EM map quality.* Structure. 2019 Feb 5;27(2):344-358.e3. doi: 10.1016/j.str.2018.10.003. Epub 2018 Nov 15. PMID: 30449687
   ***Recommended by Faculty of 1000*
2. Dambacher CM*, Worden EJ*, **Herzik MA Jr***, Martin A, Lander GC. *Atomic structure of the 26S proteasome lid reveals the mechanism of deubiquitinase inhibition*. Elife. 2016 Jan 8;5:e13027. (doi: 10.7554/eLife.13027). PMID: 26744777
   **Denotes equal contribution*
3. Zubcevic L*, **Herzik MA Jr***, Wu M*, Borschel WF, Hirschi M, Song A, Lander GC, Lee SY. *Conformational ensemble of the human TRPV3 ion channel.* Nature Communications. 2018 Nov 14;9(1):4773. doi: 10.1038/s41467-018-07117-w. PMID: 30429472
   **Denotes equal contribution*
4. **Herzik MA Jr,** Jonnalagadda R, Kuriyan J, Marletta MA. *Structural insights into the role of iron-histidine bond cleavage in NO-induced activation of H-NOX proteins*. Proc Natl Acad Sci USA. 2014 Oct 7;111(40):E4156-64. (doi: 10.1073/pnas.1416936111). PMID: 25253889
   ***Recommended by Faculty of 1000*

III. Structural Studies of Integral Membrane Proteins:

As mentioned above, I have dedicated significant effort to developing novel methodologies to further the size and resolution capabilities of single-particle cryo-EM. Alongside these efforts, I spearheaded the development of high-throughput single-particle cryo-EM approaches that allowed for the rapid screening of numerous conditions (e.g., detergents, lipids, agonists, etc.) directed towards the determination of novel 3D structures of several integral membrane protein complexes (1,2,3,4). In collaboration with the lab of Dr. Seok-Yong Lee at Duke University I was able to determine the first 3D cryo-EM structures of the Transient Receptor Potential Vanilloid-2 (TRPV2) ion channel (1), the Transient Receptor Potential Mucolipin-3 (TRPML3) ion channel (2), the TRPV3 ion channel (3), and served as a key member in determining the first full-length structures of the mitochondrial calcium uniporter (MCU) (4). During these studies, I became an expert in the purification, handling, and manipulation of mammalian integral membrane proteins for structure determination using high-throughput, high-resolution single-particle cryo-EM. These studies are evidence of my capable dedication to developing novel methodologies in order to pursue challenging biological questions and, given my track record as a leader in pushing the molecular envelope of structure determination, I am confident that we will successfully determine the structures of the challenging targets outlined in this proposal.

Research Papers:

1. Zubcevic L*, **Herzik MA Jr***, Chung BC, Liu Z, Lander GC, Lee SY. Cryo-electron microscopy structure of the TRPV2 ion channel. Nature Structural and Molecular Biology. 2016 Feb;23(2):180-6. (doi: 10.1038/nsmb.3159). Epub 2016 Jan 18. PMID: 26779611
   *Denotes equal contribution
2. Hirschi M*, **Herzik MA Jr***, Wie J, Suo Y, Borschel WF, Ren D, Lander GC, Lee SY. *Cryo-electron microscopy structure of the lysosomal calcium-permeable channel TRPML3*. Nature. 2017 Oct;550(7676):411-414. Doi: 10.1038/nature24055. PMID: 29019979
   **Denotes equal contribution*
3. Zubcevic L*, **Herzik MA Jr***, Wu M*, Borschel WF, Hirschi M, Song A, Lander GC, Lee SY. *Conformational ensemble of the human TRPV3 ion channel.* Nature Communications. 2018 Nov 14;9(1):4773. doi: 10.1038/s41467-018-07117-w. PMID: 30429472
   **Denotes equal contribution*

4. Yoo J, Wu M, Yin Y, **Herzik MA Jr**, Lander GC, Lee SY. *Cryo-EM structure of a mitochondrial calcium uniporter.* Science. 2018 Aug 3;361(6401):506-511. doi: 10.1126/science.aar4056. PubMed PMID: 29954988.

D. Additional Information: Research Support and/or Scholastic Performance

NIH R35 GM138206	Herzik (PI)	07/01/20 – 06/31/25
Towards an atomistic understanding of mitochondrial protein biogenesis.		
Searle Scholars Program	Herzik (PI)	07/01/20 – 07/01/23
Developing hybrid methods to understand dynamic mitochondrial protein assemblies		
Exploratory Project Grant – NysnoBio Neurology	Herzik (PI)	04/01/20 – 10/01/20
Molecular understanding of the progression of Parkinson's disease		

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Simpson Joseph, Ph.D.

eRA COMMONS USER NAME (credential, e.g., agency login): SIMPSONJOSEPH

POSITION TITLE: Full Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Loyola College, Madras	B. Sc.	1987	Zoology
Madurai Kamaraj University, Madurai	M. Sc.	1989	Biotechnology
University of Vermont, VT	Ph.D.	1994	Molecular Biology
University of California – Santa Cruz, CA	Post Doc	1998	Molecular Biology

A. Personal Statement

The goal of my laboratory is to study the mechanism of protein synthesis and translational regulation. As a graduate student in Prof. John Burke's laboratory, I studied ribozyme structure and catalysis. This inspired me to join Prof. Harry Noller's group for my postdoctoral research to focus on one of the most challenging problems in biology – the mechanism of protein synthesis by ribosomes. As an independent PI, I have more than 20 years of research experience performing fundamental, mechanistic studies of protein synthesis. We also developed several powerful biochemical and biophysical tools to study protein synthesis that have been widely adopted in the ribosome field. More recently, we are interested in understanding the mechanism of eukaryotic protein synthesis and translational control. The first project we are studying is the mechanism of translational control by the fragile X mental retardation protein (FMRP) family. The second project we are studying is the mechanism of translation initiation on influenza A virus mRNAs. Both projects are timely and of great biological significance. I have the training, expertise, motivation, and leadership to carry out the proposed research projects successfully. I will briefly describe some of the highlights of our past research.

- We were the first to experimentally demonstrate the interaction of the 30S ribosomal subunit with the standby site on mRNAs. We showed that during translation initiation, the 30S initiation complex deals with mRNA secondary structure by binding to a single-stranded region in the mRNA (standby site) followed by the unfolding of the mRNA secondary structure.
- We developed a rapid-kinetic method to monitor mRNA-tRNA translocation by the ribosome that is used by several groups in the field.
- Our studies showed that the universally conserved sarcin-ricin loop (SRL) of 23S rRNA is not essential for triggering GTP hydrolysis by EF-Tu and EF-G but is critical for anchoring EF-G on the ribosome during translocation.
- We showed that disrupting the interactions of the A-site codon with the ribosome accelerates translocation suggesting that the release of the mRNA from the decoding center is the rate-limiting step.
- Our studies on the mechanism of tRNA selection by the ribosome showed that "shape-recognition" is more critical than the hydrogen bonds between the codon and the decoding center of the ribosome.
- We showed that RF1 free in solution is in a closed conformation and changes to the open conformation when bound to ribosomes with a stop codon in the A-site. Our paper is considered a "classic" in the field for first demonstrating that RF1 switches from the closed to the open conformation on the ribosome.

- We have revised the “textbook” model for the mechanism of RF3-dependent dissociation of RF1 from the ribosome. Our studies showed that RF3 hydrolyzes GTP and dissociates first, followed by the release of RF1. We proposed a new model that significantly advances our understanding of the molecular mechanism of translation termination.

My contribution to the scientific community includes reviewing research proposals for NSF, NIH, and several international funding agencies. Additionally, I have reviewed manuscripts for several journals, including *Nature, Cell, Molecular Cell, RNA, Journal of Molecular Biology, Biochemistry, Nucleic Acids Research, and Nature Structural and Molecular Biology.* My laboratory has trained more than 25 undergraduate students, and several of them are co-authors on papers. I am a member of the UCSD Next Step program that advises undergraduate students about careers in science. Several minority undergraduate students from other institutions have also received research training in my lab. These include Keri Silva (Hispanic) from California State University, Northridge. Keri joined UC Berkeley for her graduate studies. Amber Pascale (African American) from the University of California, Irvine, worked as part of the STARS program funded by NSF and NIH. Amber joined Yale University for her graduate studies. David Gonzales (Hispanic) from California State University, San Marcos, performed research in my lab as part of the STARS program. He won the “Best Poster Award” at the Annual Biomedical Research Conference held in Atlanta. David joined UCSD for his graduate studies, and currently, he is a faculty at UCSD. Julio S. de Unamuno IV (Hispanic) from the University of San Diego also worked in my lab. Julio was sponsored by the USD McNair Scholars program for low-income, first-generation minority college students. Finally, Keith Sablan (Pacific Islander) from the University of Guam, Guam, worked in my lab for three summer months. I have also trained undergraduate exchange students from other countries, including Spain, Germany, and Italy.

I have participated in the Ambassadors of Academic Achievement (A^3) Program, an outreach program that brings high school students from low-income high schools to spend a day at UCSD. Many of these students are first-generation college students. My laboratory has also hosted the iGEM competition for the local high school students for several years. We help the high school students to perform experiments and provide bench space and equipment in my laboratory. In 2014, the iGEM team that we hosted won second place and the Best Poster Award at the international competition held at MIT. Finally, I have volunteered as an instructor for the Science Olympiad competition at a local middle school, teaching the students about nucleic acids, proteins, genetics, and gene expression. Thus, I have actively encouraged and passionately tried to excite students at all levels to think seriously about pursuing a career in science. The research in our lab is multidisciplinary spanning studies at the molecular, macromolecular complexes, and cellular level. Students receive excellent training in interdisciplinary research and are better prepared as a scientist. As a mentor, I take an active interest in training my students to do rigorous science and for them to develop as independent scientists.

1. P. K. Khade and S. Joseph. Messenger RNA interactions in the decoding center control the rate of translocation. **Nature Structural & Molecular Biology** 2011; 18: 1300-1302.
2. L. Garcia-Ortega, J. Stephen and S. Joseph. Precise alignment of peptidyl tRNA by the decoding center is essential for EF-G-dependent translocation. **Molecular Cell** 2008; 32: 292-299.
3. S. Studer and S. Joseph. Unfolding of mRNA secondary structure by the bacterial translation initiation complex. **Molecular Cell** 2006; 22: 105-115.
4. S. Phelps, O. Jerinic and S. Joseph. Universally conserved interactions between the ribosome and the anticodon stem-loop of A site tRNA important for translocation. **Molecular Cell** 2002; 10: 799-807.

B. Positions and Honors

Positions and Employment

1998-2004	Assistant Professor, Department of Chemistry and Biochemistry, University of California - San Diego, La Jolla, CA
2004-2008	Associate Professor, Department of Chemistry and Biochemistry, University of California - San Diego, La Jolla, CA
2008-Present	Full Professor, Department of Chemistry and Biochemistry, University of California - San Diego, La Jolla, CA

Awards and Honors

1997-1998	American Cancer Society Senior Post-doctoral Research Fellowship.
1994-1997	Lucille P. Markey Charitable Trust Fellowship from the RNA center.
1989-1994	Graduate Teaching Fellowship, University of Vermont, VT.
1987-1989	Department of Biotechnology Merit Scholarship, Government of India.
1986-1987	Recipient of Loyola Gold Medal in Zoology, Loyola College.
1985-1987	Recipient of Loyola Gold Medal in Zoology, Loyola College.
1984-1985	Recipient of Loyola Gold Medal in Zoology, Loyola College.

C. Contributions to Science

1. Mechanism of translational control by the fragile X mental retardation protein

FMRP regulates the translation of nearly 4% of the brain mRNAs. However, the precise mechanism used by FMRP to regulate translation is unknown. We used quantitative, FRET-based method and in vitro translation assays to show that FMRP binds directly to the ribosome. Additionally, we collaborated with Dr. Rajendra Agrawal to solve the first structure of FMRP bound to ribosome by cryo-EM. Our studies indicate that FMRP may inhibit translation by blocking the binding of translation factors to the ribosome. Although this was a new line of research for us, we were able to make significant contribution to this field by developing new quantitative biophysical approaches and leveraging our experience in mechanistic studies of protein synthesis.

- E. Chen, M. R. Sharma, X. Shi, R. K. Agrawal and S. Joseph. Fragile X mental retardation protein regulates translation by binding directly to the ribosome. **Molecular Cell** 2014; 54: 407-417.

2. RNA-binding specificity of the human fragile X mental retardation protein

Fragile X syndrome is the most common form of inherited intellectual disability and is caused by the lack of expression of the Fragile X Mental Retardation Protein (FMRP). FMRP is an RNA-binding protein that regulates the translation of specific mRNAs in neuronal cells. However, how FMRP binds to specific mRNAs and regulate their translation is unclear. Over the past two decades, numerous studies were undertaken to identify the RNA Recognition Element (RRE) in the mRNAs to which FMRP binds. Although several RREs have been identified by these studies, no systematic analysis of their binding affinity for FMRP was ever undertaken. We used fluorescence-based quantitative methods to determine the binding affinity of human FMRP to several of the previously identified RREs. Surprisingly, FMRP either does not bind or binds with low affinity to these RREs. We developed a new method called MIDAS to identify single-stranded RNA sequences that can bind to the FMRP KH domains. However, we find that the KH domains bind weakly to the RREs identified by MIDAS. Based on our data, we propose that the KH domains of FMRP have evolved to bind to a complex RNA structure, such as in the ribosome. These results significantly advance our understanding of the molecular mechanism used by FMRP to regulate protein synthesis.

- Y. M. Athar and S. Joseph. RNA-binding specificity of the human fragile X mental retardation protein. **J. Mol. Biol.** 2020; 432: 3851-3868.

3. Developed a simple method to purify human FMRP, FXR1, and FXR2 by overexpression in *E. coli*

Researchers have faced many difficulties in purifying the full-length versions of FMRP, FXR1, and FXR2 because of their poor expression, the production of truncated proteins, their tendency to aggregate and precipitate, and their instability in solution when not bound to RNA. We developed a simple method to purify all three proteins of the human FXP family. Our studies showed that point mutations to disrupt ribosomal stalling proline-rich motifs within the protein sequences or the co-expression of EF-P dramatically boosted proteins' expression. Additionally, the maltose-binding protein (MBP) tag and a simplified purification protocol consisting of an ammonium sulfate precipitation followed by a heparin column resulted in pure proteins at high yields. The purified proteins bound to RNA targets, demonstrating that they are functional.

- M. Edwards, M. Xu and S. Joseph. A Simple Procedure for Bacterial Expression and Purification of the Fragile X Protein Family. BioRxiv. 2020; DOI: https://doi.org/10.1101/2020.06.24.169243

4. Human FMRP inhibits the elongation step of translation through its RGG and C-terminal domain

How FMRP binds to specific mRNAs and regulate their translation is unclear. Previous studies have indicated that FMRP could inhibit the initiation and the elongation steps of protein synthesis. Using IRES-driven translation assays we showed that FMRP inhibits the elongation step of translation. Additionally, we showed that the RGG domain, together with the C-terminal tail of FMRP is sufficient to inhibit translation. Interestingly, our studies showed that the RGG domain-C-terminal tail directly binds to the ribosome suggesting that FMRP may inhibit translation by interacting with the ribosome.

- Y. M. Athar and S. Joseph. The Human Fragile X Mental Retardation Protein Inhibits the Elongation Step of Translation through its RGG and C-terminal domains. BioRxiv. 2020; DOI: https://doi.org/10.1101/2020.06.25.171967

5. **Interaction of Influenza A virus NS1 with RNA and PABP1**
The NS1 protein of influenza A virus (IAV) binds to double-stranded RNA (dsRNA), which is important for preventing the host antiviral response. Previous studies showed that NS1 may play a role in viral mRNA translation by binding to PABP1 and eIF4G. We used a new, quantitative FRET-based assay to monitor the interaction of NS1 with PABP1. Our studies showed that NS1 binds to PABP1 with high affinity: however, the binding of dsRNA to NS1 weakens the binding of NS1 to PABP1. Correspondingly, the binding of PABP1 to NS1 weakens the binding of NS1 to dsRNA. We propose that the modulation of NS1-PABP1 interaction by dsRNA may be important for the viral cycle. By developing new quantitative biophysical methods, we hope to make important contributions to understand translational initiation on influenza A virus mRNAs.

- B. Arias-Mireles, C. M. de Rozieres, K. Ly and S. Joseph. RNA modulates the interaction between influenza A virus NS1 and human PABP1. **Biochemistry** 2018; 57: 3590-3598.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/simpson.joseph.1/bibliography/40682775/public/?sort=date&direction=ascending

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

1R01 GM114261 Simpson Joseph (PI) and Rajendra Agarwal (co-PI)
National Institute of Health/NIGMS 01/01/16 – 11/30/20 (no cost extension)
Translational Control by the Fragile X Mental Retardation Protein
The major goal of this proposal is to understand the mechanism of translational regulation by the Fragile X Mental Retardation Protein (FMRP). A combination of genetic, biochemical and structural approaches will be used to characterize the function of FMRP.

63821-LS-MUR Devaraj (PI) 08/01/13 - 05/31/22
Department of Defense/Army Research Office
Dynamic Artificial Cells Composed of Synthetic Bioorthogonal Membranes
The major goal of this project is to create artificial cells with responsive genetic circuits.
Role: Co-PI

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: KOMIVES, Elizabeth A.

eRA COMMONS USER NAME (credential, e.g., agency login): ekomives

POSITION TITLE: Professor of Chemistry and Biochemistry

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Massachusetts Institute of Technology	S.B./ S.M.	06/1982	Chemistry/Toxicology
University of California San Francisco	Ph. D.	01/1987	Pharmaceutical Chem.
Harvard University	Postdoc	07/1990	Chemistry

A. Personal Statement

Research in the Komives Lab focuses on solution biophysical methods to study protein-protein interactions. Over the years we have worked on thrombin-thrombomodulin, on the NFκB transcription factor and its inhibitors, on a Cullin 5 E3 ligase, and on the urokinase plasminogen activator and its receptor. I have graduated 28 PhD students, nearly all of whom are in thriving scientific careers. Graduate education is my passion, although I have also trained a number of postdoctoral fellows. For 18 years, I was on the Steering committee of the MBTG and worked with Susan Taylor, the former PI, to oversee the program while I headed an NIDDK T32 which we decided not to renew in 2012. I became PI and renewed the MBTG in 2015. I worked with the trainees to design the curriculum they wanted with the rigor, depth, and breadth we wanted. We are implementing several creative approaches to career development that have been highly successful. I also oversee one of the graduate laboratory courses for the Training Program in Multiscale Biology.

I try to foster an inclusive and diverse environment in my laboratory and in all my teaching endeavors. Seven of my PhD students have been from underrepresented groups, and three of them are currently tenured faculty members. I am proud that two of my female graduate students are now chairs of Chemistry Departments and several others are tenured faculty members. I continue to mentor my trainees long after they have left the lab.

The research in the Komives lab utilizes a large number of different biophysical approaches, all of which require rigorous methodology and data analysis. We maintain both electronic and paper lab notebooks as well as data repositories for large and small data sets. I am happy that new students find they are able to reproduce the work of previous lab members and that we have a reputation for rigorous and unbiased experimental methodologies. I train my students to look forward to harsh reviews on their publications as this is the best way to improve the work.

Every trainee in my laboratory has weekly meetings with me and we discuss their IDP on an annual basis so that I can ensure they have all the help they need to achieve their career aspirations. We have engaging weekly lab meetings in which raw data is presented and rigorously analyzed. We work together to write papers iterating through how to structure the story and present the data. I introduce my students to faculty and researchers with whom they can network in order to achieve their best career outcomes. I also coach them on writing their job applications and first grant proposals.

Reducing the time-to-degree for my PhD students is important to me. I try to help them know how to work efficiently and how to successfully navigate graduate school hurdles in a timely manner so that they graduate on time with the skills, credentials and experiences to transition successfully into the career of their choice. That said, some of my students have chosen to start new projects and their time-to-degree can be somewhat longer. I support this choice that they make and try to ensure that they continue to make progress.

B. Positions and Honors

Positions and Employment

1990 - 1996	Assistant Professor, U. C. San Diego
1996 - 2000	Associate Professor, U. C. San Diego
2000 - 2019	Professor, U. C. San Diego
2019-present`	Distinguished Professor, U. C. San Diego

Other Experience and Professional Memberships (last 5 years)

1999-2018	Advisory Committee, UCSF Mass Spectrometry Resource
1999-present	Faculty oversight, Biomolecular and Proteomics Mass Spectrometry Facility, UCSD
2001-2004	Nominating Committee, Protein Society
2002-2005	Council, Biophysical Society
2007-present	Editorial Advisory Board, *Biochemistry*
2007	Chair, Molecular Biophysics Subgroup, Biophysical Society
2008-2019	Associate Editor, *Molecular and Cellular Proteomics*
2009-2013	NSF standing review panel on Molecular and Cellular Biophysics
2013	Co-chair, Zing conference on Enzymology entitled "New Frontiers in Enzymology: Enzyme complexes and regulation"
2014	NIH review panel for S10 grants
2014	Chair, Intrinsically Disordered Subgroup, Biophysical Society
2014-present	Awards Committee, Biophysical Society, chair since 2017
2015-2021	Editorial Board, Biophysical Journal
2015	NIH review panel for F04B fellowships
2016-2019	Council, Protein Society
2017	Co-Organizer international conference on Intrinsically Disordered Proteins (IDP 2017) IIT Mohali, December, 2017
2022	Program co-chair, Biophysical Society National Meeting

Honors

1983	Long Award for Excellence in Teaching
1984 - 1987	NIH Graduate Traineeship
1987 - 1989	NIH Postdoctoral Traineeship
1991 - 1996	Rita Allen Scholar
1992 - 1995	Searle Scholar
1999	Kaiser Permanente Award for Excellence in Teaching (First Year Medical Students)
2000	Barany Award for Contributions to Biophysics, Biophysical Society
2010 - 2015	Bruno Zimm Scholar

C. Contributions to Science

1) A Biophysical Understanding of the Thrombin-Thrombomodulin Interaction. I have been working on understanding what happens to thrombin when thrombomodulin (TM) binds for 20 years. My lab solved the NMR structures of the smallest active fragment of TM, the first glycosylated protein to be solved by NMR(1). We obtained kinetic and thermodynamic measurements of the binding interaction. We probed the dynamic changes in thrombin using amide hydrogen exchange and we demonstrated thermodynamic coupling and enthalpy-entropy compensation between the active site and anion binding exosite 1. These studies provided strong evidence of the now well-accepted concept of dynamic allostery in thrombin. Recently, we have been able to obtain high quality NMR data on thrombin (2). We used MD simulations to demonstrate the TM binding to thrombin enhances correlated motions in thrombin (3). Using HDXMS and NMR, we determined the pathways of dynamic allostery (4).

1) Fuglestad B, Gasper PM, Tonelli M, McCammon JA, Markwick PR, **Komives EA**. (2012) The dynamic structure of thrombin in solution. *Biophys J*. 103, 79-88. PMC3388214
2) Fuglestad B, Gasper PM, McCammon JA, Markwick PR, **Komives EA**. (2013) Correlated motions and residual frustration in thrombin. J Phys Chem B. 117, 12857-63. PMC3808083
3) Handley LD, Treuheit NA, Venkatesh VJ, **Komives EA**. (2015) Thrombomodulin binding selects the catalytically active form of thrombin. *Biochemistry*. 2015 54, 6650-8. PMC4697735

4) Handley, LD, Fuglestad, B, Stearns, K, Tonelli, M, Fenwick, RB, Markwick, PRL, and **Komives, EA** (2017) NMR reveals a dynamic allosteric pathway in thrombin. *Scientific Reports* 7:39575. PMC5216386

2) Development of methods for probing amide hydrogen/deuterium exchange upon protein-protein interaction. In 1998, our lab was the first to demonstrate that amide hydrogen/deuterium exchange (HDXMS) experiments could be performed by MALDI-TOF mass spectrometry. This development opened the field of HDXMS to non-mass spectrometry experts (1). We then demonstrated that protein interfaces could be mapped by labeling the surfaces of the interacting proteins by incubation for short times in deuterated water. In early experiments, we labeled the proteins separately, formed the complex, and then "washed-out" the deuterium label prior to protease digestion and mass spectrometry (2, 3). Although the "wash-out" approach yields additional information, the experiment can also be performed by exchanging the complex into deuterated water and looking for the absence of incorporation as compared to controls of each protein alone. HDXMS interface mapping experiments are now widely used by Pharmaceutical companies as well as by researchers in academia to map protein interaction interfaces (4).

1) Mandell, J. G. Baerga-Ortiz, A., Akashi, S., Takio, K. and **Komives, E. A**. (2001) "Solvent Accessibility of the Thrombin-Thrombomodulin Interface" *J. Mol. Biol. 306*, 575-589.
2) Markwick PRL, Peacock RB, **Komives EA**. (2019) Accurate Prediction of Amide Exchange in the Fast Limit Reveals Thrombin Allostery. *Biophys J*. 116(1):49-56. PMC6342732
3) Lumpkin RJ, **Komives EA**. (2019) DECA, A Comprehensive, Automatic Post-processing Program for HDX-MS Data. *Mol Cell Proteomics*. 18, 2516-2523. PMC6885705
4) Kopcho N, Chang G, **Komives EA**. (2019) Dynamics of ABC Transporter P-glycoprotein in Three Conformational States. *Sci Repts* 9, 1. 15092. PMC6805939.

3) ***Biophysical Understanding of the NFκB-IκB interaction***. In 2003, we began working on understanding the biophysical underpinnings of the complex control of the family of transcription factors called, NFκBs by their inhibitors, the IκBs. The NFκB family of transcription factors is involved in stress response and turn on hundreds of genes, so their activity is under exquisitely careful control in cells. In this project, we collaborate with cell biologists, structural biologists, and theorists to deeply understand the kinetic control of the transcriptional regulatory system. We have made many contributions to understanding this system. In the first high quality measurements of the binding affinity of the IκBs for NFκBs, the affinity was found to be much tighter than originally thought, making sense of cell-biological results. The C-terminal ankyrin repeats of IκBα were shown to be intrinsically disordered and we now know there is a degron in this region that is exposed causing the short intracellular half-life of IκBα. Using single molecule FRET, we reported one of the first observations of fluctuations on long time scales of a disordered protein region (1). We demonstrated that IκBα strips NFκB from the DNA (2) and showed that the rate of molecular stripping controls the rate of nuclear export in cells (3). Recently, we have begun to analyze the complex dynamics of the NFκB dimers (4).

1) Lamboy, J. A., Kim, H., Lee, K. S., Ha, T. and **Komives, E. A.** (2011) Visualization of the nanospring dynamics of the IκBα ankyrin repeat domain in real time *Proc. Nat. Acad. Sci. U S A.* 108, 10178-83. PMC3121830
2) Alverdi V, Hetrick B, Joseph S, **Komives EA** (2014) Direct observation of a transient ternary complex during IκBα-mediated dissociation of NFκB from DNA. *Proc Nat Acad Sci USA* 111(1):225-30. PMC3890772
3) Dembinski, HD, Wismer, K, Vargas, JD, Suryawanshi, GW, Kern, N, Kroon, GJA, Dyson, HJ, Hoffmann, A, **Komives, EA** (2017) Functional importance of stripping in NFκB signaling revealed by a stripping-impaired IκBα mutant. *Proc Natl Acad Sci U S A 114*, 1916-1921. PMC5338396
4) Narang D, Chen W, Ricci CG, **Komives EA**. (2018) RelA-containing NFκB dimers have strikingly different DNA-binding cavities in the absence of DNA. *J Mol Biol*. 430(10):1510-1520. PMC5951767

4) Biophysics of Ubiquitin transfer E3 ligases. In 2016, we began a new project characterizing the Ankyrin and SOCS Box (ASBs) E3 ligase substrate receptors. These ankyrin repeat proteins are a major class of substrate receptors that bind substrates to CUL5-Rbx2 E3 ligases. We found that ASB9 binds a dimer of creatine kinase (CK) with extremely high affinity (1), and we built and verified a model of this substrate-substrate receptor interaction (2). We recently were able to solve the structure of full-length CUL5-Rbx2 and also of the ASB9-CK which we used to build a model of the full E3 ligase. Using HDXMS, we showed long-range dynamics changes are propagated through the ligase by substrate binding as well as by Neddylation (3).

1) Balasubramaniam D, Schiffer J, Parnell J, Mir SP, Amaro RE, **Komives EA**. (2015) How the Ankyrin and SOCS Box Protein, ASB9, Binds to Creatine Kinase. *Biochemistry* 108(9):2350-61. PMC4348336

2) Schiffer JM, Malmstrom RD, Parnell J, Ramirez-Sarmiento C, Reyes J, Amaro RE, **Komives EA** (2016) Model of the Ankyrin and SOCS Box Protein, ASB9, E3 Ligase Reveals a Mechanism for Dynamic Ubiquitin Transfer. *Structure* 24(8):1248-56. PMC4972691
3) Lumpkin RJ, Baker RW, Leschziner AE, **Komives EA**. (2020) Structure and dynamics of the ASB9 CUL-RING E3 Ligase. *Nat Commun*. 11(1):2866. PMC7280518

5) Biophysical Understanding of urokinase plasminogen activator (uPA)-receptor interactions. In 2017, we began working on understanding the dynamics of murine urokinase plasminogen activator when Dr. Tobias Kromann-Hansen joined the lab as a postdoctoral fellow. He had followed our work on thrombin and hypothesized that dynamic allostery may also be occurring in uPA. We demonstrated that his crystal structure of the alternate form of muPA was also occurring in solution (1) and that the equilibrium between these two very different chymotrypsin and non-chymotrypsin-like folds could be regulated by nanobody and substrate binding (2). Dr. Kromann-Hansen returned to Denmark unexpectedly early, but we have continued the project extending his work in murine uPA to human uPA and also to the full-length protein. We are currently writing up our first paper on the human protein, which has different dynamics from the murine in line with their different physiological behaviors.

1) Kromann-Hansen T, Lange EL, Sørensen HP, Hassanzadeh-Ghassabeh G, Huang M, Jensen JK, Muyldermans S, Declerck PJ, **Komives EA**, Andreasen PA. (2017) Discovery of a novel conformational equilibrium in urokinase-type plasminogen activator. *Sci Rep*. 7(1):3385 PMC5469797
2) Kromann-Hansen T, Lange EL, Lund IK, Høyer-Hansen G, Andreasen PA, **Komives EA**. (2018) Ligand binding modulates the structural dynamics and activity of urokinase-type plasminogen activator: A possible mechanism of plasminogen activation. *PLoS One*. 13(2):e0192661. PMC5805342

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/elizabeth.komives.1/bibliography/public/

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

R01HL127041-04 Komives (PI) 01/15/16-12/31/2020 (NCE)

NHLBI

Title: Functional Dynamics of Thrombin

The goal of this project is to understand how the internal dynamics of thrombin are allosterically modulated by thrombomodulin.

Role: PI

NSF-MCB 1817774 Komives (PI) 07/01/2018 – 06/30/2022

Molecular and Cellular Biosciences

Title: The role of dynamics in E3 ligase function

The goal of this project is to combine cryo-EM and amide hydrogen-deuterium exchange mass spectrometry to gain an understanding of how CUL5 E3 ligases transfer ubiquitin to their substrates.

Role: PI

Completed Research Support

P01 GM071862-10 Komives (PI) 05/01/12 - 02/28/17 (NCE through 02/28/18)

NIGMS

Title: IκB/NFκB Recognition In Silico, In Vitro, In Vivo

The major goals of this Program Project are to combine theory, biophysical experiments and in vivo cellular biochemistry to understand signaling through the NF-kB system.

Role: PI of overall project and of Project 1

BIOGRAPHICAL SKETCH

DO NOT EXCEED FIVE PAGES.

NAME: Taylor, Susan S.

eRA COMMONS USER NAME: staylor

POSITION TITLE: Professor of Chemistry & Biochemistry and Professor of Pharmacology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
University of Wisconsin, Madison, WI	B.A.	06/1964	Chemistry
The Johns Hopkins University, Baltimore, MD	Ph.D.	10/1968	Physiological Chemistry
MRC Laboratory Molecular Biology, Cambridge	Postdoc	12/1971	Protein Chemistry
University of California, San Diego, CA	Postdoc	03/1972	Protein Chemistry

A. Personal Statement. Over many decades my laboratory has established a multi-scale approach to study the structure, function, dynamics, and cellular localization of cAMP-dependent protein kinase (PKA) and its associated proteins. Our interdisciplinary platform that includes crystallography, NMR, SAXS/SANS, and high-power computing has established PKA as the prototypical transducer for the large protein kinase superfamily. A guiding principle is that structure will lead to an enhanced understanding of function at both molecular and cellular levels, and this strategy has been validated repeatedly. These are the underlying principles that I try to convey to all students and fellows who train in my laboratory in addition to training them to be rigorous in their experiments. Reaching across scales and building collaborative partnerships are part of the toolbox of skills that each trainee learns in my laboratory. Through bi-weekly group meetings and one-on-one meetings they go over the details of their findings and also learn to trouble shoot. They interact with skilled research scientists to learn state-of-the-art technologies in crystallography and imaging. They also present their work at research rounds that are held weekly in the Pharmacology department. All have also completed their theses in less than six years. Finally I am committed to and passionate about recruiting and training URG students.

Most recently we are adding cryo EM to our toolbox of approaches that we use to elucidate structure and dynamics. In parallel, we have established cell imaging and high-resolution mosaic imaging of PKA isoforms at the tissue level. Our structure of the PKA catalytic subunit, the first protein kinase structure to be solved, represents a fully active kinase bound to an inhibitor peptide and ATP while subsequent structures of holoenzyme complexes and various AKAP complexes provide a solid foundation for mapping the unique properties of any protein associated with PKA signaling. Our next challenge is to move beyond holoenzymes to signalosomes where each PKA contributes in new ways to new communities. At the same time, we are profiling the molecular and cellular properties of disease-associated proteins such as the Cα fusion protein that drives fibrolamellar hepatocellular cancer (FLHCC), point mutants in Cα that drive Cushing's Disease and in RIα that drive Carney Complex Disease and Acrodysostosis.

I have demonstrated **leadership and service** at many levels throughout my career. At NIH, I served on the GM Council and on the Board of Scientific Councilors for NIHLB, NIDDK, and NCI. I am presently on the BSC for NICHD. I have served on the Council for ASBMB and then as its president and have organized many ASBMB meetings, most recently ASBMB Pseudokinase meetings in 2015 and 2018. I was also on the Council for the Protein Society and for the National Academy of Sciences. I am a passionate advocate for interdisciplinary science and especially for **training the next generation of scientists**. In addition to mentoring my own graduate students and fellows, I was on the Burroughs Welcome Advisory Committee for Career Awards in Interdisciplinary Science and on the Council for the Human Frontiers in Science Program. I served for two decades on the Packard Scientific Review Panel for selecting new Packard Fellows. At UCSD I served for 20 years as PI of our T32 Molecular Biophysics Training Grant and am Co-PI on our T32 Interfaces in Science Training Grant. Here we have always had a commitment to recruiting and training URM students; it

is a part of our culture. As evidence of my continued commitment, I am now teaching a course in ethics, mentoring and communication skills to our first year Chemistry/Biochemistry graduate students and am head of our departmental Equity, Diversity, and Inclusion committee. I am also a leader in the protein phosphorylation community and have always strived to promote an open and collaborative environment where ideas are exchanged freely and collaborations encouraged. In terms of **sharing reagents,** our structure coordinates are released immediately upon or prior to publication. Plasmids, antibodies, and proteins are also shared freely. Our recent deposition of the brain imaging data into the Cell Imaging Library has been highly successful.

B. Positions and Honors

Positions and Employment

1964-1968	Graduate Student, Dept. Physiological Chemistry, The Johns Hopkins University (E.C. Heath)
1969-1971	Postdoc. Fellow, MRC Laboratory of Molecular Biology, Cambridge, England (B.S. Hartley)
1971-1972	Postdoc. Fellow, Dept. Chemistry, University of California, San Diego, CA (with N.O. Kaplan)
1972-1974	Assistant Professor in Residence, Dept. Chemistry, University of California, San Diego, CA
1974-1979	Assistant Professor of Chemistry, University of California, San Diego, CA
1979-1985	Associate Professor of Chemistry, University of California, San Diego, CA
1980-1981	Fogarty Fellow, MRC Laboratory of Molecular Biology, Cambridge England (with A. Klug)
1985-	Professor of Chemistry and Biochemistry, University of California, San Diego, CA
1997-2014	Howard Hughes Medical Institute Investigator
2004-	Professor of Pharmacology, University of California, San Diego, CA

Honors (Selected)

Eli Lilly Lecturer, Mich. St. U. (1991); Hellerman Mem. Lecturer, Johns Hopkins U. (1992); Burroughs-Wellcome Visiting Prof. in Pharm., Rochester U. (1992); Drummond Memorial Lecturer, U. Calgary (1992); **Elected to Am. Acad. Arts & Sci. (1992)**; Forefronts of Large Scale Computation Award (1993); Hans Lindner Memorial Lecture, Weizmann Institute, Israel (1995); Advisory Board, Max Planck Institute for Molecular Physiology, Dortmund, Germany (1995-2008);Merit Award, NIH GM19301 (1996); **Elected into the National Academy of Sciences (1997)**; **Elected into Institute of Medicine (1997)**; Howard Hughes Medical Institute Investigator (1997); Burroughs-Wellcome Visiting Professor in Pharmacology, U. North Carolina (1998); Outstanding Scientist Award, San Diego Am.Chem. Soc. (1998); Outstanding Achievement Award, Miami Winter Symposium (1999); 2000 National Lecturer, Biophysicial Society (2000); **Garvan-Olin Medal, Am. Chem. Soc. (2001)**; 2007 William C. Rose Award, ASBMB (2006); AAAS Fellow Award (2008); Vanderbilt Prize in Biomedical Sciences (2009); **FASEB Excellence in Science Award (2010)**; PABMB Lecture at 35th Annual Reunion of SBBM de Chile (2012); 2014 Centenary Award, Biochemistry Society, UK (2013); UCSD Chancellor's Associates Faculty Excellence Award (2014); **ASBMB Earl and Thressa Stadtman Distinguished Scientist Award (2017)**; **Harvey Lecture, Rockefeller U. (2017)**.

Service (Selected)

NIH Biochemistry Study Section (1978-82); ACS Study Section: Nucleic Acids and Prot. Synth. (1983-87); Chair of Gordon Conf. on Second Messengers & Prot. Phosphorylation (1986); Ed. Board, *J. Biol. Chem*. (1985-90); ASBMB Council (1989-92), Board of Scientific Councilors, Nat. Heart, Lung & Blood Inst. (1987-92), Chair 1990-91; Council, Prot. Soc. (1992-95); NRC/Commission on Life Science (1992-95); Co-chair ASBMB Mtg. on Prot. Phosphorylation (1992); Council for Research/Clinical Investigation Awards Am. Can. Soc. (1993-96); FASEB Summer Conf. on Prot. Kinases (Vice-Chair, 93; Chair, 95), ASBMB Satellite Meeting "Prot. Kinases and Phosphatases" (Co-chair 1994); ASBMB President (1995-96); Board of Scientific Councilors, National Cancer Institute (1996); General Motors Assembly (1997); Burroughs Wellcome Advisory Committee, Career Awards at the Scientific Interface (2001-2007), Advisory Committee, Human Frontiers in Science Program (2010-2012); Packard Foundation Fellowships Advisory Panel (1998-2016)

C. Contributions to Science

1. Establishing the Catalytic Subunit as the Prototype for the Kinome. Our interdisciplinary strategy for identifying active site residues and then elucidating the structure and function of the PKA C-subunit has established PKA-C as the prototype for the protein kinase superfamily. Since solving the first kinase structure in 1991, we have trapped all steps of the catalytic cycle in crystal lattices. We also showed how the C-terminal tail that lies outside the conserved catalytic core is a conserved feature of all AGC protein kinases and an essential part of ATP binding and catalysis. We solved structures of the myristylated PKA-C and used computational and fluorescence approaches to understand how the C-subunit senses the myristyl moiety. By comparing all active and inactive kinases we discovered the hydrophobic regulatory (R) and catalytic (C) spines that form the core architecture for every protein kinase. This is another fundamental concept that came

from my laboratory. Protein kinases are dynamic molecular switches and the assembly of the R-spine defines the activation switch, and the constitutive assembly of the R-spine is a feature that defines many oncogenes. Most recently, by carrying out many 50 μsec simulations, we described a Community Map analysis of the C-subunit. This allows us to go beyond 1°, 2°, and 3° structure to understand how correlated motions are achieved and allosteric sites integrated with the overall catalytic mechanism. We then showed how a Mutation far from the active site destroys the community network. The spine concept coupled with ComMaps compares Allostery in kinases with fine-tuning of a violin. In this section I include three of my five most significant contributions (*), two with graduate students as first authors.

a. *Affinity Labeling of cAMP-dependent Protein Kinase with *p*-Fluorosulfonylbenzoyl Adenosine: Covalent Modification of Lysine 71. Zoller, M.J., Nelson, N.C., and **Taylor, S.S.** *J. Biol. Chem.* **256**:10837-10842 (1981)
b. *Crystal Structure of the Catalytic Subunit of cAMP-dependent Protein Kinase. Knighton, D.R., Zheng, J., Ten Eyck, L.F., Ashford, V.A., Xuong, Ng. H., **Taylor, S.S.**, and Sowadski, J.M. *Science* **253**:407-414 (1991)
c. *Surface Comparison of Active and Inactive Protein Kinases Identifies a Conserved Activation Mechanism. Kornev, A.P., Haste, N.M., **Taylor, S.S.,** Ten Eyck, L.F. *Proc. Natl. Acad. Sci.* **103**: 17783-17788 (2006).
d. The Dynamic Architecture of a Protein Kinase. McClendon, C.L., Kornev, A.P., Gilson, M.K. and **Taylor, S.S.** *Proc. Natl. Acad. Sci. USA* 111:E4623-31 (2014). PMCID: PMC4217441

2. Allosteric activation of PKA by cAMP is embedded in the Regulatory subunits. In parallel with the C-subunit structure/function studies, we have characterized the PKA regulatory (R) subunits where allosteric activation of PKA is embedded in the cyclic nucleotide binding (CNB) domains. There are four functionally non-redundant isoforms of PKA R-subunits, and we have characterized and solved structures of not only the free R subunits but also the R_2 dimer and an RC heterodimer including mutant R-subunit that drives a disease phenotype. With SAXS/SANS we demonstrated unambiguously that the structures of the isoforms were different even though each R-subunit dimer has the same domain architecture. RIα has been studied in most depth, and this now includes the structure of an RIa-dimer, NMR structures, a Markov State Model of the CNB domains, CNC and ACRDYS mutants, and single molecule optical tweezers. This multi-scale approach is unraveling the allosteric regulation. All of the listed papers were first authored by graduate students.

a. *Regulatory Subunit of Protein Kinase A: Structure of Deletion Mutant with cAMP Binding Domains. Su, Y., Dostmann, W.R.G., Herberg, F.W., Durick, K., Xuong, Ng. H., Ten Eyck, L.F., **Taylor, S.S.**, and Varughese, K.I. *Science* 269:807-813 (1995).
b. Molecular Basis for Regulatory Subunit Diversity in cAMP-dependent Protein Kinase: Crystal Structure of the Type IIβ Regulatory Subunit. Diller, T.C., Madhusudan, Xuong, Ng. H., and **Taylor, S.S.** *Structure* 9**:**73-82 (2001).
c. Structure of a PKA RIa Recurrent Acrodysostosis Mutant Explains Defective cAMP-dependent Activation. Bruystens, J.G., Wu, J., Fortezzok A., Del Rio, J., Nielsen, C., Blumenthal, D.K., Rock, R., Stefan, E. and **Taylor, S.S.** *J. Mol. Biol.* 428(24 Pt B):4890-4904 (2016). PMCID: PMC5149412
d. Integrated Method to Attach DNA Handles and Functionally Select Proteins to Study Folding and Protein-Ligand Ineractions with Optical Tweezers. Hao, Y., Canavan, C., **Taylor, S.S.** and Maillard, R.A. *Sci. Reports* 7(1):10843 (2017) PMCID: PMC5589850

3. Dynamic assembly of isoform-specific holoenzymes. While we learned much from individual R- and C-subunits and from R:C heterodimers, we did not understand the functional non-redundancy of the R-subunits nor did we understand Allostery. This required full-length proteins and will eventually require that we look beyond to the multicomponent PKA signaling complexes that are assembled at membranes and organelles. Our first holoenzyme structures allowed us to see the amazing symmetry of each holoenzyme and to appreciate that each holoenzyme was structurally distinct as SAXS/SANS had predicted. The holoenzyme structures also explained their functional non-redundancy.

a. *Structure and Allostery of the PKA RIIβ Tetrameric Holoenzyme. Zhang, P., Smith-Nguyen, E.V., Keshwani, M.M. Deal, M.S., Kornev, A.P. and **Taylor, S.S.** *Science* 335:712-716 (2012). PMCID: PMC3985767
b. Assembly of allosteric macromolecular switches: lessons from PKA. **Taylor SS**, Ilouz R, Zhang P, Kornev AP. *Nat Rev Mol Cell Biol.* 13:646-58(2012) PMCID: PMC3985763

c. Structures of the PKA RIa Holoenzyme with the FLHCC Driver J-PKAca or Wildtype PKAca. Cao, B., Lu, T.-W., Fiesco, J.A.M., Tomasini, M., Fan, L., Simon, S.M., **Taylor, S.S.** and Zhang, P. *Structure* 27:816-28 (2019) PMCID:PMC6506387

d. Two PKA RIa Holoenzyme States Define ATP as an Isoform-specific Orthosteric Inhibitor that Competes with the Allosteric Activator, cAMP. Lu, T.W., Wu, J., Aoto, P.C., Weng, J.H., Ahuja, L.G., Sun, N., Cheng, C.Y., Zhang, P. and **Taylor, S.S.** *PNAS* 116:16347-56 (2019) PMCID:PMC66978791

4. Building PKA Scaffolds and Signaling Communities. Localization is an essential feature for determining PKA specificity. Scaffold proteins such as A Kinase Anchoring Proteins (AKAPs) create a signaling community in close proximity to dedicated substrates. The AKAP amphipathic helix docks onto the dimerization/docking domain of the R-subunit. Our discovery of dual specific AKAPS, dAKAP1 and dAKAP2, showed that RI subunits could also bind to AKAPs. Elucidating structures of this AKAP motif and identifying RI-specific AKAPs has been a major goal over the past decade. Our discovery of the small acylated AKAP, smAKP that targets RI to membranes and most recently of GPR161 that has an RI-specific AKAP embedded within its C-terminal tail are opening new doors into our appreciation of the role of RI signaling at membranes. Three of the listed significant papers hsd graduate students as first authors.

a *A-kinase-interacting Protein Localizes Protein Kinase A in the Nucleus. Sastri, M., Barraclough, D.M., Carmichael, P.T., and **Taylor, S.S.** *Proc. Natl. Acad. Sci. USA* 102**:**349-354 (2005). PMCID: PMC544310

b *D-AKAP2-PKA RII-PDZK1 Ternary Complex Structure: Insights from the Nucleation of a Polyvalent Scaffold. Sarma, G.N., Moody, I.S., Ilouz, R., Phan, R.H., Sankaran, B., and **Taylor, S.S**. *Protein Sci.* 24:105-16 (2014). PMCID: PMC4282416

c Structure of smAKAP and its Regulation by PKA-mediated Phosphorylation. Burgers, P.P., Bruystens, J., Burnley, R., Nikolaev, V., Keshwani, M., Wu, J., Janssen, B., **Taylor, S.S.,** Heck, A.J.R. and Scholten, A. *FASEB J.* 283:2132-48 (2016). PMCID: PMC4980077

d GPR161 Anchoring of PKA Consolidates GPCR and cAMP Signaling. Bachmann, V., Mayrhofer, J., Ilouz, R., Tschaikner, P., Raffeiner, P., Rock, R., Courcelles, M., Apeit, F., Lu, T.-W., Baillie, G.S., Thibault, P., Aanstad, P., Stelzl, U., **Taylor, S.S.** and Stefan, E., *Proc Natl Acad. Sci. USA* 113:7786-91 (2016). PMCID: PMC4948347

5. Visualizing PKA in cells. In addition to elucidating structures and understanding the dynamic properties of PKA, it is essential to understand how PKA functions in live cells. With R. Tsien we developed the first FRET reporter for cAMP and discovered the Nuclear Export Signal (NES) in PKI. Later with Zhang and Tsien we designed the first protein kinase activity reporter (AKAR). In collaboration with the National Center for Microscopy and Imaging Research (NCMIR), we defined how PKA and PKA substrates are targeted to mitochondria where they help to control organelle dynamics. A new technology, miniSOG, allows us to do correlated light and electron microscopy to more precisely map localization of proteins associated with PKA signaling while High Resolution Mosaic Imaging provides a portrait of PKA isoform distribution in tissues.

a. *****Identification of a Signal for Rapid Export of Proteins from the Nucleus. Wen, W., Meinkoth, J.L. Tsien, R.Y., and **Taylor, S.S.** *Cell* **82**:463-473 (1995).

b. *****Genetically Encoded Reporters of Protein Kinase A Activity Reveal Impact of Substrate Tethering. Zhang, J., Ma, Y., **Taylor, S.S.**, and Tsien, R.Y. *Proc. Natl. Acad. Sci. USA* 98:14997-15002 (2001). PMCID: PMC64972

c. A Kinase interacting protein (AKIP1) is a key regulator of cardiac stress. Sastri M, Haushalter KJ, Panneerselvam M, Chang P, Fridolfsson H, Finley JC, Ng D, Schilling JM, Miyanohara A, Day ME, Hakozaki H, Petrosyan S, Koller A, King CC, Darshi M, Blumenthal DK, Ali SS, Roth DM, Patel HH, **Taylor SS**. *Proc Natl Acad. Sci. USA* 110:E387-96 (2013) PMCID: PMC356278

d. *Isoform-specific Subcellular Localization and Function of Protein Kinase A Identified by Mosaic Brain Mapping. Ilouz, R., Lev-Ram, V., Bushong, E.A., Stiles, T., Friedmann-Morvinski, D., Douglas, C., Goldberg, G., Ellisman, M.H. and **Taylor, S.S.** *eLife* 6:e17681 (2017). PMCID: PMC5300705

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/40423766/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

PHS/NIH: 1R35 GM130389 Taylor (PI) 01/01/19 - 12/31/23
"Lessons Learned from PKA: Assembly of Dynamic Macromolecular Switches"
With cryoEM and high-resolution mosaic imaging, the major goals of this grant is to establish PKA as the prototype for the assembly of macromolecular polyvalent signaling complexes at the molecular and cellular level and show how these "machines" are structurally and functionally altered in disease.
Role: PI

MJFF: 11425.07 Taylor (PI) 08/01/20– 07/31/21
"Structural Window into LRRK2: Kinase or Pseudokinase?"
The major goal of this grant is to characterize LRRK2 conformational states using mutagenesis, crystallography and electron microscopy (EM).
Role: PI

Lilly Research Award Program Taylor (PI) 02/25/19 – 02/24/21
"Dynamics Driven Allostery in Rsk" The major goal of this grant is to analyze entropy-driven thermal dynamics of RSK1 complexes using computational methods, X-ray crystallography, cryoEM, HDX and biochemical analysis.
Role: PI

Completed Research Support

UC-NL-CRT: LFR-17-476732 Consortium PI: James Fraser 03/01/17 – 02/28/20
"Macromolecular Movements by Simulation and Diffuse Scatter"
The major goals of this grant are to make quantitative comparisons of allosteric networks based on simulations and experimental analysis of diffuse scattering. The allosteric networks will be tested with mutations and eventually small molecules for their ability to alter protein function dynamically. New network model refinement software using open source tools will be incorporated into a leading package for X-ray refinement (Phenix).
Role: Site PI

DRG/NIH: 1P01 DK54441 Taylor (PI) 04/01/13 – 03/31/19 (NCE)
"PKA and PKC Targeting Mechanisms"
PI (Project I): Susan S. Taylor
"Novel Isoform-specific Targeting of PKA "
This PPG is focused on targeting mechanisms for PKC and PKA. It includes 4 PIs: S. Taylor, J. Olefsky, and A. Newton at UCSD and J. Scott at the U. Wahsington and 4 Core Directors. The goals for the Taylor lab are to characterize the cellular architecture of PKA scaffolds that are assembled at the mitochondria and how these scaffolds change in response to cAMP and as a function of diet and disease.
Role: PI

PHS/NIH: R03TR002947 Taylor (PI) 09/01/19 - 08/31/20
"Illuminating the Role of understudied PRKACB Splice Variants in PKA Signaling"
The major goal of this project is to characterize the Cβ isoforms of PKA. This isoform is associated with cancer and autoimmune diseases and a splice variant is highly expressed in lymphocytes. It has been designated as a "neglected" kinase that is likely important for disease.
Role: PI

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Toor, Navtej Singh

eRA COMMONS USER NAME (credential, e.g., agency login): nstoor

POSITION TITLE: Associate Professor of Biochemistry

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Calgary	B.Sc.	05/1996	Biochemistry
University of Calgary	Ph.D.	11/2004	RNA Biochemistry
Yale University / Howard Hughes Medical Institute	Postdoc	06/2009	RNA Structural Biology

A. Personal Statement

The goal of our research is to gain insight into the structure and function of non-coding regions of eukaryotic and prokaryotic genomes. Spliceosomal introns and non-LTR retroelements comprise the majority of this “junk DNA”, which comprises ~50% of the human genome. Both of these genetic elements are thought to have evolved from a common ancestor called the group II intron. A group II intron is a self-splicing catalytic RNA that can also undergo reverse splicing reactions into DNA with the assistance of an intron-encoded protein. Group II introns are considered to be ancestral to the spliceosome. The spliceosome is a multi-megadalton, ribonucleoprotein complex which is responsible for catalyzing RNA splicing in all eukaryotes. We are currently working to determine the crystal structures of both group II introns and spliceosomal complexes to gain insight into the molecular basis for their function.

Mentoring and teaching students are integral parts of my research activities. There are currently four Ph.D. graduate students in my lab: Tim Wiryaman, Anastassia Hirlinger, Jason Hingey, and Boris Rudolfs. I meet with these students on a daily basis to discuss experimental design and research progress. Three Ph.D. students have graduated from my lab: Russell Chan, Jessica Peters, and Daniel Haack. I have also served as the first year adviser for incoming graduate students from 2010 to 2018. In this role I advised students on appropriate courses for their research interests and more importantly, help guide them in choosing a lab for their thesis work.

I teach both undergraduate and graduate courses in biochemistry and structural biology. In my graduate course, we discuss recent papers in class and debate the merits and disadvantages of a wide variety of experimental techniques. Students have told me that after completing this class, they feel that they can better judge and understand papers that they read in the literature. In my undergraduate class, I make sure to present material to the students that goes beyond what is normally shown in the textbooks. I present the background and personalities behind significant breakthroughs in biology. I try to introduce undergraduate students to the concept of doing basic biochemical research at the university level and try to integrate recent scientific discoveries into lectures.

Our research is centered on studying RNA structure and function in the context of pre-mRNA splicing. As the PI on an NIH-funded grant, my laboratory has made fundamental discoveries about the mechanism of eukaryotic RNA splicing. I personally take great care to train my students in good experimental design and appropriate controls combined with an objective analysis of the resulting data. I also fully support my students attending research conferences as well as career-oriented events to help them decide their future career directions. In this regards, I regularly meet with my students to evaluate their progress and their career trajectories. In terms of diversity, I strongly believe in encouraging underrepresented groups to participate in

science. It is possible for anyone to excel at research given the appropriate environment and intellectual stimulation. As a result, I have mentored many diverse students at the undergraduate and graduate levels.

1. Robart AR, Chan RT, Peters JK, Rajashankar KR, & Toor N. (2014). Crystal structure of a eukaryotic group II intron lariat. ***Nature*** 514: 193-197. *PMCID: PMC25252982*
2. Toor N, Keating KS, Taylor SD, & Pyle AM. (2008). Crystal structure of a self-spliced group II intron. ***Science*** 320: 77-82. *PMID: 18388288*
3. Haack DB, Yan X, Zhang C, Hingey J, Lyumkis D, Baker TS & Toor N. (2019). Cryo-EM Structures of a Group II Intron Reverse Splicing into DNA. ***Cell.*** 178: 612-623.

B. Positions and Honors

Positions and Employment

2009-2015 Assistant Professor, Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA.

2016-present Associate Professor, Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA.

Honors

1991-1993 Canada Scholarship Award, Government of Canada

1999 Research Assistantship Award, University of Calgary, Canada

2012 Hellman Faculty Fellowship Award

C. Contributions to Science

1. Elucidation of the mechanism of RNA splicing.

Both the spliceosome and the group II intron share a conserved core RNA structure that is thought to catalyze RNA splicing in all eukaryotes, including humans. This RNA structure is known as the U2/U6 snRNA in the spliceosome and domain V in group II introns. This common structure consists of an RNA stem loop containing a two-nucleotide bulge and a conserved catalytic triad of residues. This domain is highly conserved from bacteria to humans; however, its exact function in splicing had remained a mystery for many years. To solve this problem, I determined the **first crystal structure of a group II intron**. The structure **revealed that RNA splicing is catalyzed by two metal ions** coordinated to the highly conserved domain V between the two-nucleotide bulge and the catalytic triad. Therefore, RNA splicing utilizes a two-metal-ion mechanism in which one metal activates the attacking nucleophile and other one stabilizes the transition state. Group II introns are thought to share a common ancestor with the spliceosome. Given this evolutionary connection, it is likely that the spliceosome also utilizes a two-metal-ion mechanism of catalysis. Therefore, this structure gave the **very first molecular insight into the mechanism of eukaryotic RNA splicing**. I was a co-corresponding author on this study, in addition to being first author.

a. Toor N, Keating KS, Taylor SD, & Pyle AM. (2008). Crystal structure of a self-spliced group II intron. ***Science*** 320: 77-82. *PMID: 18388288*

b. Chan RT, Robart AR, Rajashankar KR, Pyle AM, & Toor N. (2012). Crystal structure of a group II intron in the pre-catalytic state. ***Nature Structural and Molecular Biology*** 19: 555-557. *PMCID: PMC22484319*

2. ***First crystal structure of an intron lariat.***

RNA splicing is the excision of non-coding introns from pre-mRNAs prior to translation. The branched RNA structure, known as the lariat, is formed during the splicing of both group II and spliceosomal introns that comprise ~25% of mammalian genomes. **Lariat formation is a hallmark of eukaryotic RNA splicing** and is indicative of a shared ancestry between the two types of introns. The lariat consists of an unusual 2′-5′ phosphodiester bond between a bulged adenosine residue and the 5′ end of the spliced intron. Defects in lariat formation can result in aberrant splice site selection and human disease. However, since the first discovery of the lariat over 30 years ago, there were no high-resolution structures giving insight into the formation of this ubiquitous RNA linkage. In this regard, this work represents the **first crystal structure of a 2′-5′ branched lariat RNA**. This finally revealed the location of domain VI, which contains the bulged adenosine responsible for lariat formation. Domain VI is analogous to the branch site of

spliceosomal introns. In the structure, two tandem tetraloop-receptor interactions with domain VI position the bulged adenosine nucleophile in the catalytic core. In the active site, a four-magnesium-ion cluster is responsible for both catalysis and proper positioning of the 5′ end of the intron. The **evolutionarily-related spliceosome is likely to have a similar active site arrangement**. This also represents the **largest protein-free RNA ever crystallized**. I was the sole corresponding author on this study.

a. Robart AR, Chan RT, Peters JK, Rajashankar KR, & Toor N. (2014). Crystal structure of a eukaryotic group II intron lariat. ***Nature*** 514: 193-197. *PMCID: PMC25252982*

b. Chan RT, Peters JK, Robart AR, Wiryaman T, Rajashankar KR, & Toor N. (2019). Structural basis for the second step of group II intron splicing. ***Nature Communications*** 9: 4676. *PMCID: PMC6224600*

3. First structure of a retroelement invading DNA

Group II introns are a class of retroelements that invade DNA through a copy-and-paste mechanism known as retrotransposition. Their coordinated activities occur within a complex that includes a maturase protein, which promotes splicing through an unknown mechanism. The mechanism of splice site exchange within the RNA active site during catalysis also remains unclear. We determined two cryo-EM structures at 3.6 Å resolution of a group II intron reverse splicing into DNA. These structures reveal that the branch-site domain VI helix swings 90°, enabling substrate exchange during DNA integration. The maturase assists catalysis through a transient RNA-protein contact with domain VI that positions the branch-site adenosine for lariat formation during forward splicing. These findings provide the first direct evidence for the role the maturase plays during group II intron catalysis. The domain VI dynamics closely parallel spliceosomal branch-site helix movement and provide strong evidence for a retroelement origin of the spliceosome. This also represents the **first structural insight into DNA strand invasion by a retroelement**.

a. Haack DB, Yan X, Zhang C, Hingey J, Lyumkis D, Baker TS & Toor N. (2019). Cryo-EM Structures of a Group II Intron Reverse Splicing into DNA. ***Cell*** 178: 612-623.

Complete List of Published Work in MyBibliography:

http://www.ncbi.nlm.nih.gov/sites/myncbi/navtej.toor.1/bibliography/47810850/public/?sort=date&direction=descending

D. Research Support

Ongoing Research Support

NIH R01 GM102216-03 Toor (PI) 07/15/17 - 07/01/21
Structural Biology of Retrotransposition
The goal of this study is to determine the structural basis of retrotransposition, which is responsible for the replication and dispersal of retroelements in both prokaryotic and eukaryotic genomes (including that of humans).
Role: PI

Completed Research Support

NIH R01 GM102216 Toor (PI) 07/16/12 - 05/31/18
Structural Biology of RNA Splicing
The goal of this study is to determine the structural basis of intron lariat formation, which results in the formation of an unusual 2′-5′ phosphodiester bond during RNA splicing in eukaryotes.
Role: PI

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Zid, Brian M.

eRA COMMONS USER NAME (credential, e.g., agency login): BRIANZID

POSITION TITLE: Assistant Professor of Biochemistry

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Truman State Univ, Kirksville MO	BS	08/2000	Chemistry
California Inst of Tech, Pasadena CA	PhD	06/2008	Biology
Harvard University, Cambridge MA	Postdoctoral	06/2015	Systems Biology

A. Personal Statement

The long-term focus of my lab is to use a combination of biochemical, genomic, imaging, and computational approaches to understand how gene expression is controlled during stress and disease. Specifically, we study the control of mRNA localization to phase separated RNA-protein granules in both yeast and mammalian cells. This approach requires the use of various, interdisciplinary techniques and I am confident that my prior training will enable me to make novel, impactful findings that advance our understanding of this process and its relevance to disease and aging while simultaneously uncovering the basic mechanisms that underlie our discoveries. My graduate advisor Seymour Benzer encouraged his lab members to ask high-risk questions to generate novel, impactful findings that could change or even start new fields. On the other hand, my postdoctoral advisor Erin O'Shea stressed the importance of exploring detailed mechanisms that drive biological systems. Both mentalities inform my approach to research to this day.

While a postdoctoral fellow I saw the benefit of approaching scientific questions from a multitude of directions with varied techniques and in my own lab I am working to create a similarly diverse and inclusive environment for my trainees. Along with my appointment in Chemistry and Biochemistry, I am also the department's representative to the larger quantitative Biology (qBio) PhD specialization at the university. I have recruited two postdoctoral fellows one who specializes in RNA biology and quantitative microscopy and the other who has expertise in microfluidic development and mRNA localization measurements. I also have several graduate students with varied interests and backgrounds that span organic synthesis to plant genetics. Two of them are part of the Biology graduate program, while three others are part of the Biochemistry and Biophysics graduate program. One PhD student is part of the Cell and Molecular Genetics Program at UCSD. Another is part of the qBio specialization and a third joined the Interfaces Graduate Program in Multi-Scale Biology which I am part of, while another student who recently joined was a physics undergraduate student and brings a strong modeling background to the lab. I value the multidisciplinary makeup of my lab and actively mentor my group members to combine their varied perspectives and technical skills. I also train my students to be rigorous and unbiased in pursuing questions of interest. The questions of how mRNAs are localized to phase separated granules and the impact this phase separation has on gene expression as well as the use of diverse methodologies to tackle these questions are well suited to training students in molecular biophysics.

To further help trainees in their progression through academic research I organize a monthly San Diego-wide RNA club where two students or postdocs present their research to the local RNA community. This includes arranging an annual seminar+Q&A session from local RNA industry members to discuss potential career

pathways outside of academia. Along with presenting at the San Diego RNA club I also encourage my trainees to present their research to diverse audiences both internally and at external conferences.

B. Positions and Honors

Positions and Employment

2015- Assistant Professor, Department of Chemistry & Biochemistry, UC San Diego, La Jolla CA
2017- Organizer of San Diego-wide RNA seminar series

Honors

2011-2013 Derek C. Bok Award, Certificate of Distinction in Teaching
2011-2013 American Cancer Society Funding a Cure Postdoctoral Fellow
2014 Platform Talk Cold Spring Harbor Meeting on Translational Control - *Promoter sequences determine cytoplasmic localization and translation of mRNAs during starvation in yeast*
2014 Poster Prize Winner, Integrative RNA Biology Conference
2016 Minisymposium Talk American Society for Cell Biology Annual Meeting – *The role of translation elongation in differential gene expression during stress*
2017-2019 Organizer of San Diego-wide RNA Seminar Series – Funded by the RNA Society
2018 Oral Session RNA Meeting – *Regulated translation elongation as a mechanism of differential protein synthesis during stress*
2018-2019 Selected as a 2018,2019 *Chemical Machinery of the Cell* – Scialog Fellow

C. Contributions to Science

1. **Identified the TOR pathway as a lifespan extension pathway that mediates the effects of dietary restriction.**
   During my time as a graduate student in the lab of Seymour Benzer at Caltech, I was interested in investigating how nutrients impinge on lifespan. While most of the aging literature at the time focused on Sir2 and the insulin-like signaling pathway, we wanted to investigate whether another nutrient-sensing growth pathway, the target of rapamycin (TOR) pathway, plays a role in the lifespan extension. From this work we made the novel finding that downregulation of the TOR pathway in Drosophila extends lifespan in a nutrient-dependent manner. Additionally, I found that the TOR effector d4EBP, a translational regulator, is necessary and sufficient for lifespan extension due to dietary restriction (DR). I then performed the first genome-wide translation study under DR and made the novel discovery that mitochondrial genes are translationally upregulated upon DR and that this upregulation is necessary for lifespan extension from DR. The importance of this research is exemplified by the TOR pathway currently being a major field of study in aging research, with subsequent work from many other labs showing that the TOR pathway is a conserved lifespan extension pathway that has protective effects against many neurodegenerative diseases. I was a second author for the publication identifying the importance of the TOR pathway in lifespan and the lead author as well as a corresponding author on the paper showing the role that d4EBP and translation play in the DR process.

   a. Kapahi P, Zid BM, Harper T, Koslover D, Sapin V, Benzer S (2004) Regulation of lifespan in Drosophila by modulation of genes in the TOR signaling pathway. *Current Biology*, 14(10):885-90. PMID: 15186745
   b. Kapahi P, Zid B (2004) TOR pathway: linking nutrient sensing to life span. *Sci Aging Knowledge Environ*. (36):PE34. PMID: 15356349
   c. Zid BM, Rogers A, Katewa S, Vargas MA, Kolipinski M, Lu TA, Benzer S, Kapahi P (2009) 4E-BP Extends Lifespan upon Dietary Restriction by Enhancing Mitochondrial Activity in Drosophila. *Cell*, 139(1):149-160. PMID: 19804760

2. **Identified a link between promoter sequences and the cytoplasmic fate of mRNA during nutrient deprivation.**
   My work on DR stimulated my interest in understanding how nutrients control gene expression at a basic, mechanistic level. Towards this goal, I joined the lab of Erin O'Shea at Harvard University for my postdoctoral research to study how cells respond to nutrient deprivation at the translational level. While the

O'Shea lab did not have experience in translational control, their expertise in using quantitative tools at a systems-wide level made it an ideal place to pursue this question. To monitor translation genome-wide in a quantitative manner, I established ribosome profiling in the lab. In collaboration with a biophysics postdoc I investigated the mechanistic basis of differential protein production under amino acid limitation in E. coli. By using quantitative modeling of ribosome profiling data in combination with biochemical experiments, we made the novel observations that differential aminoacylation and ribosomal abortion are key determinants of protein production during stress. Using the above methodology along with quantitative single-cell microscopy, I monitored global translational changes during glucose deprivation in yeast. I found that during glucose limitation transcriptionally upregulated mRNAs could be segregated into two classes: (1) those that are preferentially translated and are diffusely localized in the cytoplasm, and (2) those that are poorly translated and are concentrated in membrane-less compartments. Remarkably, the information specifying differential localization and translation of these two classes of mRNAs is encoded in the promoter sequence. This work altered the paradigm that in eukaryotes transcription and translation are disconnected processes. Instead, we found that these spatially distinct processes can be coordinated during nutrient limitation.

a. Subramaniam, AR, Zid BM, O'Shea EK (2014) An integrated approach reveals regulatory controls on bacterial translation elongation. *Cell*, 159(5):1200–1211. PMID: 25416955
b. Zid BM, O'Shea EK (2014) Promoter sequences determine cytoplasmic localization and translation of mRNAs during starvation in yeast. *Nature*, 514(7520):117-121. PMID: 25119046

3. **Identified the changing mitochondrial volume fraction as mediator of nuclear-encoded mitochondrial mRNA localization and translational control.**
Mitochondria are hubs for metabolite and energy generation and have been shown to be very important for age-related processes, including cancer and neurodegeneration, yet the mechanism of localized translation to these organelles and the impact this has on mitochondrial function is poorly understood. We found that nuclear-encoded mRNAs are not just localized to the mitochondria or diffusely localized but can be more dynamic in nature as certain nuclear-encoded mitochondrial mRNAs have a switch-like behavior in their mitochondrial localization. During vegetative conditions when mitochondrial respiration is low, these mRNAs are diffusely localized and generally not associated with the mitochondria, while under respiratory conditions, these mRNAs switch to become associated with the mitochondria. This enhanced localization during respiratory conditions can be explained by changes in the geometric constraints of the cell, as the fraction of the cytoplasm that is mitochondria increases, the probability of mRNA interaction with the mitochondria increases and this drives nuclear-encoded mitochondrial mRNA association for these mRNAs. These localization changes are correlated with enhanced protein levels, and we show that mRNA localization to the mitochondria is necessary and sufficient to drive increased protein levels. This represents a novel mechanism of gene expression control where protein synthesis can be regulated by simple geometrical properties (mitochondrial volume fraction) without the need to have secondary protein regulatory factors at the nuclear or cytoplasmic level. This work opens a new direction to explore how the geometric constraints of the cell regulate gene expression in a variety of cellular states.

a. Tsuboi, T., Viana, M., Xu, F., Yu, J., Chanchani, R.,Arceo, X.G.,Tutucci, E., Choi, J., Chen, Y.S., Singer, R.S., Rafelski, S.M., Zid, B. M. (2019). Mitochondrial volume fraction and translation speed impact mRNA localization and production of nuclear-encoded mitochondrial proteins. *bioRxiv*, doi: http://dx.doi.org/10.1101/529289

Complete List of Published Works in My Bibliography:
https://www.ncbi.nlm.nih.gov/pubmed/?term=Zid+b

D. Research Support

Ongoing Research Support

R35 GM128798-01 Zid (PI) 7/2018 – 6/2023
Causes and consequences of differential mRNA localization to mRNP granules

The goals of this study are to explore 1) the role that promoter elements have on cytoplasmic mRNA regulation 2) how mRNA localization impacts gene expression during stress and 3) the function of stress-induced phase-separated granules in mammalian cells.
Role: PI

Completed Research Support

R35GM128798-02S1 Zid (PI) 7/2019 – 6/2020
Alzheimer's Administrative Supplement
The goals of this study are to use yeast and microfluidics to 1) explore the impact of aging on TDP-43 toxicity and localization and 2) identify potential modifiers of age-induced TDP-43 pathology
Role: PI

Hellman Fellows Award Zid (PI) 7/2018 – 6/2019
The role of RNA/protein mislocalization during aging
The major goals of this project are to 1) Explore the dynamics of RNA-binding protein aggregate formation during yeast aging. 2) Identify mRNAs differentially localized to RNA-protein granules and decipher the mechanistic basis of this differential localization.
Role: PI

AFAR 20163907 Zid (PI) 7/2016 – 6/2018
American Federation of Aging Research Junior Faculty Award
Aggregation of RNA-Binding Proteins and Their Effects on Gene Expression During Aging in *S. cerevisiae*
The major goals of this project are to 1) categorize the localization of aggregation-prone RNA-binding proteins during aging 2) identify mRNAs differentially localized to RNA-protein granules and decipher the control mechanisms of this differential localization. 3) quantify the changes in gene expression that is driven by the aberrant aggregation of mRNPs during aging.
Role: PI

COPY FROM 2020–21 UC SAN DIEGO GENERAL CATALOG

Interim Update (February 3, 2021)

Chemistry and Biochemistry (graduate curriculum)

Chemistry and Biochemistry

[undergraduate program | courses | faculty]

Chair's Office
2040 Urey Hall Addition
(858) 534-5489
http://chemistry.ucsd.edu

Undergraduate Student Affairs
Revelle College, 4010 York Hall
(858) 534-4856

Graduate Student Affairs
Revelle College, 4010 York Hall
(858) 822-6014

All courses, faculty listings, and curricular and degree requirements described herein are subject to change or deletion without notice.

The Graduate Programs

~~Graduate students are accepted to the~~The Chemistry Program in the Department of Chemistry and Biochemistry accepts students for study toward the MS in ~~c~~Chemistry, the PhD in ~~c~~Chemistry, the PhD in ~~c~~Chemistry with ~~s~~Specialization in ~~b~~Bioinformatics, the PhD with ~~s~~Specialization in ~~c~~Computational ~~s~~Science, the PhD with ~~s~~Specialization in ~~m~~Multiscale ~~b~~Biology, and the PhD with ~~s~~Specialization in ~~q~~Quantitative ~~b~~Biology.

The Biochemistry and Molecular Biophysics Program in the Department of Chemistry and Biochemistry accepts students for study toward the MS in Biochemistry and Molecular Biophysics and the PhD in Biochemistry and Molecular Biophysics.

Chemistry Program (CHEM)

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Master of Science

A Plan I (Thesis) MS in chemistry and a Plan II (Comprehensive Examination) MS in chemistry are offered. The former allows specialization in one area as well as research experience. The latter encourages breadth and offers opportunities to broaden one's scientific background.

Admissions: Students are admitted for fall quarter entrance only. Eligibility requirements for admission include solid training in the chemical sciences as judged by the undergraduate record, a minimum 3.0 GPA in chemistry courses completed, and a minimum 3.0 overall GPA.

Students who attended the University of California San Diego are eligible to apply for either the Plan I (Thesis) or Plan II (Comprehensive Examination) master's program. Those who wish to apply to the Thesis Plan must have a

letter of support from the proposed thesis adviser. All other students are admitted to the Plan II (Comprehensive Examination) master's program only.

The GRE general test is required of all applicants. Foreign applicants must submit a TOEFL score; TWE scores are strongly recommended.

Residency and Time-to-Degree: Master's students must register at UC San Diego for a minimum of three quarters, and complete at least twenty units per academic year. Full-time Comprehensive Examination Plan students can complete the degree in three quarters. Thesis Plan students typically take eighteen to twenty-four months to graduate.

Plan I (Thesis)

Purpose: To prepare students for research careers or for doctoral or professional studies.

Advancement to Candidacy: A minimum of thirty-six units with an overall minimum GPA of 3.0 must be completed. Complete a minimum of eighteen units of Thesis Research (CHEM 299). At least eight units of graduate level chemistry courses must be completed for a letter grade. Four units of teaching apprenticeship (CHEM 500) and two units for the teaching seminar (CHEM 509) may be applied (see "Doctoral Program," "Teaching," and "Language Requirement" sections). Additional/Elective courses taken to meet the 36-unit requirement must be upper-division or graduate Chemistry courses. Students must obtain department approval to apply courses from other departments. Contact the Chemistry & Biochemistry Student Affairs Office for full information.

Thesis: Students must give an oral presentation and defense of their thesis project to a thesis committee. A student graduates after the thesis has been defended and the written dissertation approved by his or her committee, the department, and the Graduate Division, and then filed with the university archivist. The thesis committee consists of at least three faculty: (1) the thesis adviser, (2) a faculty member from the Department of Chemistry and Biochemistry familiar with the student's research area, and (3) a faculty member from either this or another department whose research is in an area different from that of the thesis.

Plan II (Comprehensive Exam)

Purpose: To prepare students for doctoral or professional studies, or for teaching at the community college or high school level, or for career work in industry.

Advancement to Candidacy: A minimum of thirty-six units with an overall minimum GPA of 3.0 must be completed. A minimum of sixteen units must be letter-graded chemistry graduate courses. Four units of teaching apprenticeship (CHEM 500) and two units for the teaching seminar (CHEM 509) may be applied (see "Doctoral Program," "Teaching," and "Language Requirement" sections). Four units of non-thesis research (CHEM 297 or CHEM 298) and four units of Research Survival Skills (CHEM 250) are allowed (enrollment in CHEM 250 is only permitted for students who are pursuing a Ph.D. degree). Additional/Elective courses taken to meet the 36-unit requirement must be upper-division or graduate Chemistry courses. Students must obtain department approval to apply courses from other departments. Plan II students may not use CHEM 299 units toward their degree. Contact the Chemistry & Biochemistry Student Affairs Office for full information.

Comprehensive Examination: The purpose of this requirement is to confirm that students have achieved an advanced understanding of, and a comprehensive training in, the chemical sciences. The tests cover a wide range of material, so that students will have a chance to show what they have learned. For master's students, the department administers exams in biochemistry and in analytical/instrumental, inorganic, organic, and physical chemistry.

Students must pass three of the exams in order to graduate. For doctoral students earning a Plan II MS on the way to the PhD, the written and oral Departmental Examination components fulfill this requirement.

Doctoral Program

The goal of the PhD in chemistry is to prepare students for careers in science by expanding their knowledge of chemistry while developing their ability for critical analysis, creativity, and independent study. The program is designed to encourage initiative and to stimulate enjoyment and development of the student's area of research expertise as well as the broader aspects of scientific inquiry and enlightenment.

Research

Students choose their research concentration from program tracks in Analytical and Atmospheric Chemistry, Physical Chemistry, Inorganic Chemistry, Organic Chemistry, Chemical Biology, Theoretical and Computational Chemistry, and Biochemistry and Biophysics. Opportunities for scientific discovery are also abundant through the department's extensive collaborations with investigators in other physical, biological, and engineering sciences. This includes on-campus collaborations with faculty in the Materials Science Program, School of Medicine, School of Pharmacy and Pharmaceutical Sciences, and Scripps Institution of Oceanography. There are off-campus interactions with scientists at nearby research facilities such as the Salk Institute and The Scripps Research Institute. State-of-the-art facilities and equipment support all the research programs. The department's Industrial Relations Program interfaces with national and local chemical, biotechnology, and pharmaceutical industries to encourage technology transfer and to assist postgraduates interested in industrial careers.

Research Adviser

A first-year faculty adviser guides students until a research adviser is chosen. Most of a student's efforts in graduate school are directed toward research for the doctoral dissertation, and selection of a research adviser is of utmost importance. To assist students with this critical decision, all chemistry and biochemistry faculty describe their current research activities early in the fall quarter. Students then rotate in laboratories or consult with faculty to discuss research opportunities. Although students have until the end of the first year to join a laboratory, most start their research by midyear.

Placement Examinations and Course Work

There will be two required examinations for incoming doctoral students: one General Exam and one In-Track Exam (in the student's area of research specialization). These examinations will cover undergraduate-level course material in chemistry and biochemistry The In-track Exam will focus on the student's area of research and the General Exam will encompass topics from all subdisciplines of chemistry and biochemistry: biochemistry, inorganic chemistry, organic chemistry, physical chemistry, and analytical/instrumental analysis. To meet the Placement Examination requirement, students must show proficiency at the upper-division level on the topics covered in the General Exam and the In-Track Exam by the end of Spring quarter of the student's first year. Students must demonstrate proficiency by passing both Placement Exams, or by completing prescribed coursework with a grade of B or higher if they do not pass one or both Exams.

Departmental Examination

In the second year, a student's progress in research and graduate studies is evaluated through the departmental examination, which includes a written component and oral defense of the student's research proposal. Students are

also evaluated on their general knowledge of their particular field of study and students may be asked about progress on their dissertation.

Qualifying Examination

By the end of the third year, students defend the topic, preliminary findings, and future research plans of their dissertation. Passing this defense qualifies the student to advance to candidacy for the dissertation. A dissertation committee composed of five faculty, one of whom is the research adviser, provides consultation and evaluation for the dissertation project.

Dissertation

The dissertation is normally completed in the fourth or fifth year. This body of research is expected to make an innovative contribution to the field of chemistry. PhD candidates present a seminar summarizing their research accomplishments and defend their thesis in an oral examination before their dissertation committee.

Teaching

Experience in teaching is a vital and integral part of every graduate student's training, and all students participate in the instructional activities of the undergraduate curriculum. Course credit for the teaching apprenticeship is earned by enrolling in CHEM 500. Excellence in teaching is stressed, and the department provides a thorough training program covering the fundamentals of teaching as well as other useful information and techniques for effective instruction. Students are required to enroll in the CHEM 509 teaching training seminar in their first quarter as a chemistry/biochemistry graduate TA at UC San Diego. Further training is provided by the campus's Center for Teaching Development. Faculty and the students taught evaluate the performance of teaching assistants every quarter and awards are bestowed annually for outstanding performance as a teaching assistant.

Language Requirement

Students whose native language is not English must demonstrate a mastery of English adequate to complete the teaching requirement. Deficiencies must be remedied by the end of the first year of academic residency. For native English speakers, there is no foreign language requirement.

Time Limits

In accordance with UC San Diego policy, students must advance to candidacy by the end of four years. Total university support cannot exceed six and one-third years. Total registered time at UC San Diego cannot exceed seven and one-third years.

Seminars

Seminars by researchers from other universities, national laboratories, and industry are another important aspect of the graduate curriculum. Seminars are presented weekly in biochemistry, inorganic, organic, and physical chemistry. Department colloquia are given on topics of general interest to the department. Seminars are also sponsored by many other departments and institutes, both on the UC San Diego campus and at our neighbor institutions.

Financial Support

The department supports all first-year students in good academic standing from a variety of sources, including teaching and research assistantships, training grants, fellowships, and awards. A stipend is paid in addition to fees and, if applicable, tuition. Continuing students who do not have fellowships or awards are normally supported on training grants or on research assistantships by their thesis advisers.

Admissions

The department seeks bright, motivated doctoral students and welcomes all such applications. To make admissions decisions, the department considers an applicant's statement of purpose and research interests, GRE scores on the general test plus either the advanced chemistry or advanced biochemistry test, undergraduate record, quality of the undergraduate university, letters of recommendation, and research experience and publications. Applicants whose native language is not English must also submit TOEFL scores; TWE scores are strongly recommended. Admission to the doctoral program is for fall quarter.

PhD in Chemistry with Specialization in Computational Science

Since fall 2007, the UC San Diego campus has offered a comprehensive PhD specialization in Computational Science that is available to doctoral candidates in participating science, mathematics, and engineering departments. This PhD specialization is designed to allow students to obtain training in their chosen field of science, mathematics, or engineering along with a specialization in computational science integrated into their graduate studies. Prospective students must apply and be admitted into the PhD program in Chemistry/Biochemistry described previously.

PhD in Chemistry and Biochemistry with Specialization in Multiscale Biology

Since fall 2009, the UC San Diego campus has offered a PhD specialization in Multiscale Biology that is available to doctoral candidates in participating programs that span four divisions: Biological Sciences, Physical Sciences, Jacobs School of Engineering, and Health Sciences. This PhD specialization is designed to allow students to obtain training in their chosen field within the biological sciences, physical sciences, engineering, and health sciences along with training in integrative and quantitative analysis across multiple scales of biological organization from molecule to organism to health and disease. It educates a new cadre of PhD scientists to undertake interdisciplinary work at the interfaces between the biological, medical, physical, and engineering sciences.

PhD in Chemistry with Specialization in Quantitative Biology

A specialization in Quantitative Biology spanning four divisions—Biological Sciences, Physical Sciences, Jacobs School of Engineering, and Health Sciences—is available to doctoral candidates in the Department of Chemistry and Biochemistry. This PhD specialization is designed to train students to develop and apply quantitative theoretical and experimental approaches to studying fundamental principles of living systems. The core of this specialization

comprises of one year of theory courses and one year of lab courses, with most of these courses substitutable for chemistry elective courses. For more information students should contact the Student Affairs Office.

PhD in Chemistry with Specialization in Interdisciplinary Environmental Research

A graduate specialization in Interdisciplinary Environmental Research (PIER) is available for select doctoral students in chemistry. PIER students seek solutions to today's environmental challenges.

The PhD specialization is designed to allow students to obtain standard training in their chosen field and an opportunity to interact with peers in different disciplines throughout the duration of their PhD projects. Such communication across disciplines is key to fostering a capacity for interdisciplinary "language" skills and conceptual flexibility.

Specialization Requirements

- Complete all course work, dissertation, and other requirements of the chemistry PhD
- 16-unit interdisciplinary boot camp (Summer Session, SIO 295S-295LS)
- 8 units from a secondary field (outside the home department)
- 6 units (3 quarters) Interdisciplinary Environmental Research Forum (SIO 296)
- At least one chapter of the dissertation will be broadly related to environmental research and will be interdisciplinary in nature.

Application Requirements

We advise students to begin PIER in their third year upon completion of core chemistry course requirements.

The following items should be combined into a single PDF document and submitted to cmbc@ucsd.edu.

- Student's CV
- Half-page abstract of proposed thesis work
- Up to one-page statement of student's interest in interdisciplinary environmental research including career goals.
- Nomination letter from adviser acknowledging student's academic ability and interdisciplinary environmental interest. The letter must include a commitment for summer stipend support.

Admission to the Specialization

Students are admitted into the chemistry doctoral program. Admission to PIER is a competitive process with six to eight students granted admission each year from across ten participating UC San Diego departments. Selected applicants will have the opportunity to enroll in the specialization.

PIER Fellowships

When funding is available, all applicants will be considered for one year of PIER fellowship support.

COPY FROM 2020–21 UC SAN DIEGO GENERAL CATALOG

Interim Update (February 3, 2021)

Chemistry and Biochemistry (graduate curriculum)

Biochemistry and Molecular Biophysics Program (BIOC)

Doctoral Program

The goal of the PhD in Biochemistry and Molecular Biophysics is to prepare students for careers in science by expanding their knowledge of biochemistry, molecular biophysics, and structural biology while developing their ability for critical analysis, creativity, and independent study. The program is designed to encourage initiative and to stimulate enjoyment and development of the student's area of research expertise as well as the broader aspects of scientific inquiry and enlightenment.

Master's Degree: Plan II (Comprehensive Exam)

For students in the Biochemistry and Molecular Biophysics PhD program, they may earn a Plan II MS degree in Biochemistry and Molecular Biophysics on the way to the PhD. The Departmental Examination (written and oral components) fulfill the comprehensive examination requirement for the MS degree. See above under "Chemistry Program" for full degree requirements.

Research

Students choose their research concentration in broad areas of biochemistry, molecular biophysics, and structural biology. Opportunities for scientific discovery are also abundant through the department's extensive collaborations with investigators in other physical, biological, health, and engineering sciences. This includes on-campus collaborations, for example, with faculty in the Biological Sciences, School of Medicine, School of Pharmacy and Pharmaceutical Sciences, and Physics. There are off-campus interactions with scientists at nearby research facilities such as the Salk Institute and The Scripps Research Institute. State-of-the-art facilities and equipment support all the research programs. The department's Industrial Relations Program interfaces with national and local chemical, biotechnology, and pharmaceutical industries to encourage technology transfer and to assist postgraduates interested in industrial careers.

Research Adviser

A first-year faculty adviser guides students until a research adviser is chosen. Most of a student's efforts in graduate school are directed toward research for the doctoral dissertation, and selection of a research adviser is of utmost importance. To assist students with this critical decision, all biochemistry and molecular biophysics faculty describe their current research activities early in the fall quarter. Students then rotate in laboratories or consult with faculty to discuss research opportunities. Although students have until the end of the first year to join a laboratory, most start their research by midyear.

Placement Examinations and Course Work

Entering students take written placement examinations in general chemistry and biochemistry. The purposes of these exams are to assist with advising and to assure that students have the breadth and level of competence needed for graduate studies. Deficiencies must be remedied in the first year.

First-year students typically take six graduate courses based on the results of their placement examinations, their research programs, and their specialized interests. CHEM 250, CHEM 509, and CHEM 500 are required. Undergraduate courses and courses offered through other departments may also be taken, depending on the student's

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research area. By the second year, the emphasis is on thesis research, and a lighter load of courses is taken, although participation in seminars and informal study groups continues.

Departmental Examination

See above under "Chemistry Program".

Qualifying Examination

See above under "Chemistry Program".

Dissertation

See above under "Chemistry Program".

Teaching

See above under "Chemistry Program".

Language Requirement

See above under "Chemistry Program".

Time Limits

See above under "Chemistry Program".

Seminars

See above under "Chemistry Program".

Financial Support

See above under "Chemistry Program".

Admissions

See above under "Chemistry Program".

Joint Doctoral Program with San Diego State University

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Interim Update (February 3, 2021)

Chemistry and Biochemistry (graduate curriculum)

The Department of Chemistry and Biochemistry at UC San Diego and the Department of Chemistry at San Diego State University offer a joint program of graduate study leading to the PhD in chemistry. More information is available in the current edition of the Bulletin of the Graduate Division of San Diego State University.