TRAINING PROGRAM PLAN

Training Program

This proposal requests support to further establish our Graduate Training Program in Quantitative and Chemical Biology (QCB TP) at Indiana University, which is now entering its ninth year. We outline a topical interdepartmental program at the *Chemistry-Biology Interface (CBI)* on the Bloomington campus that was initiated in Fall 2010 with significant institutional support and won a first cycle of federal support from 2014-2019. Our program involves a highly collaborative group of 34 trainers drawn from the Departments of Chemistry, Biology, and Physics, and three interdepartmental graduate programs, including Biochemistry and Neuroscience in the College of Arts and Sciences, and in Cell, Molecular and Cancer Biology (CMCB) at the Indiana University School of Medicine-Bloomington (**Table 1**).

As described in greater detail below, our QCB graduate training program is unique in a number of ways. We have strived to develop a training culture that provides cutting-edge, interdisciplinary research training opportunities to trainees in a way that does not abandon, but rather enhances, disciplinary depth. Further, we have done so in an environment that features seamless integration of training in *both* chemical and physical biology. This orientation of our QCB program provides a platform in which to educate students as broadly as possible, spanning biomedical science disciplines and approaches, while leveraging deep, disciplinary training that largely occurs in specific departments and programs. This scientific training is complemented with a number of didactic and non-didactic opportunities to develop the soft-skills necessary to be successful scientists in the modern era. Indeed, major advances in biomedical science will be ever more dependent on scientists trained in this way, to understand *both* the chemical and physical logic of biological systems in quantitative terms as well as to have the requisite presentation and communication skills to thrive in a multitude of scientific careers.

I. Rationale, Training Objectives and Overall Training Program

I.A. Rationale

Research and training ecosystem. Indiana University has significant historical strengths in the chemical and biological sciences dating back to mid-century and earlier. The Department of Chemistry, as host department for the QCB TP, has historical strengths in organic and physical chemistry, and is well regarded for its highly-ranked program in analytical chemistry. Major fundamental discoveries in ion mobility mass spectrometry, atomic spectroscopy, electrochemistry, capillary electrophoresis and glycomics have occurred here. A major ongoing objective of our training program is to integrate these strengths in analytical chemistry and instrumentation development with other historical strengths and recent institutional developments, through training program-specific didactic courses and research opportunities that provide comprehensive interdisciplinary training in chemical and physical biology.

An evolving Department of Chemistry, where over half of the faculty, including twelve of the 17 QCB TP preceptors based in Chemistry (**Table 2**), have arrived here on or after 2007, continues to catalyze collaborative research on campus. The impact of a strong materials chemistry faculty and the addition of significant physical facilities in the areas of nanoscience, chemical synthesis, chemical biology, biophysical chemistry and structural biology continue to enhance the landscape for interdisciplinary training that this program seeks to exploit. Other major institutional changes are driving the continued development and evolution of our training program. Indiana University has added significant new state-of-the-art research space on the campus, with the construction of Simon Hall (2007), the first multidisciplinary building ever built on the Bloomington campus, and Multidisciplinary Science Building II (MSBII; 2013) a few blocks north. Both buildings feature “open lab” concepts with investigators drawn from multiple departments and units working side-by-side, with significant common social space that promotes collaboration, while hosting core research laboratories that serve the needs of faculty and student trainees alike (see **Facilities and Environment**). Simon Hall is the home of the Department of Molecular and Cellular Biochemistry (MCB), and sits in the yard between the Medical Sciences CMCB faculty and the Departments of Chemistry, Physics and Biology, while housing investigators from all six participating QCB TP trainer departments and programs (**Table 1**). Simon Hall and MSBII have strongly catalyzed interdisciplinary and collaborative research on which our program seeks to expand, specifically with the addition of four new trainers associated with the Program in Neuroscience, whose laboratory space is in MSBII (**Tables 1, 2**). Major

animal and whole animal imaging facilities are housed in MSBII. The addition of these trainers, coupled with new trainer appointments in MCB and in Chemistry, will catalyze the development of what we anticipate will be a new, highly dynamic "molecular signaling" research node as part of our QCB training program (**Section VI**). Our campus also boasts a rich history in organismal and developmental biology and genetics (Salvadore Luria and the *Paramecium* biologist Tracey Sonneborn were faculty members here) and more recent strengths in cancer biology and virus assembly. Our training program continues to drive extensive collaborations among biologists, chemists and physicists in solving problems in developmental biology and infectious disease (**Section VI**).

Finally, a number of other major institutional developments, enabled in many ways by the success of both Simon Hall and MSBII to catalyze interdisciplinary science, continue to transform graduate education on the Bloomington campus. One was the formal creation of a Department of Molecular and Cellular Biochemistry (MCB) in 2009. The growth of MCB, now chaired by QCB TP Steering Committee member Steve Bell, has allowed our campus to significantly enlarge its research footprint in DNA metabolism and cancer biology; four members of MCB, including two Assistant Professors, are trainers on this program (**Table 2**). This led to a recent (2018) comprehensive and topical redesign of how we teach students in the Biochemistry Ph.D. program that the QCB training program is poised to embrace, in much the same way that the establishment and growth of two new interdepartmental graduate programs, in Cell, Molecular and Cancer Biology (CMCB; 2016) and Neuroscience (2013) are expected to do (**Tables 1, 2**).

A second major institutional development is the Grand Challenges Program, a Presidential-level research initiative that seeks to build bridges across traditional disciplines to solve a number of large, complex problems that face our society. Significant numbers of QCB TP trainers are associated with the first funded Grand Challenge, the Precision Health Initiative (PHI, 2016-2021). The PHI is a $120M faculty hiring and infrastructure project that spans the IU School of Medicine in Indianapolis and the IU Bloomington campuses, with the goal to broadly employ precision medicine to accelerate the pace of discovery of new therapeutics that target triple negative breast cancer, multiple myeloma and devastating childhood and neurological diseases. The Chemical Biology Pillar of the PHI provides significant start-up funding for new faculty and QCB preceptors in Chemistry, Biology and MCB and resources to acquire new instrumentation in mass spectrometry and structural biology that are integral to the research programs of these faculty. QCB TP Program Director (PD) Giedroc is a member of the PHI Steering Committee, thus ensuring that these substantial resources, alongside QCB training faculty in CMCB and Neuroscience programs (**Table 2**), can be leveraged to significantly enhance the QCB trainee research experience in therapeutic target identification and characterization, and drug discovery.

Instrumentation. QCB trainers play important administrative leadership roles in a host of core research laboratories that support the research projects of QCB trainees, with significant enhancements coming online over the last five years (see **Facilities and Environment**). In addition, these core laboratories are expertly managed by non-tenure track Ph.D.-level Scientists, most on 12-month college-budgeted appointments, allowing us to keep research costs to a minimum. The mass spectrometry (MS) capabilities are organized under the Waters Center of Excellence, so-designated in honor of QCP TP preceptor and Distinguished Professor David Clemmer, in recognition of his significant contributions to ion mobility mass spectrometry. The Waters Center hosts the Laboratory for Biological Mass Spectrometry (LBMS) under the direction of Associate Scientist Jon Trinidad, which provides significant analytical expertise and instrumentation for global proteomics and post-translational modification studies. The LBMS works hand-in-hand with the Mass Spectrometry Facility, which provides GC-MS and MS-MS support for high mass accuracy metabolomics studies. The Nanoscale Characterization Facility (NCF) enables research in materials and nanobiology and hosts a number of atomic force microscopes and a Focused Ion Beam (FIB) instrument, used for high resolution cryo-electron microscopy, image reconstruction and electron cryo-tomography, allowing trainees to investigate macromolecular assemblies, *e.g.,* viruses, to organelles and cells, using state-of-the-art tools. The closely associated Electron Microscopy Center (EMC) provides cryo-electron microscopy in the form of a 300 keV cryo-TEM equipped with a direct electron detection camera and a new 1400 TEM in the Department of Biology. The EMC enjoys strong, recurring support as a College of Arts and Sciences Research Center and will add an FEI Glacios 200 kV dedicated cryo-TEM, slated for installation in early 2019 and shared by QCB trainers in Chemistry, Biology and MCB. These departments have partnered to provide four Scientists who operate and maintain

instrumentation associated with the NCF and the EMC. Other structural biology instrumentation and associated staff expertise in NMR spectroscopy and x-ray crystallography include 600 and 800 MHz Agilent NMR spectrometers (with the 600 now converted to a Bruker instrument, June 2018) both equipped with cryoprobe systems, and significant x-ray crystallographic and robotics capabilities associated with the Macromolecular Crystallography Facility in Simon Hall. The Light Microscopy Imaging Center (LMIC), supported by the Office of the Vice Provost for Research and by the College of Arts and Sciences, houses an impressive collection of instrumentation for all types of light microscopy, including a new OMX 3D-structured illumination super-resolution imaging system, which is ideally suited for imaging of bacterial cells, a particular programmatic strength on campus. These facilities, coupled with significant MRI-based and other animal imaging modalities available in MSBII make the Bloomington campus an outstanding venue in which to implement cross-disciplinary graduate training in QCB.

Support for Graduate Education. Indiana University was founded in 1820 and since awarding its first Ph.D. in 1882 now offers doctorates in 85 different disciplines on the Bloomington campus. The administrative home of five of the six participating departments and programs in this proposed training program (Biology, Chemistry, Molecular and Cellular Biochemistry, the Program in Neuroscience and Physics) is the College of Arts and Sciences. The administrative structure of the College features an Executive Dean, and Executive Associate Dean and three Associate Deans (AD), including one AD in Natural and Mathematical Sciences. Another AD, Michael McGinnis, serves as the AD for Graduate Education. Dr. McGinnis is and will continue to serve as a member of the internal advisory committee for the QCB TP (**Section III.A**). This administrative organization allows the College to more effectively engage departments and the University Graduate School to target high achieving students from STIM (Science, Technology, Informatics and Mathematics) disciplines and other underrepresented groups for institutional fellowship support of students who show an interest in the QCB training program and other affiliated departmental programs that feed into the program. A proactive Office of the Vice President for Diversity, Equity, and Multicultural Affairs (OVPDEMA), led by Dr. James Wimbush, is strongly integrated into the University Graduate School (UGS), as the Dean of the UGS is also Dr. Wimbush. This creates a nimble administrative structure that seeks to drive QCB trainee diversity (see **Institutional Letters of Support**), while sponsoring workshops on the importance of prioritizing the recruitment and retention of highly qualified trainees from underrepresented groups (see **Recruitment Plan**). Indiana University is strongly committed to these efforts, and as an institutional member of the National Center for Faculty Development and Diversity (NCFDD), provides additional resources to recruit and retain diverse faculty and graduate students, with expertise in mentoring and skill building, both important for future success. Additional resources available to graduate trainees to improve their mentoring and writing skills are available in the Graduate Mentoring Center of the University Graduate School (see **Retention Plan**).

Snapshot of the Training Environments of the QCB TP Participating Departments. **Table 1** reveals that the six departments and programs participating in the QCB Training Program collectively host 191 unique faculty who are currently training 558 graduate students and 104 postdoctoral scientists. The 34 QCB preceptors are responsible for training 168 (30% of total) and 29 (28%) graduate and postdoctoral trainees, respectively, and thus comprise a core component of this collective graduate training mission. Of the 168 total graduate trainees in QCB trainer groups, 117 (70%) are eligible for support by this training program. **Table 2** lists the 34 QCB TP preceptors with their primary (and secondary) departmental and programmatic affiliations, a summary of their research interests and graduate and post-graduate training records. These data reveal a tremendous breadth of expertise in chemical and physical biology, and a highly-experienced training faculty, with 226 total graduate students having completed doctoral training under their tutelage in the last 10 years (6.6 per QCB trainer), with 86% continuing in research-intensive or related careers. The trainer group also boasts significant postdoctoral training experience, with 115 postdoctoral scientists having completed their training, and 94% continuing in research careers.

Table 3 shows that there are five existing T32 training grant programs on the Bloomington campus including this NIGMS-funded CBI program in QCB. Three of the remaining four training programs are based in the Department of Psychological and Brain Sciences (PBS), home to the Program in Neuroscience, and are either strongly thematic, specifically oriented toward drug abuse or post-natal behavioral development, or clinical-translational in nature, and involve only QCB trainers Mackie, Lu and Hohmann, all based in Neuroscience. A fourth training program, focused on behavioral and evolutionary

aspects of sex, gender and reproduction, is based in the Department of Biology, with no faculty overlap with this CBI program. *Our training program in Quantitative and Chemical Biology (QCB) is the only one on the Bloomington campus that provides broad-based, interdisciplinary molecular-level predoctoral training that is currently funded by NIGMS*. **Table 4** lists all single PI/PD and MPI external research and contract grant support of the 34 QCB preceptors, which exceeds $5.0M in the current year in direct costs, or nearly $150,000 per trainer, and includes 42 unique single PI/PD or MPI NIH grants.

1.B. Training Mission

The overall training mission of the QCB Training Program is *to transform graduate education in the molecular sciences on the Bloomington campus*, by facilitating interdisciplinary and collaborative research training in the chemical, physical and biological sciences to address important problems in biology and medicine. The program does this by providing a core didactic and extracurricular experience in chemical and physical biology that seamlessly integrates quantitative and rigorous training into traditional disciplines defined by the six Ph.D.-granting graduate programs that nominate trainees for support by the program. This creates a highly diverse trainee cohort from a wide range of disciplinary cultures and scientific backgrounds that organically enhances broad, scientific literacy across the group, while simultaneously providing for the highest quality mentored research experience. Thus, an overriding objective of our program is to move trainees beyond their disciplinary "comfort zones" *at the right time in their graduate careers*, whether it be the descriptive realm of biology or the rigor of the physical and chemical sciences, to a common intersection that coalesces around solutions to biologically important problems.

Meeting the following four objectives will allow us to achieve our goal of sustaining trainee interest in working toward meaningful, collaborative and research-intensive careers by reaching attrition (≤10%), time-to-degree (5.0 years) and trainee cohort diversity (≥20%) metrics that *exceed* those of the component participating graduate programs from which the training program draws.

1.C. Objectives

Objective 1. *Create a transformative graduate training program that is unique, strongly value-added and embraced by the upper administration.* The QCB TP is readily distinguished from other graduate programs on campus in that it formalizes high impact, interdisciplinary and collaborative training opportunities for trainees from one of six distinct academic backgrounds. Our six graduate feeder programs that support the QCB TP are by definition, discipline-specific; as such our program complements these more traditional graduate programs. In satisfying the curricular requirements of the training program which includes six (6) credits of QCB TP core and elective courses (**Section I.D**), trainees earn a graduate school-approved minor in Chemical and Physical Biology (CPB), superimposed on a discipline-specific Ph.D. degree. Indiana University and in particular, the College of Arts and Sciences, is strongly supportive of this type of graduate training, as evidenced by the significant numbers of matching slots provided by the College of Arts and Sciences and the University Graduate School (see **Institutional Letters of Support**).

Objective 2. *Catalyze collaboration, quantitative reasoning and cross-disciplinary training among trainees from a variety of scientific backgrounds.* The Bloomington campus provides a highly collegial and collaborative research environment that is strongly facilitated by the physical proximity of QCB TP trainer laboratories (see **Facilities and Environment**). As described in more detail below, the QCB TP Steering Committee, in consultation with our Internal Advisory Committee (**Section III**), recently (2017-2018) updated the QCB training faculty by removing inactive trainers and adding new trainers, which adds considerably to our biological expertise in cancer biology, molecular neuroscience and signaling, and membrane protein structure and proteostasis, while strategically pairing outstanding new hires with established investigators across four departments and programs (**Section VI**). These new trainers not only enhance the QCB trainer group's ability to apply cutting-edge chemical and physical tools to solve a wider array of biological problems, but also provide new opportunities to bring an emphasis on scientific reasoning, research design and methods and quantitative analysis to a wider range of trainees from diverse scientific backgrounds. These enhancements to the training environment are integrated into QCB Journal Club (**Section I.D**) (see **Plan for Instruction in Methods for Enhancing Reproducibility**). QCB Journal Club also hosts an eight contact-hour intensive course in the Responsible Conduct of Research (RCR), thus elevating instruction in research responsibility, integrity and reproducibility to that of a didactic

class requirement of the training program (see **Plan for the Instruction in the Responsible Conduct of Research**).

Objective 3. *Provide value-added extracurricular activities that expose trainees to a wide range of research areas, while teaching essential communication and professional leadership skills.* We have developed a number of innovative extracurricular features that collectively provide opportunities beyond QCB Journal Club for students from the chemical, physical and biological sciences to interact and learn together (**Section I.D**). These include the annual Watanabe Symposium in Chemical Biology, which brings 4-5 internationally renowned scientists in chemical and physical biology to Bloomington each Fall, while also featuring a poster session that highlights the research activities of trainees, students and postdocs in QCB TP preceptor laboratories. Two other innovative events are QCB Evenings and QCB-trainee Invited Seminar Series, which are now entirely trainee-run, organized and publicized on social media (@iuqcb) by our two QCB ambassadors. QCB ambassadors are current QCB trainees appointed by the Steering Committee for one-year terms (**Section III.A**) and serve as liaisons between the trainee cohort and program leadership and represent a deliberate strategy to establish trainee ownership of their training program. Both QCB Evenings and QCB-trainee Invited Seminar Series provide significant leadership opportunities for trainees. These activities, in addition to the Watanabe Symposium, also provide significant one-on-one networking opportunities, while exposing trainees to the breadth of careers and biomedical research topics integral to our molecular understanding of human health, physiology and disease.

Objective 4. *Develop a diverse pool of well-trained scientists who are prepared for a wide range of career choices.* Satisfying this objective derives from our deliberate efforts to diversify the trainee cohort, not only in terms of the racial, ethnic, socioeconomic and disabilities status, but also in terms of disciplinary field of study (**Section I.D**). We then take this diverse pool of students and provide them opportunities to perform research between traditional disciplines, while exposing them to a very wide range of research interests that collectively characterize the QCB trainee cohort. Superimposed on this are significant career development opportunities built into the QCB training program itself, as well as additional career activities, including the IU Career Development Symposium, sponsored by the Department of Chemistry, most recently in partnership with the Walter Center for Career Achievement in the College of Arts and Sciences. This event was initiated in 2015 by Chemistry graduate students and has occurred annually since then; in the upcoming project period, our QCB trainee cohort proposes to add panelists and participants who can speak to the breadth of careers available to QCB TP students more broadly (**Section II**).

I.D. Overall Training Plan

Didactic Training/Core Curriculum. The QCB training program is designed to attract students with undergraduate degrees in chemistry, biology, biochemistry, biophysics, neuroscience or physics who seek to develop and utilize leading-edge quantitative and chemical approaches to explore biological problems important in human health and disease. The *overriding principle* that governs development and evolution of the curriculum is that it is value-added on a traditional core disciplinary program of study. We establish the program in this way since the program itself is not degree-granting. Prospective trainees are admitted to Graduate School in one of three degree-granting department-based programs, in Chemistry, Biology, and Physics, or in one of three interdepartmental programs, in Biochemistry (administratively housed in MCB), Cell, Molecular and Cancer Biology (CMCB, housed in the Bloomington campus of the IU School of Medicine), or the Program in Neuroscience (housed in the Department of Psychology and Brain Sciences, PBS). In Chemistry, students typically begin their formal classwork in one of six subdisciplines in the Fall of year 1, *e.g.,* analytical chemistry, chemical biology, inorganic chemistry, materials chemistry, organic chemistry or physical chemistry, and ultimately earn their degrees specializing in that subdiscipline. In addition, Physics

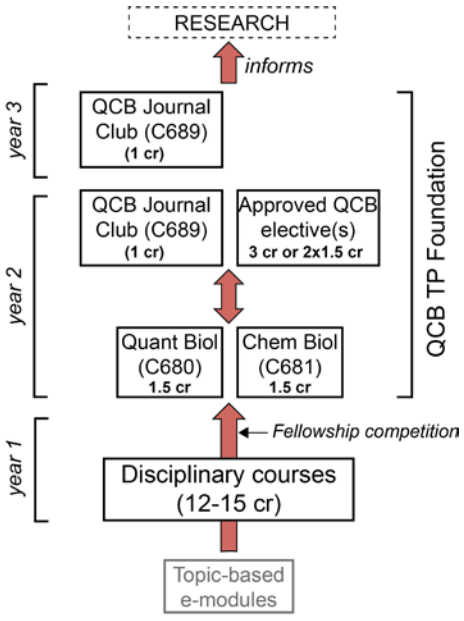

Fig. 1. The QCB TP construct.

has established a biophysics track as an option to a traditional degree program in Physics. Although these disciplinary programs encompass anywhere from 12-27 credits, 6 credits of elective courses are always required and are used to satisfy a University requirement for a declared minor. As such, the Graduate School has approved a minor in Chemical and Physical Biology (CPB), which is satisfied by the six core credits of the core curriculum of QCB TP (***Fig. 1***). CPB also doubles as one of three "minor" tracks in the Biochemistry Ph.D. program, and thus serves both purposes. This 6-credit core is programmatically supplemented by two semesters of QCB Journal Club (CHEM C689) in the Fall of their second and third years, and continuous participation in other extracurricular activities associated with the program.

The proposed QCB TP construct (***Fig. 1*****)** (see ***Table C*** below for sample curricula) emphasizes the centrality of QCB TP requirements on what is otherwise a standard, distinct disciplinary focus. The two core didactic courses (CHEM C680 and CHEM C681) are designed to arm the student with a fundamental "language" or "tool-box" of chemical and physical biology that enables him/her to develop dissertation projects in interdisciplinary areas as a result of interacting with colleagues in other areas of chemistry, physics or biology. This is a *central and unique aspect of the proposed program* and is motivated by the fact that the often-forced separation of chemistry, sometimes defined as the making and breaking of bonds, from physical principles and measurement science, is not in our trainee's best interests. For example, advances in natural products synthesis and discovery will increasingly rely on innovations in separations science and mass spectrometry, just like enhancements in single molecule methods and macromolecular dynamics are critically dependent on protein and nucleic acid labeling strategies, advances in surface science, and innovations in optical spectroscopy or spin physics. These are just two of many examples that highlight the importance of training the next generation of scientists broadly across the chemistry-biology interface. QCB Journal Club coupled with an additional three credits of approved QCB TP electives (discussed below) reinforces and expands the concepts learned in these two core courses.

Two didactic 1.5 cr (8 week) courses and a program-specific journal club were developed specifically for this training program and are discussed in more detail below. They are Introduction to Quantitative Biology and Measurement (CHEM C680), Introduction to Chemical Biology I (CHEM C681) and QCB Journal Club (CHEM C689). Both C680 and the C681 have each been taught four times during the current funding cycle; note that CHEM C681 is actually a first course of a full semester (3 cr) sequence, which is followed by CHEM C682, Introduction to Chemical Biology II. As shown in the QCB TP construct (***Fig. 1***), C681 is a 1.5 cr core course in the QCP TP *for all students*, with C682 left as an elective (**Section I.D.e**).

Our experience in developing C680, C681 and C689 is that students from diverse disciplines often have varying gaps in past training that need to be bridged in order to maximize the pedagogical impact of our core classes. No single class can possibly serve such a function without the danger of boring some students and losing others depending on the area discussed. However, smaller teaching modules on demand could serve such a function. *Therefore, we propose to continue a key component of the QCB TP moving forward, which is the development of small topic-based e-learning modules with incorporated learning assessments created entirely by trainees with training faculty input.* The goals for the development of these online training units are 1) to solidify student knowledge of scientific concepts and content and increase trainee communication skills by having them teach others; 2) to develop trainee skills in communicating in and working in multidisciplinary teams centered around a common goal—specifically a coauthored e-learning module; 3) to build a repository of mini-classes on topics related to quantitative and chemical biology and its foundations, serving not only trainees but also the broader scientific community on campus; and 4) to allow trainees and other scientists a facile method to easily learn (or brush up on) the fundamentals of techniques, experiments, and knowledge in order to form a shared community centered on a common language. During the current award cycle, students have completed a number of these learning assist e-modules under the direction of co-Director Pohl as part of CHEM C681, and now include terpene biosynthesis, high-throughput screening methods, molecular imaging, natural products and biological targets, and oligosaccharide synthesis.

I.D.a. Topic-based e-learning modules. Based on the success of these existing e-modules to meet the needs of diverse students, and follow-up discussions from currently supported QCB trainees, these initially developed e-modules will be supplemented in the upcoming project period by those focused more heavily on fundamental concepts in biology, chemistry and physics, for use as background material, and

a number designed to further reinforce concepts in rigor and reproducibility. Proposed training e-modules to be developed are 1) basic methods for the statistical analysis of data from biological replicates (*p*-values, various tests of significance, variance, propagation of errors, etc.); 2) general cell biology and biochemistry basics; 3) organic chemical reactions commonly used in chemical biology; 4) basic protein and nucleic acid structure and quantitative and qualitative characterization techniques; and 5) the basics of biological mass spectrometry. *Currently or previously supported trainees* who feel very knowledgeable in a particular area will work in teams of 2-4 students in C681 to develop these modules over the course of the next 2-3 years. This group will reach a consensus on the key concepts that the learning module will need to include as well as the sequence of content to create an ≈hour-long module. The task to generate specific PowerPoint slides will then be divided among the team members; once the module is created, team members will then evaluate it by providing a series of problems or questions to other groups of students not involved in preparing the module, to assess their understanding. Other trainee groups will develop new modules that will be of interest to the group. The campus also has a strong instructional technology group at the Center for Innovative Teaching and Learning (CITL) who have been critical in providing insights into the development of online learning methods and who are readily available for consultation.

I.D.b. Introduction to Chemical Biology (C681/C682; N. Pohl or M. VanNieuwenhze, instructors). C681, Introduction to Chemical Biology I and C682, Introduction to Chemical Biology II, are sequential 1.5 cr (8 week) courses (see **Appendix B.1** for C681/C682 syllabi for Spring 2017 and Spring 2018 taught by two different instructors*). C681* is more of an applications in chemical biology course and covers microarray technology, protein labeling, chemical genetics, small molecule interactions with proteins/DNA, modulation of protein-protein interactions, RNA aptamers and molecular evolution. *C682*, on the other hand, has a stronger synthetic focus, incorporating basic elements of chemical biology including peptide synthesis and chemical ligation methods, oligonucleotide and oligosaccharide synthesis, diversity oriented synthesis and combinatorial libraries, bioorthogonal reactions, high throughput screening methods and their use in drug discovery, and secondary metabolism. We are fortunate in that two different instructors now have significant experience with C681 (from Spring 2015-2018), and both have designed this course to be readily accessible to trainees *not* specializing in organic chemistry, *e.g.,* those currently in physical or analytical chemistry, physics, biology or biochemistry, and requires only a solid undergraduate course in organic chemistry. New trainees from the neuroscience program should likewise have no particular difficulties with this course. As outlined above, topics-based e-modules to be developed by trainees should help to fill in any remaining knowledge gaps that students encounter (***Fig. 1)***.

I.D.c. Introduction to Quantitative Biology and Measurement (C680, 1.5 cr; B. Dragnea or D. Giedroc, instructors). This second core course of the QCB TP curriculum is CHEM C680 (see **Appendix B.2** for with a recent syllabus and schedule of classes, for Fall 2017). This course, most recently taught by PD Giedroc (Fall 2016, Fall 2017) is a hybrid course that incorporates strong elements of quantitative data acquisition, analysis and interpretation presented in the context of an introduction to the "tools of physical biology." The course is divided into four sections of approximately equal duration. They include 1) equilibrium binding; 2) single-molecule science; 3) biological mass spectrometry, and 4) electron microscopy, all topics with which QCB trainees should have some familiarity. In addition to Dr. Giedroc, two staff Research Scientists, Dr. Jon Karty, Director of the Mass Spectrometry Facility (MSF) and Dr. Joe Wang, of the EM Center, teach the sections on mass spectrometry and (cryo)-electron microscopy. C680 features the foundational concepts of energy levels and macromolecular equilibria, binding polynomials and partition functions that are developed alongside a comprehensive discussion of timescales and conformational dynamics, and how various dynamics might be probed by which approaches. This is followed by a discussion of quantitative proteomic and metabolomic profiling, including post-translational modifications (PTMs), and modern electron microscopy, from negative strain to cryo-TEM and new direct electron detection methods to single particle reconstruction. CHEM C680 therefore has two complementary objectives. The first is to introduce students to the cutting-edge instrumentation available for use in their dissertation research, with a focus on capabilities and measurement (data analysis, sensitivity, resolution, quantitative strengths and limitations of each approach) and comparatively less so on the theory of the measurement. This prepares students who take this course to take an advanced elective(s) that better covers the theoretical underpinnings and applications of each approach in much more depth (see ***Table C***, below), *i.e.,* much like C681 is a "feeder" course for advanced electives in

chemical biology and biocatalysis, C680 becomes a feeder course for advanced electives on the biophysics side of the QCB Training Program. *As can be seen, this course directly develops the concepts of rigor and reproducibility for trainees in a very concrete way, from a variety of perspectives* (see **Plan for Instruction in Methods for Enhancing Reproducibility**). The second equally important objective is that this course allows us to cover topical research findings and new approaches in QCB Journal Club (C689), thus enhancing the value of the discussion as an essential part of this course, led by the students.

Table A. Discussion Topics covered in QCB Journal Club (CHEM C689), 2014-2017

Semester	Topic	Instructor
Fall 2014	*Allostery and the Conformational Ensemble*	**Giedroc**[1]
	Mechanochemistry of DNA replication	Bell
	Metals in Medicine/Water Oxidation	Zaleski
	Mechanisms of Peptidoglycan Hydrolysis	Winkler
Fall 2015	*Directed Protein Evolution*	Bochman[2]
	Employing Electron Microscopy to Learn Biology	Mukhopadhyay
	Bioengineering and the Immune Response	Douglas
	Protein Kinase Profiling Strategies	Cook
Fall 2016	***Ethics and RCR I**: Two 2-hr sessions*[3]	**Dann**[1]
	Advances in Genome Editing	Hollenhorst
	Functional Versatility in the ABC Transporter Superfamily	Oakley
	***Ethics and RCR II**: Two 2-hr sessions*[3]	**Dann**
	Application of Small Molecule Probes to Study Peptidoglycan Biosynthesis and Dynamics	VanNieuwenhze
Fall 2017	***Ethics and RCR I**: Two 2-hr sessions*[3]	**Dann**
	Chemical Biology and Drug Discovery	Cook
	Membrane Protein Quality Control	Schlebach
	***Ethics and RCR II**: Two 2-hr sessions*[3]	**Dann**
	Physical Perspectives on Allostery	Setayeshgar
	Advanced Live Cell High Resolution Imaging	Shaw

[1]Course coordinator in bold. [2]Dr. Giedroc was course coordinator. [3]See **Plan for Instruction in the Responsible Conduct of Research** for additional details.

d. QCB Journal Club (C689) (1 cr, twice). QCB Journal Club is a 1 cr student seminar-based course and is designed to bring together graduate trainees, postdoctoral associates and QCB TP preceptors to discuss recent literature in the broad, interdisciplinary area of Quantitative and Chemical Biology. Effective Fall 2014, this course was offered in the Fall semester only, which has allowed us to maintain the intensity and broad interdisciplinary participation by both faculty and trainees alike. C689 provides coverage of three to four separate topics to be decided upon by each of three to four participating faculty instructors. Each topic or section of the course encompasses 3-4 student-led presentations (***Table A***). Prior to the first presentation in a series, the faculty instructor provides an overview of the general topic highlighting the broad context of the material to be presented in that section. Each presentation is given by a single student (the Presenter), with an assigned Discussion Leader charged with developing discussion questions and leading the open discussion that follows the presentation (see **Appendix B.3** for a sample syllabus). Feedback on trainee surveys (**Section IX**) reveals that C689 is a very popular course. Fourteen (14) of the current QCB TP preceptors have now participated in C689 over the last four years (***Table A***). The topics that have been discussed span an enormous range of research areas of interest to QCB TP trainers and trainees alike. On average, 10-12 students attend these presentations at any one time. Students can register for this course up to two times for graduate credit. This course satisfies the general student seminar requirement in Chemistry (chemical biology) and Biochemistry degree programs (C800, B600) and other “journal club” requirements in other feeder graduate programs, and thus has no substantive impact on individual Ph.D. curricular requirements or time-to-degree. QCB students supported by the grant are required to register for the course twice, with the other registrants/speakers drawn from students and trainees in QCB TP preceptor laboratories.

In Fall 2016, C689 course director Charles Dann added four two-hour sessions on Research Ethics and the Responsible Conduct of Research (RCR) to ensure that all QCB trainees are exposed to a consistent research ethics and RCR training experience that is strongly integrated into their graduate training (***Table A***). This training utilizes a small group discussion format, covers six NIH-mandated topics

and involves extensive use of case studies and is further discussed elsewhere (see **Plan for the Instruction in the Responsible Conduct of Research**).

Table B. QCB TP approved electives[1]

Course number	Credits	Title (brief description)	Existing course?	Instructor
B525/C585	1.5	Membranes and Membrane Proteins[2]	–[3]	**Schlebach**
B530/C581	1.5	Macromolecular Structure and Function	–	**Dann**
B531/C882	1.5	Biomolecular Analysis and Interactions	–	**Giedroc**
B540/C588	1.5	Fundamentals of Biochemical Catalysis	–	Widlanski/**Lewis**
B541/C589	1.5	Enzyme Mechanisms	–	Widlanski/**Lewis**
C682	1.5	Introduction to Chemical Biology II	–	**Pohl/ VanNieuwenhze**
C502	3	Inorganic Spectroscopy		**Zaleski**
C620	3	Measurement Science	–	**Baker**[4]
C632	3	Structure/Function Spectroscopy of Metals		**Zaleski**
B680/C687	1.5	Special Topics: Biomolecular NMR Spectroscopy	–	**Giedroc**
Z620/B680	1.5	Special Topics: Electron Microscopy	–	Morgan/Stein
Z620/B680	1.5	Special Topics: Digital Imaging and Light Microscopy	–	**Shaw**
B511	3	Duplicating and Expressing the Genome	–	**Bell**
BIOL L519	3	Bioinformatics: Theory and Application	–	Hahn
MSCI M508	2	Precision Medicine of Cancer	–	Nephew
MSCI M580	3	Molecular Biology of Cancer	–	Forrester/Mitra/ **Hollenhorst**
NEUS N566	3	Developmental and Cellular Neuroscience	--	Prieto
PSY P667	3	Neuropsychopharmacology	--	**Hohmann/Mackie**
PHYS P575	3	Introduction to Biophysics[5]	–	**Setayeshgar**
PHYS P581	3	Modeling and Computation in Biophysics[5]	–	Glazier
PHYS P582	3	Biological and Artificial Neural Networks	–	De Ruyter
PHYS P583	3	Signal Processing and Information Theory	–	Beggs
PHYS P676	3	Selected Topics in Biophysics	–	**Setayeshgar**

[1]These courses flow from the two required 1.5 cr courses in Quantitative Biology and Measurement (C680) and Chemical Biology (C681). Bxyz, Biochemistry (BIOC) course listing; Cxzy, Chemistry (CHEM) course listing. [2]Taught as a new course in Spring 2018 as a Special Topics course (B680/C687); [3]"–", existing course. [4]Multi-institutional course shared via videoconference with Purdue and Notre Dame Universities. [5]Core courses in the Biophysics Track in the Department of Physics.

I.D.e. QCB TP advanced electives. Three credits of graduate electives round out the QCB TP curriculum and coupled with required core C680/C681 satisfy the six-credit minor requirement of the Graduate School in Chemical and Physical Biology (CPB) (***Fig. 1***). ***Table B*** provides a listing of all 1.5 and 3 cr courses that currently satisfy the QCB elective requirement (a fuller description of these courses is provided in **Appendix B.4**). These courses allow a student to *customize* his/her graduate education by selecting those that are most directly relevant to their research interests. The Curriculum Committee (**Section III**) considers on a rolling basis new course additions to this roster of courses as needed. QCB TP trainees will enroll in two of these 1.5 cr courses or a single 3 cr course to satisfy the six-credit requirements of the program (***Table B;*** *QCB trainers highlighted in* ***bold***). As these courses continue to come online, we anticipate that the disciplinary (departmental and subdisciplinary) component of the QCB TP construct (currently 12 cr; ***Fig. 1***) will be reduced, allowing students to organically incorporate additional didactic interdisciplinary training into this and other future training programs in other areas. Thus, it is our sense that the NIGMS support will continue to catalyze a transformation of the graduate training culture on campus (**Section 1.B**).

I.D.f. Rotations, Dissertation Research, Candidacy Examinations and the Final Defense.

First year: The details of these first-year processes typically follow departmental or program-specific conventions. Students currently join laboratories in the Fall semester of the first year (in Chemistry, Physics, Neuroscience) or immediately following the Fall semester of year 1 (Biochemistry, Biology, CMCB). Students who enter through Biochemistry, Biology and CMCB do one semester of three research rotations, each of ≈5 weeks duration, prior to choosing a thesis laboratory at the end of the Fall semester. Every effort is made to match students with their first-choice research advisor, in a process that is managed by the Directors of Graduate Studies (DGS) in each program, in consultation with students and prospective mentors. We provide all students sufficient tools to make an informed decision by encouraging discussions

with the DGS, other faculty and students, and the prospective advisor. Students officially join groups on January 1 of their first year.

In the three programs that don't currently require research rotations (Chemistry, Physics and Neuroscience), we are currently implementing, effective Fall 2019, an "opt-in" QCB program-specific, one semester research rotation requirement, as a *pre-condition* for consideration for a fellowship award in our annual Spring QCB Fellowship competition, which considers upcoming second-year students for support in years 2-3 (***Fig. 1***). In Chemistry, students enroll in CHEM C500, a two semester-long independent research course which requires mid-term and final reports to be submitted by the student to the Graduate Office (see **Plan for Instruction in Methods for Enhancing Reproducibility**). As part of C500, students initially learn about research opportunities at a Fall semester, year 1 poster session, and by further educating themselves about research opportunities by attending weekly group meetings and/or working on their classwork in a lab(s) of their choice. They are then matched with a laboratory mentor in early October of the first semester by mutual consent, and begin working on a C500 project through the end of the spring semester of year 1. The "opt-in" QCB TP rotation requirement would allow students originally targeted for admission by the QCB Recruitment Committee (**Section III.A**) and therefore interested in joining a QCB trainer laboratory in Chemistry, to tailor their C500 experience to incorporate three 5-week rotations, with the first of these to end on October 1 (the time at which other students in chemistry join groups). These students would then complete two additional five-week rotations, one of which must be taken with a QCB trainer outside that student's core divisional (chemistry) or departmental affiliation, to be followed by submission of a mid-term (December) C500 report that describes their research experiences in each of three laboratories. Students are then matched by the DGS to thesis laboratories, and join groups on January 1, with the final C500 report submitted in the usual way.

Implementation of this "opt-in" QCB rotation requirement is facilitated by the fact that the DGS in Chemistry (A. Flood) is also chair of the QCB Curriculum Committee (**Section III.A**). We plan to implement an exactly parallel process in Neuroscience and in Physics with the analogous requirement that one of these three rotations be carried out in a QCB trainer laboratory outside of a student's primary program (Neuroscience) or departmental (Physics) affiliation. We view this as an important mechanism to enhance cohesion and collaboration among both trainers and the prospective trainee cohort, while making our training program specific activities fully available to other students and trainees in feeder graduate programs. At the same time, this common research rotation experience satisfies one of our core training objectives, which is to expose students to the broadest possible research training experience in the context of disciplinary depth (**Section 1.C**). We also anticipate that, at least in Chemistry, this "opt-in" arrangement will readily spread to the rest of the department, consistent with the desire of students to have a stronger impact in how their graduate careers unfold. On April 15 of their first year, prospective trainees submit an application for support by the QCB TP (**Section VII**), begin their dissertation projects, and register for a slate of classes consistent with their research interests, while satisfying the QCB TP programmatic and curricular requirements outlined above.

Second year: For those incoming second-year students awarded two-year QCB fellowships, the major form of second-year trainee evaluation is performance in didactic year 2 courses, including the QCB required curriculum; success (GPA≥3.0) in these courses will allow students to stand for their preliminary (candidacy) examinations in the 5th semester or Fall semester, year 3, as is common practice at Indiana University. Prior to standing for 5th semester examinations, the QCB training program will introduce one additional formal requirement prior releasing funds for this second year of support. This requirement will be due May 15 (after completion of classes) and will consist of a two-page research progress report (outline of research objectives; progress toward those objectives, with any conference abstracts or publications clearly indicated; see **Appendix C.1** for the annual progress report form) as well as trainee permission for the QCB TP steering committee to retrieve complete IU transcripts. These reports will be submitted via an online submission portal on our website, similar to that already established for the fellowship application process. One member of the QCB program Steering Committee (assigned by the PD) will evaluate these progress reports, and meet with the student one-on-one to discuss. After this meeting, the program will provide brief feedback in the form of written comments and specific recommendations on progress toward the development of technical, operational and professional development skills of the trainee, suitable for transmission to both the trainee and the primary research advisor(s).

Table C. Sample representative curricula for QCB TP students entering through the Program in Neuroscience (PNS) and in Physics.[1]

PNS:			**Physics (Biophysics)**		
Fall Year 1		cr	*Fall Year 1*		cr
NEUS N500	Neural Science I	3	PHYS P581	Classical Mechanics	3
PSY P595	First Year Research Seminar	3	PHYS P506	Electricity and Magnetism I	4
NEUS N510	Cell & Molecular Neuroscience	3	PHYS P575	Introduction to Biophysics	3
NEUS N650	Neuroscience Seminar	1	PHYS P800	Research	
NEUS N800	Research				
Spring Year 1			*Spring Year 1*		
NEUS N501	Neural Science II	3	PHYS P556	Thermodynamics/Stat Mech	4
NEUS N566	Developmental Neuroscience	3	PHYS P581	Modeling Computation Biophys	3
PSY P677	Neuropsychopharmacology	3			
NEUS N650	Neuroscience Seminar	1			
NEUS N800	Research		PHYS P800	Research	
Fall Year 2			*Fall Year 2*		
NEUS N650	Neuroscience seminar	1	PHYS P511	Introduction to Quantum Mech	4
CHEM C680	**Quant Biol Measurement**	**1.5**	PHYS P609	Computational Physics	3
CHEM C681	**Intro Chemical Biology**	**1.5**	**CHEM C680**	**Quant Biol Measurement**	**1.5**
CHEM C689	**QCB Journal Club**	**1**	**CHEM C681**	**Intro Chemical Biology**	**1.5**
NEUS N800	Research		**CHEM C689**	**QCB Journal Club**	**1**
			BIOL L800	Research	
Spring Year 2			*Spring Year 2*		
NEUS N650	Neuroscience seminar	1	PHYS P582	Biol Artificial Neural Networks	3
TBA[2]	**QCB Elective(s)**	**3**	**TBA[2]**	**QCB Elective(s)**	**3**
NEUS N800	Research		P800	Research	
Fall Year 3			*Fall Year 3*		
CHEM C689	**QCB Journal Club**	**1**	**CHEM C689**	**QCB Journal Club**	**1**
NEUS N800	Research		CHEM P800	Research	
	5th Sem Candidacy Exams			***5th Sem Candidacy Exams***	
Spring Year 3			*Spring Year 3*		
NEUS N800	Research	1	BIOL Z620	Research Ethics	1
			PHYS G901	Research	
Years 4-5			*Years 4-5*		
NEUS G901	Research (1 cr semester)	1	PHYS G901	Research (1 cr semester)	1

[1]See **Section I.D.g.iv** for representative list of courses for previously supported trainees entering through Ph.D. programs in various divisions of Chemistry, Biochemistry and Biology. Disciplinary requirements in these majors range from 12-18 credits vs. 16 cr in Biology, 21 cr in PNS, and 27 cr in Physics. QCB TP programmatic requirements (**bold**) will be taken in years 2 and 3 (indicated above) for these majors.
[2]See ***Table B*** for a list of QCB TP electives.

Third year and beyond: Although all 5th semester candidacy examination procedures incorporate both written and oral defense components irrespective of graduate degree, the specific programmatic details differ slightly. In Biology and CMCB, the written proposal is submitted beginning in summer after the fourth semester followed by an oral defense in the 5th semester; in the Chemical Biology division of Chemistry and in the Neuroscience and Biochemistry programs, the written exam is taken three weeks prior to the oral defense, both of which occur in the 5th semester. In the analytical, inorganic, materials, physical chemistry divisions of Chemistry, the written "cumulative exam" requirement is satisfied by student-seminar courses CHEM A800, N800, M800 and P800 (1 cr, twice); in organic chemistry, students must pass a series of written cumulative exams prior to the oral defense. In the biophysics track in Physics, students take a two-day written examination that tests their general knowledge in physics, biophysics and computational methods at the end of the first year. In all cases, satisfactory performance on the written exam is required to stand for the oral defense of a comprehensive written document that outlines the background and significance, previous work and proposed work to be undertaken during the dissertation research phase of the program.

After successful completion of the preliminary examinations, students are admitted to candidacy and work toward completion of their original research projects essentially full-time. In Biology, Biochemistry, CMCB and Neuroscience, it is required that students hold annual committee meetings in which they report on research progress. In Chemistry and in Physics, this is not currently a formal requirement; however, here again we introduce a QCB program-specific requirement. All trainees in these latter two departments supported by a QCB TP fellowship will be required to submit a yearly written report to the Director of the Program (**Appendix C.1**) by May 15 of every year, and coincident with that, call a meeting of their advisory committees to report on progress (**Section VII**). During these meetings, the advisory committee will evaluate research progress, as well as progress toward professional development objectives, and recommend what steps are needed to ensure a successful final defense, timely graduation from the

program and adequate professional development preparation for a career after graduate school. Representative curricula of students entering through non-traditional departmental and program portals while completing the requirements of the QCB TP are shown below (***Table C***).

I.D.g. Extracurricular Value-added Programmatic Activities. An important training objective of our graduate training program is to hold events outside of the classroom that bring together trainers and trainees from disciplinary programs that otherwise would not interact. A small number of "signature events" that highlight the QCB TP and research from preceptor laboratories then become integral components of the training environment. We will continue to host the following activities:

I.D.g.i. Watanabe Symposium in Chemical Biology. Saturday, September 30, 2017 marked the eighth of what has become an annual programmatic event that highlights the QCB training program (**Appendix B.5**). This one-day symposium is hosted by PD Giedroc and former Chemistry faculty member and QCB trainer Richard DiMarchi and features oral presentations by four or five internationally recognized speakers from academia and industry, short presentations by several QCB TP preceptors and a poster session that showcases research activities of trainees in QCB TP laboratories. Our 2017 symposium on Biomolecular Machines featured four members of the US National Academy of Sciences, including Bob Sauer (MIT), Angela Gronenborn (University of Pittsburgh), Jody Puglisi (Stanford) and Taekjip Ha (Johns Hopkins) with ≈25 lunchtime poster presentations by QCB trainees and others in trainer groups. The 2018 symposium has been organized by QCB TP trainer Adam Zlotnick around the theme of virology and antivirals, continuing the thematic orientation of these symposia. In the next project period, the Recruitment Committee proposes to use this “signature” event of our training program to aggressively promote our program in the Midwest, by inviting prospective trainees and their undergraduate research mentors from small colleges and HBCU institutions within a four-hour drive of Bloomington (St. Louis, Nashville, Cincinnati, Columbus, Chicago) to the symposium in an effort to generate new graduate applications.

I.D.g.ii. QCB Evenings**.** QCB Evenings are scheduled 4-6 times per academic year. Each QCB Evenings event invites two trainees, students or postdocs from different QCB trainer laboratories to present their work, with a dinner of pizza and refreshments sandwiched between the two presentations. These events start at 5:30 pm, typically on a Wednesday, and finish by 7:00 pm. Speakers need not be directly supported by the training grant, but must be working in a QCB TP preceptor laboratory; however, all trainees previously supported by a fellowship, *i.e.,* the trainee cohort, are required to present to the group prior to graduation. QCB Evenings have undergone significant revisions in the last year, entirely as a result of surveying current students and alumni of the training program (**Section IX**). These events are now fully student-run (trainers are not permitted to attend), and organized by our two QCB ambassadors in consultation with the trainee cohort. This event was originally modeled on the highly successful ChemGRC seminar series in Chemistry, and after a brief retooling hiatus in Fall 2017, is again going strong (**Appendix B.6** provides representative announcements).

I.D.g.iii. QCB Seminar Series. The Chemical Biology division of the Department of Chemistry and the Program in Biochemistry sponsor an active weekly seminar series in which outstanding scientists are brought to campus, interact with faculty and students alike, and present a seminar on their work (Fridays, 2:30 pm). Chemistry endowment funds are used to support this activity. Chemical Biology hosts approximately half of these visits over the course of an academic year. QCB seminar series was originally created as a faculty-hosted event, in which QCB trainees had an opportunity to interact with the 2-4 invited speakers per year over a catered lunch, where trainees gave short talks (with 2-3 slides) about their projects. Upon consulting with trainees, we changed to a “no slides” format, and allowed students to use only the blackboard, thus increasing opportunities for unscripted discussion. The evolution of QCB Seminar Series is now complete, and as of April 2018, now features a QCB trainee-invited seminar speaker. The trainee cohort meets, arrives at a consensus choice, and a QCB ambassador personally extends the invitation on behalf of the program. They create the itinerary (with administrative help), host the speaker for a lunchtime “elevator pitch” of their research as described above, and for dinner at the end of the day. Our program recently hosted Profs. Josh Wand (Univ. Pennsylvania) using elements of the old format, and Jie Xiao (Johns Hopkins; B. Rued, trainee host) as our first true QCB trainee-invited seminar speaker (see **Appendix B.7** for announcements). Prof. Xiao’s seminar was an enormous success with extensive participation by both the trainee cohort and QCB training faculty. Trainee-invited seminar

speakers are now being extended invitations for the 2018-2019 academic year. Other distinguished seminar series complement these efforts, including an annual Harry G. Day Lecturer, named for the co-discoverer of stannous fluoride (the active ingredient in Crest toothpaste). In Fall 2017, QCB trainer David Clemmer hosted Dame Carol Robinson from the University of Oxford, whose career trajectory was non-traditional, and thus was of particularly strong interest to female faculty and trainees alike.

I.D.g.iv. Snapshots of Individual Trainees Supported by the Program (2014-2018). The research and training activities of seven trainees are provided here, as representative of students who enroll at Indiana University into distinct degree programs with vastly different backgrounds that our program seeks to support. These students entered either the Biochemistry, Biology or Chemistry Ph.D. programs, the latter in one of four separate subdisciplines (analytical, inorganic, materials, organic). This snapshot as well as ***Tables C-D*** provide an accounting of foundational coursework available to graduate trainees in our program, and the breadth of collaborative research activities exemplified by current and future trainees in QCB TP preceptor laboratories. All of these courses are graded courses (A+–F), with the exception of QCB Journal Club (C689) and various journal clubs and student seminar series (A600, B800, A800, M800, N800, etc.), which are evaluated as S/U (satisfactory/ unsatisfactory). The instructor is indicated below only when a QCB preceptor taught the indicated course; CHEM C500, research credits and student seminar courses are not shown for clarity.

Britta Rued, Biology (Microbiology) is a 5th year trainee and former (2017) QCB Ambassador jointly mentored by her major advisor Malcolm Winkler and co-advisor David Giedroc. Britta entered the Microbiology Program at Indiana University after completing a B.A. in Biology (minor, Chemistry) at the University of Wisconsin River Falls. Britta has developed a collaborative project that seeks to understand the structure and function of the integral membrane protein FtsX in cell division in *Streptococcus pneumoniae*. She has carried out extensive microbial physiology experiments on mutant *S. pneumoniae* strains that harbor FtsX mutant alleles guided by our NMR solution structure of a functionally important extracellular domain, coupled with biophysical studies (ITC) of the physical interaction between this domain and an essential peptidoglycan hydrolase. Britta is co-author on four publications thus far, with one major manuscript in preparation (**Table 5**). Her formal didactic training includes:

BIOC B511	3 cr	Duplicating and Expressing the Genome	Bell
BIOL L585	3	Genetics and Bioinformatics	
BIOC B503	3	Critical Analysis of the Scientific Literature	
BIOC B504	3	Biomolecular Catalysis	
BIOL M511	3	Molecular Biology of Prokaryotes	
BIOC B680	1.5	Electron Microscopy	
BIOL Z620	1.5	Digital Imaging and Light Microscopy	Shaw
CHEM C687	1.5	Special Topics: Biomolecular NMR Spectrosc	Giedroc
CHEM C680	1.5	Intro Quantitative Biology and Measurement	Dragnea
CHEM C681	1.5	Introduction to Chemical Biology I	VanNieuwenzhe
CHEM C689	1	QCB Journal Club	QCB Faculty

Lucero Sanchez, Materials Chemistry, is a 5th year trainee and former (2017) QCB Ambassador in the laboratory of Yan Yu. Ms. Sanchez entered the graduate program after finishing a B.S. in Chemistry and in Biochemistry at the University of Iowa. Lucy's project focuses on membrane dynamics of immune cells, and specifically involves the synthesis of bioinspired Janus particles and live cell single-particle tracking techniques in an effort to elucidate the mechanism for phagocytosis by immune cells. Lucy is co-author on seven papers (**Table 5**). Her didactic training includes:

CHEM C501	4 cr	Chemical Instrumentation	
CHEM C611	3	Electroanalytical chemistry	Baker
CHEM C612	2	Spectrochemical Methods of Analysis	
CHEM C613	2	Mass Spectrometry and Stable Isotopes	Clemmer
CHEM C614	2	Chromatography	Jacobson
CHEM M501	3	Fundamentals of Materials I	Dragnea
CHEM M502	3	Fundamentals of Materials II	Yu

CHEM M503	3	Supramolecular Chemistry	Flood
CHEM C680	1.5	Intro Quantitative Biology and Measurement	Dragnea
CHEM C681	1.5	Introduction to Chemical Biology	VanNieuwenhze
CHEM C689	1	QCB Journal Club	QCB Faculty

Chelsea Rintelmann, Organic Chemistry, is a current QCB Ambassador and third-year trainee in the laboratory of co-PD Nicola Pohl. Ms. Rintelmann earned her B.S. in Chemistry from Allegheny (Pa.) College, joined the graduate program and Prof. Pohl's group in Fall 2015, and successfully passed her candidacy examinations in Fall 2017. Her research interests include the synthesis of biologically important carbohydrate-based probes and carbohydrate containing molecules as pathogen-associated molecular probes for anti-leishmaniasis vaccine design, and high mannose-type N-glycans. Chelsea has successfully completed the multi-step synthesis of a new molecular probe to investigate immune responses to a *L. major* infection. Chelsea is co-author on one paper thus far (**Table 5**). Her classroom training consists of:

CHEM C503	3 cr	Spectrochem Methods Structure Determination	
CHEM C540	3	Advanced Organic Chemistry	Brown
CHEM C543	3	Organic Reactions	
CHEM C643	3	Organic Natural Products	
CHEM C582	1.5	Biomolecular Analysis and Interactions	Giedroc
CHEM C680	1.5	Intro Quantitative Biology and Measurement	Giedroc
CHEM C681	1.5	Introduction to Chemical Biology I	Pohl
CHEM C682	1.5	Introduction to Chemical Biology II	Pohl
CHEM C689	1	QCB Journal Club	QCB Faculty

Julie Button, Biochemistry, is currently a third-year student with Tuli Mukhopadhyay. Ms. Button is a graduate of West Virginia University having earned a B.S. in Chemistry (GPA 3.98). She entered the Ph.D. program in Biochemistry in Fall 2015, and successfully passed her candidacy examinations in Fall 2017. Her research interests focus on the mechanisms of alphavirus nucleocapsid assembly. She has not yet published, but has presented her work at one national meeting. His formal coursework is:

BIOC B501	3 cr	Integrated Biochemistry	
BIOC B502	1.5	Analysis of the Biochemical Literature	
BIOC B530	1.5	Macromolecular Structure and Interactions	Dann
BIOC B531	1.5	Biomolecular Analysis and Interactions	Dann
BIOC B540	1.5	Fundamentals of Biochemical Catalysis	
BIOC B541	1.5	Enzyme Mechanisms	
BIOC B506	1.5	Integrated Biochemistry II	
BIOC B680	1.5	Special Topics in Biochemistry: Grant Writing	
BIOC B600	1	Seminar in Biochemistry	Giedroc
CHEM C680	1.5	Intro Quantitative Biology and Measurement	Giedroc
CHEM C681	1.5	Introduction to Chemical Biology I	VanNieuwenhze
CHEM C689	1	QCB Journal Club	QCB Faculty

Stephen Ratvasky, Inorganic Chemistry, is currently a second-year trainee with Jeff Zaleski. Mr. Ratvasky completed his B.S. in Chemistry at Duquesne University (GPA 3.94) and joined Prof. Zaleski's group in Fall 2016. He will take his candidacy examinations in the Fall 2018. Mr. Ratvasky's research interests are focused on the development of therapeutic antitumor enediyne-containing metal complexes. Current work is focused on the synthesis of cisplatin analogues bearing thermally triggerable enediyne diamine ligands, which should bind DNA and induce radical-based DNA cleavage. He has also incorporated the same enediyne ligand above into an established DNA-binding Cu(II) metallodrug scaffold in an effort to circumvent toxicity associated with heavy metal-based chemotherapeutics, such as cisplatin. He has not yet published but has presented his work at a number of local symposia. His didactic training consists of:

CHEM C502	3 cr	Inorganic Spectroscopy	Zaleski
CHEM C630	3	Structure and Bonding	
CHEM C562	3	Computational Quantum Chemistry	

CHEM C636	3	Organometallic Chemistry and Catalysis	
CHEM C634	3	Transition Metal Chemistry	
CHEM C637	3	Physical Methods in Structural Chemistry	
CHEM C680	1.5	Intro Quantitative Biology and Measurement	Giedroc
CHEM C681	1.5	Introduction to Chemical Biology I	Pohl
CHEM C689	1	QCB Journal Club	QCB Faculty

Joseph (J.B.) Holmes, Physics, is a third-year student carrying out research in the laboratory of Bogdan Dragnea in collaboration with Sima Setayeshgar. Mr. Holmes completed his undergraduate degree in Physics at Houston Baptist University (GPA 3.49) and enrolled at IU as an MS student on the biophysics track in our American Physical Society Bridge Program. The Bridge Program is aimed at increasing the diversity and number of URM students in Physics Ph.D. programs where students begin their formal coursework in 300-400-level undergraduate courses while performing graduate research. Mr. Holmes has since been admitted to the Ph.D. program, having passed his written qualifying examinations. He is developing a project focused on experimental and computational studies of optical interactions in bioinspired lattices. His didactic training includes:

PHYS P331	3 cr	Theory of Electricity & Magnetism I	
PHYS P441	3	Analytical Mechanics I	
PHYS P575	3	Introduction to Biophysics	
PHYS P332	3	Theory of Electricity & Magnetism II	
PHYS P460	3	Modern Optics	
PHYS P548	3	Mathematical Methods for Biology	
PHYS P506	4	Electricity & Magnetism I	
PHYS P511	4	Quantum Mechanics I	
PHYS P521	3	Classical Mechanics	
PHYS P556	3	Statistical Physics	
PHYS P557	3	Solid State Physics	
CHEM C680	1.5	Intro Quantitative Biology and Measurement	Giedroc
CHEM C681	1.5	Introduction to Chemical Biology	Pohl
CHEM C689	1	QCB Journal Club	QCB Faculty

Brooke Brown, Analytical Chemistry, is a first-year student in the laboratory of David Clemmer. Ms. Brown is a non-traditional graduate student, and attended Baylor University after completing a stint in the US Army as a medic in Afghanistan. She earned a B.S. in Chemistry and did undergraduate research with Touradj Solouki. In the Clemmer group, Ms. Brown is developing a multi-modal mass spectrometry-based method to monitor the structures of temperature-induced unfolding intermediate structures by hydrogen/deuterium exchange ion mobility spectrometry-mass spectrometry (HDX-IMS-MS). Her model system is ubiquitin, and involves the use of prototype temperature-controlled ESI-source; success with ubiquitin allows future applications to the study of proteostasis, particularly those aberrant processes that lead to neurodegenerative disease. Her coursework thus far includes:

CHEM C501	4 cr	Chemical Instrumentation	
CHEM C612	2	Spectrochemical Methods of Analysis	Thielges
CHEM C613	2	Mass Spectrometry and Stable Isotopes	
CHEM C615	2	Bioanalytical Chemistry	Clemmer

II. Career Development

Although the extensive breadth of the QCB TP research activities ensures that trainees are exposed to a variety of career options in the chemical and biomedical science fields, other more deliberate strategies are required to ensure that trainees are purposefully developing a top-flight communications skill-set, essential for any career path, while actively thinking about career and workforce options *throughout* their time in graduate school. We believe that specific career development activities in which student trainees

productively engage change as a student navigates graduate school. Years 1-2.5 constitute the first major phase of graduate training, while the second phase corresponds to mid-third year to degree completion.

Pre-Ph.D. candidacy career development. In this first phase, major objectives are familiarizing the trainee with his/her field and the foundational premise of the research project, while providing tools and opportunities for trainees to learn the fundamentals of successful scientific communication, in short- and long oral-, poster- and "elevator pitch"- style formats. Our strategy toward meeting those pre-candidacy objectives for *all trainees* features two approaches: 1) all two-year fellowship recipients will enroll in MSCI M509 (1 cr), Basics of Scientific Communication in the Spring semester of their second year, just prior to attendance at what might be their first major national meeting in the summer between their second- and third years (**Appendix B.8** for a recent syllabus). This course, organized by QCB Steering Committee member Claire Walczak, takes students through a series of exercises that expose them to various forms of communication, from writing an abstract, to preparing figures for papers vs. posters vs. various oral presentation formats, while touching on successful conventions that distinguish science communication to different audiences. Students on one-year, third-year fellowships will enroll in the course in the third year, or be encouraged to register in their second year if they are considering applying for a QCB fellowship.

The second feature in pre-candidacy career development leverages presentation skill development that occurs organically in student seminar courses (B600, x800 courses in chemistry, etc.) and journal clubs (*e.g.,* C689) that characterizes all graduate curricula. This prepares QCB trainees for further developing presentation skills at local (IU and Indiana) and regional conferences and symposia, and was a major motivation for creating a poster session for QCB trainees during the annual Watanabe Symposium. In addition, the Midwest features a large palette of regional meetings, including the Turkey Run Analytical Conference, PINDU (an inorganic chemistry-focused conference), GRASP NMR, the Gibbs Conference on Biothermodynamics, the Rustbelt RNA meeting, the Chicago Cytoskeleton Meeting, and the Midwest Protein Folding, Assemblies and Molecular Motions meetings, as well as regional meetings of the American Chemistry Society. Small conferences like these provide valuable networking opportunities for younger trainees, while allowing them to hone presentation skills in a nurturing environment.

Post-Ph.D. candidacy career development. This phase of career development endows more senior, post-candidacy students with presentation skills that position them to be *successful* during the post-candidacy phase and beyond. Here, trainees will have opportunities to attend national and international meetings to present their work in a more impactful way, while taking advantage of career development programs and symposia that are routinely offered at national "society" conferences, *e.g.,* the National Symposia of the American Chemical Society or annual meetings of the Biophysical Society, Pittcon, Protein Society, RNA Society, ASBMB, American Society of Microbiology, and American Society of Cell Biology. These symposia routinely offer valuable information on the wide variety of careers in the chemical and biomedical research community, beyond that of the academic scientist.

QCB trainees will also be encouraged to participate in the IU Career Development Symposium in partnership with the Walter Center for Career Achievement in the College of Arts and Sciences. This event was initiated in 2015 by Chemistry students, and is now an annual event, with the 4th symposium, in August 2018, in the final planning stages (**Appendix B.9**). This symposium is organized by the Department of Chemistry and the Chemistry Graduate Representative Committee (ChemGRC) and enjoys strong industrial support, while featuring a significant chemical biology flavor. For example, the 2016 symposium hosted former QCB trainer and entrepreneur Richard DiMarchi as keynote speaker, and QCB trainees and students from trainer groups participated in the poster session and a follow-up career fair (**Appendix B.9**). In upcoming symposia, our trainee cohort proposes to add panelists and participants that speak to an even broader range of careers available to all QCB trainees. In addition, we propose to better leverage our 10 alumni of the QCB training program in the upcoming project period (iuqcb.indiana.edu), which include several who have gone directly into non-traditional post-Ph.D. permanent positions and postdoctoral appointments in industry (**Table 8A**). Trainees propose to bring one or two alumni to campus to participate in the Career Development Symposium and host a roundtable discussion with current QCB trainees. Finally, Chemistry (including QCB trainers Brown and Cook) recently (2018) established an annual Novartis Chemical Science Lectureship, in partnership with Novartis. This half-day symposium in April featured three prominent speakers working in the areas of synthetic transformations, chemical biology and

drug discovery. The inaugural symposium featured Dale Boger of Scripps and Jason Elliot of Novartis Institute for Biomedical Research, providing students in QCB trainer groups a view of industrial-academic partnership opportunities from multiple perspectives. Past Watanabe Symposia and QCB Seminar series have also featured speakers from the pharmaceutical and biotechnology sectors (**Appendices B.5-B.6**).

The training program will also encourage students interested in industry/entrepreneurship to actively participate in events organized by the Johnson Center for Entrepreneurship and Innovation in Simon Hall, affiliated with the Kelley School of Business, notably the Velocity Conference organized by IU Chemistry Ph.D. alumnus and inventor Jack M. Gill. Others interested in academic careers will be encouraged to participate in the annual Preparing Future Faculty Conference, sponsored by the University Graduate School. This conference was last held in February 2018, and included panel discussions on various career options, balancing research/teaching/service, navigating the job market, and developing innovative teaching strategies and related events. Finally, the Biotechnology Program at IU runs a Thursday evening seminar series in Simon Hall that hosts speakers from the biotechnology and pharmaceutical industries, with plenty of time to allow significant interaction between students and industry leaders after each seminar; these discussions often include personal insights about career transitions and advice to students for how to follow these paths. In addition, Dr. William Carroll, an IU Chemistry alumnus and former president of the American Chemical Society, also presents semi-annual workshops and engages students one-on-one about how to be competitive for industrial jobs in today's climate.

III. Program Oversight, Preceptor Selection and Preceptor Training

III.A. Oversight

The program is directed by PD David Giedroc and co-Director Nicola Pohl (**Section V**). They are also members of the QCB TP Steering Committee that serves as the governing body of the program. The Steering Committee has administered the program since inception in 2010 and is composed of members drawn from all major participating departments and programs, including Chemistry (Drs. Giedroc and Pohl), Biology (Sid Shaw), Biochemistry (Stephen Bell), Cell, Molecular and Cancer Biology (CMCB, Claire Walczak), Physics (Dr. Shaw, joint in Physics) and Neuroscience (Ken Mackie). The committee is responsible for evaluating preceptors for inclusion or reappointment (see below). In addition, this committee solicits and evaluates applications for program financial support and makes these appointments for 1-2 years. This committee also oversees student progress and thus has a major role in ensuring retention of trainees in the program (see below). Membership on the Steering Committee is voted upon by current Training Faculty. Members do not serve for a set term and will rotate off periodically. In the event the Director or co-Director steps down, remaining members of the Steering Committee elect his/her replacement from current Training Faculty.

Two additional committees, composed of three-four faculty trainers each, will report to the Steering Committee, and are charged with the recruitment of graduate trainees into the program (the Recruitment Committee) and providing curricular oversight of the training program (the Curriculum Committee). We have deliberately kept these committees small (this is a change from the past) so as enable a rapid and nimble response to issues as they arise. The major focus of the Recruitment Committee will be the identification of highly qualified potential trainees, particularly from underrepresented groups suitable for recruitment to the program, and for increasing the size and diversity of the applicant pool. Members of this committee will work closely with the graduate admissions committees of participating departments and programs to identify those students who are eligible and interested in being considered for support by the training grant, as they progress to become second-year students. The chair of this committee is Charles Dann (Chemistry), who has extensive experience in graduate admissions in both Chemistry and the Biochemistry Program. He is slated to become Director of Graduate Studies and chair of the Biochemistry Graduate Standards Committee and is also a member of the Diversity Affairs Committee in Chemistry, and thus these QCB TP administrative functions are highly complementary to those roles. Dr. Dann will orchestrate the recruitment of trainees from the Chemistry and Biochemistry admissions portals. Other members of the committee are Peter Hollenhorst (CMCB), who will work closely with admissions directors in CMCB (QCB TP trainer and CMCB Director of Graduate Studies Heather Hundley) and in Biology, Sima Setayeshgar (Physics), who as Director of the Biophysics program in Physics is well-positioned to oversee trainee recruitment in Physics, and Andrea Hohmann (Neuroscience), who will spearhead recruiting there.

The Curriculum Committee will be responsible for all curricular matters, including identifying Training Faculty to teach in the QCB Journal Club, and proposing and generally overseeing the development of new 1.5 cr or 3 cr electives for the QCB TP that satisfy the requirements of the academic minor in Chemical and Physical Biology (**Section I.D.e**). This committee will be composed of a Chair and two additional Training Faculty not currently serving on the Steering Committee but intimately familiar with departmental graduate programs. The chair of the committee is Amar Flood (Chemistry) who has extensive experience as Director of Graduate Studies in Chemistry (2014 to present), with Suchetana Mukhopadhyay (Biology), incoming Director of Graduate Studies in Biology, and Hui-Chen Lu (Neuroscience) as members.

Both Recruitment and Curriculum Committees are also served by one of two QCB Ambassadors. QCB ambassadors are appointed to a one-calendar year term by the Steering Committee and are currently or recently supported NRSA trainees. They are charged with developing, overseeing and maintaining (with administrative help; see below) our internet presence, including a social media presence (Twitter @iuqcb), while also calling periodic (quarterly) meetings of the trainee cohort. Maintaining an up-to-date and exciting web presence is critically important in making us competitive for training program applicants, and these efforts interface well with the Recruitment Committee. Trainee meetings on the other hand, are used to organize QCB TP-associated extracurricular activities, including QCB Evenings, QCB-trainee selected seminar series, the Watanabe Symposium in Chemical Biology and all career development and social activities of the program. These activities impact the Curriculum Committee. The QCB Ambassadors program was initiated in January 2017 with Britta Rued (Winker/Giedroc, Biology) and Lucy Sanchez (Yu, Chemistry) in CY2017 and now features Chelsea Rintelmann (Pohl, Chemistry) and Paul Marcyk (Cook, Chemistry) as CY2018 ambassadors and has proven to be extremely effective. One member of the trainee cohort serves as host for a *consensus* QCB-trainee-invited seminar speaker, the first of whom, Dr. Jie Xiao of Johns Hopkins University (**Appendix B.7**), was hosted by former QCB ambassador B. Rued.

The day-to-day administration of the QCB Training Program is carried out by the Program Director in consultation with the co-Director. They are assisted by administrative staff in the home department (Chemistry), currently Maria Sievers Perotti as Administrative Director and Compliance and Reporting Manager, Caitlin Watkins, Pre-Award Specialist, and Misty Theodore, Post-Award Specialist. Ms. Sievers Perotti will continue to serve as the administrative contact for all trainees and Training Faculty, calling meetings of the various committees, notifying trainees of their selection as trainees, soliciting trainee progress reports, interfacing with the graduate offices of participating departments, and generally providing administrative oversight of program. She will be responsible for overseeing all financial aspects of the program, including identifying sources of matching stipend support and travel expenses, in close consultation with the Director of Business in Chemistry and Ms. Theodore. Ms. Watkins' responsibility will be to serve as primary interface with QCB ambassadors and the collective trainee cohort, in maintaining the website and social media presence.

An Internal Advisory Committee (IAC) composed of the chairs of participating departments (Chemistry, Biology, Physics) and Directors of Graduate Studies in participating programs (CMCB, Biochemistry, Neuroscience) and Prof. Michael McGinnis, Associate Dean for Graduate Education in the College of Arts and Sciences, will be convened at least once every two years and more frequently, if needed. This committee last met in January 2018 to review the progress and training record of the existing training program. The IAC's primary role is advisory, so as to ensure integration and consistency of QCB TP curricular requirements with existing departmental and programmatic degree requirements, while advising the Director of any changes that need to be made. For example, the Steering Committee decided to add trainers from the Program in Neuroscience on the advice of the IAC, all of whom are new additions to training faculty, effective April 2018 (**Section VI**). An external advisory committee, likely drawn from QCB-trainee invited seminar speakers or Watanabe Symposium speakers, will be appointed by the Steering Committee in consultation with the Internal Advisory Committee, as our program matures.

III.B. Selection and Evaluation of Preceptors

Selection. A primary criterion for appointment as a Preceptor is an emerging or documented track record of graduate student training, a strong research orientation toward "molecules and mechanism", either within their own laboratories or via collaboration with other groups (see below), and an excitement about his/her participation in the both the curricular and extracurricular activities of the QCB training

program. We favor preceptors that are naturally collaborative, who bring biology to physics and chemistry and vice versa, coupled with a desire to teach in the curriculum designed specifically for this program. Since our curriculum is built around a graduate minor in Chemical and Physical Biology, this ensures that the standards of scientific rigor associated with the program are imparted by the Training Faculty to our trainees. QCB Journal Club plays an important role in this process, by featuring a discussion of primary research findings in quantitative and chemical biology, which by necessity overtly explores the concepts of reproducibility and statistical significance. In addition, the course director of QCB Journal Club rotates among the training faculty and that individual is responsible for teaching 4 2-hr sessions on the Responsible Conduct of Research in C689 (see **Plan for the Instruction in the Responsible Conduct of Research**) thus enhancing the connectively of this material to scientific topics under discussion. A demonstrated track record of securing extramural funding from private foundations and/or federal agencies is also required for selection as a trainer. Finally, in order to facilitate future collaboration among QCB trainers, we place some consideration on research interests that naturally connect biologists to analytical chemists, structural biologists, biophysicists or other chemists as a way to bridge graduate feeder programs and enhance co-mentorship of prospective QCB trainees. Addition of all new Training Faculty requires a nomination from any member of the Training Faculty and submission of a full CV; the Steering Committee considers and acts on the nomination via closed ballot with majority rule.

Evaluation. A review of the Training Faculty is carried out annually by the Steering Committee, with the last comprehensive review carried out in Spring 2017, and most recently in January 2018 based on discussions with the IAC, which led to addition of four new trainers in or affiliated with the Program in Neuroscience. Once appointed, ongoing appointment on the Training Faculty derives from consistent participation in program events, including regular attendance and willingness to direct or organize research themes for QCB Journal Club, the periodic nomination of a highly qualified prospective trainee from their research groups for a fellowship award, and maintaining an externally funded research program that features graduate students. Training Faculty attendance and trainee group student participation at all extracurricular activities are also evaluated, as is participation in the weekly invited seminar in Chemical Biology or Biochemistry (Fridays, 2:30 pm).

III.C. Preceptor Training

As can be seen from the data compiled in Table 1, graduate students outnumber postdoctoral trainees in QCB trainer laboratories by ≈5-fold, as is typical for an Arts and Sciences campus in a college town; thus, all of our trainers are well-versed in the challenges and opportunities of graduate education. The training faculty also features four current or incoming Directors of Graduate Studies (in Chemistry, CMCB, Biology and Biochemistry) who are intimately familiar with the expectations of students and graduate mentors alike. All have been engaged in the development of their graduate handbooks, which spell out these expectations for all training faculty in individual graduate feeder programs. This includes Conflict Resolution Protocols (**Appendix D**), which differ slightly from department to department but generally provide opportunities within and outside the department for trainees to resolve conflicts with their primary advisor. Any QCB trainer that consistently displays poor judgement in mentorship, including placing formerly supported trainees back on teaching assistants after the fellowship period ends, beyond those required to meet a minimal Ph.D. program-specific teaching requirement (typically one semester), will be removed from the training faculty. Once fellowships are awarded to trainees, the PD meets with their mentors to describe the mentoring expectations of the program; in addition, all prospective QCB trainee mentors must agree in writing to major terms and conditions that come with hosting a QCB trainee (**Appendix E.3**). The quality of the trainer mentorship will be tracked by evaluation of the annual progress reports to be submitted by trainees (**Appendix C.1**), and individual meetings with a steering committee member. In addition, the PD meets with the entire training faculty at least annually, typically in August, to review the trainer responsibilities in order to ensure that they function in the best interests of the trainee. These responsibilities include encouraging QCB fellowship recipients to explore new research directions while cultivating their own interests consistent with their evolving career goals, in the broad context, of course, of the mentor's funded research program, and strongly encouraging applications for individual predoctoral fellowships, *e.g.,* F31, once the fellowship period ends. This builds trainee independence and ownership of their projects, thus catalyzing a successful transition to the next stage of their careers.

IV. Institutional and Departmental Commitments to our Program

Strong evidence of support by the College of Arts and Sciences is provided by the considerable investment in internally funded QCB TP slots to date, which now totals 26 training slots since inception (Fall 2010), in addition to "top-off" funding used to raise the NIH-mandated NRSA stipend to $25,000 for each of 20 NIGMS-funded slots (2014-2019, 2/4/4/4/6 slots in years 01-05). This program also enjoys the strong support of the University Graduate School (UGS) and all participating department chairs and program directors (see ***Institutional Letters of Support***), entirely consistent with the historical commitment of matching funds for successful instrumentation proposals that have brought new instrumentation to campus. The UGS has again committed five (5) training slots during the next funding cycle (as 1/1/1/1/1 in years 01-05, which equals their level of support in the previous cycle), with the same stipulation that this support be used to fund trainees from underrepresented groups, which we have done (see **Trainee Retention Plan**). The College of Arts and Sciences has agreed to continue their current level of stipend support in this next five-year funding cycle by providing 10 training slots distributed 2/2/2/2/2 (years 01-05) as matching funds for the current application (see ***Institutional Letters of Support***).

V. Training Program Directors

David Giedroc, Program Director (PD). Prof. Giedroc is the Lilly Chemistry Alumni Professor and founding Director of this Chemistry-Biology Interface Training Program in QCB at Indiana University. Dr. Giedroc earned a Ph.D. in Biochemistry (minor: Chemistry) in 1984 from Vanderbilt University School of Medicine, and following postdoctoral training at Yale University, joined the Department of Biochemistry and Biophysics at Texas A&M University, serving on the faculty there for 19 years (1988-2007). During that time, he assumed a number of administrative roles including founding Director of the Biomolecular NMR Laboratory and founding co-Director of the Center for Advanced Biomolecular Research (CABR). CABR served as one of the catalysts for the establishment of an NIGMS-funded CBI training program (T32 GM008523), on which Dr. Giedroc served as a trainer. Dr. Giedroc then played a leading role in establishing an NIGMS-funded training program in Molecular Biophysics at Texas A&M (T32 GM065088), first as a preceptor and member of the steering committee, and ultimately as Director in 2005. In 2007, he moved to the Department of Chemistry at Indiana University as Professor, and served as Chair of the Department from 2010 to 2015. As chair, he was a regular attendee at the Open Chemistry Collaborative in Diversity Equity (OXIDE)-organized National Diversity Equity Workshops for chemistry chairs, and was named the inaugural (2015) Diversity Catalyst Lecturer for his proactive efforts to increase the number of female faculty in the department, and his establishment of a departmental Diversity Affairs Committee (see **Recruitment Plan**). Since stepping down as chair, PD Giedroc has served in a number of administrative roles related to graduate education, including service as chair of the Committee on Research, Creative Activity and Graduation Education, assembled to create a new Strategic Plan for the College of Arts and Sciences at Indiana University. He is also founding chair of the Graduate Standards Committee in the Biochemistry graduate program, leading a total redesign of the curriculum (2016-2018). He is also co-Director of the Chemical Biology Pillar of the Precision Health Initiative, an IU Bloomington-IU School of Medicine Indianapolis collaborative venture, where he also serves as a member of the Steering Committee. Prof. Giedroc has served as an *ad hoc* reviewer for NIH and NSF study sections and a full term on the NIGMS Biomedical Research Training (BRT-B) study section (2006-2010).

PD Giedroc's research training encompasses biophysical chemistry, bioinorganic chemistry and structural biology, in particular, biomolecular NMR spectroscopy. His research activities are organized under a common umbrella, the *Biophysical Chemistry of Infectious Disease* and is currently (since 2016) supported by an NIGMS Maximizing Investigators' Research Award (MIRA) and as PI on a collaborative MPI grant with investigators at Vanderbilt University. He has extensive experience in graduate and postdoctoral education, having graduated 23 Ph.D. and 9 M.S. students, and now leads a group of eight Ph.D. students (one jointly mentored with QCB preceptor Winkler) and three postdoctoral scientists. Four former Ph.D. students (3 females) have secured faculty positions at R1 institutions, including the University of Michigan, the University of Missouri, Columbia, and the University of Alabama (deceased). One current Argentine postdoctoral trainee is winner of a highly competitive 2015 Pew Latin American Fellowship, while five others, including one URM African-American and one URM Native American, now hold tenure-track positions at universities and PUIs in the US and in Korea. At Indiana University, PD Giedroc has developed

three courses that serve either as a core course (CHEM C680, Introduction to Quantitative Biology and Measurement) or an elective (CHEM C687, Special Topics in Biomolecular NMR Spectroscopy) in the QCB TP curriculum and is a founding coordinator in CHEM C689, QCB Journal Club.

Nicola Pohl, co-Program Director. Dr. Giedroc is assisted in the administration of the program by a co-Director, Dr. Nicola Pohl, a carbohydrate chemist and Marvin and Joan Carmack Chair in Bioorganic Chemistry. Prof. Pohl has strong credentials in synthetic chemistry and chemical biology and as such is complementary to the research expertise of Dr. Giedroc, which lies on the biophysical (quantitative) side of our QCB Training Program. Dr. Pohl has served as primary or co-mentor for over 30 graduate students since starting her independent career in 2000. She earned her Ph.D. from the University of Wisconsin in Madison as one of Prof. Laura Kiessling's first students. Her graduate work involved the synthesis of oligosaccharides, including the synthesis of multivalent galectin inhibitors using ring-opening metathesis polymerization. Following an NIH-sponsored postdoctoral position in the Department of Chemical Engineering at Stanford University with Prof. Chaitan Khosla working on metabolic engineering of polyketide antibiotic and anticancer compounds, Dr. Pohl started her independent career at Iowa State University. She left her position there as Wilkinson Professor of Interdisciplinary Engineering and as Professor of Chemistry and of Chemical and Biological Engineering in 2012 to join the IU faculty. She has served as an *ad hoc* member of numerous NIH study sections and NSF panels in addition to serving on the scientific advisory board of the Research Corporation for Science Advancement and is past Chair of the Carbohydrate Division of the American Chemical Society. She is currently a member of the NIGMS Training and Workforce Development B (TWD-B) study section (from 2017). She has taught numerous graduate and undergraduate classes, and served as member and chair of the chemistry curriculum committee at Iowa State; at IU she has taught the Introduction to Chemical Biology I, II courses (C681/C682) in the QCB TP curriculum. Dr. Pohl's laboratory works in the area of glycobiology to address key synthetic and automation bottlenecks in the field, most recently with applications to infectious disease, and in the development of improved methods for the synthesis and conformational analysis of structurally well-defined carbohydrates.

VI. Training Program Faculty

The training faculty consists of 34 trainers in 6 different academic units on the Bloomington campus (**Table 2**) that boasts considerable diversity (26% female) while drawing on trainers at all academic ranks, including 6 assistant professors, 10 associate professors and 18 full professors (as of July 1, 2018). The training faculty has external grant support that exceeds $5.0M per year ($149,900 per trainer in the current year) (**Table 4**). 33 of 34 trainers have current extramural grant support, many with more than one award, including over 40 active NIH awards in total, with just one trainer currently between grants. Furthermore, virtually all trainers boast impressive track records of continuous extramural funding throughout their careers (see **Faculty Biosketches**). Research interests span a wide range of techniques, approaches and biological interests, characterized by four broad biological research foci in the areas of virus assembly, microbial infectious disease, cancer biology and molecular neuroscience and signaling (***Fig. 2***). Specific areas of technical expertise that underpin this biology include chemical synthesis of bioactive molecules and therapeutics, synthetic methodologies, supramolecular chemistry and directed evolution of biosynthetic catalysts (Brown, Cook, Flood, Lewis, Pohl, VanNieuwenhze and Zaleski), analytical and bioanalytical chemistry, metabolomics and instrumentation development (Baker, Clemmer, Jacobson, McKinlay, Pohl), biomaterials chemistry and physical cell biology (Douglas, Dragnea, Flood, Setayeshgar, Yu), NMR spectroscopy, electron microscopy, x-ray crystallography and laser spectroscopy (Dann, Giedroc, Thielges, Ziarek, Zlotnick), biophysical chemistry (Clemmer, Giedroc, Schlebach, Thielges, Ziarek) and cellular dynamics/microscopy of living cells (Shaw, VanNieuwenhze, Walczak, Winkler, Yu). Included among the training faculty are several strong microbiologists (Fuqua, McKinlay, Winkler), virologists (Mukhopadhyay, Zlotnick) and biochemists with interests in DNA replication and repair, RNA

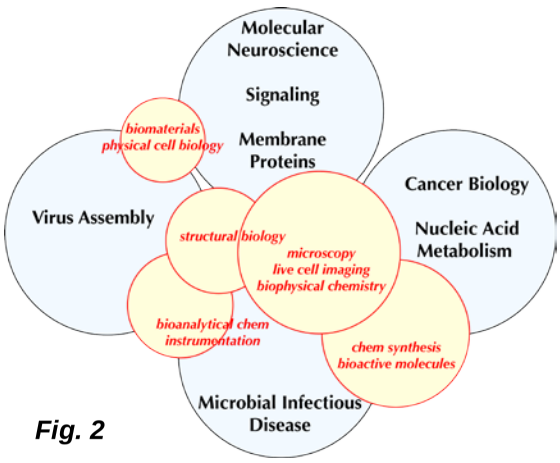

Fig. 2

editing, transcriptional regulation in cancer (Bell, Bochman, Hollenhorst, Hundley), all of whom have a history and interest in obtaining chemical and physical insights into their biology. Finally, in the last academic year we have assembled a core membrane protein proteostasis, structural biology, and molecular neuroscience group (Schlebach, Flood, Hohmann, Lu, Mackie, Tracey, Ziarek) with which we hope to develop a major future node of broad collaboration among QCB training faculty. We believe that full integration of these groups into the QCB Training Faculty and all associated educational and extracurricular activities "brings the biology to the chemists and physicists" thus avoiding the "chemical or physical biology ghetto." This arrangement allows biologists and more physically or chemically-inclined graduate students to work side-by-side in the same laboratory, without regard to prior training or degree program; this in turn, leads to joint publications and joint grant submissions, while enriching the educational experience for trainees and mentors alike. The QCB training faculty has a collective excellent past record of predoctoral training (**Table 2)**, with 226 total predoctoral students having completed their Ph.D. training over the past ten-year period, with the vast majority of these Ph.D. graduates (86%) continuing in research-related careers. Likewise, the trainer group has considerable postdoctoral training experience with 115 total postdoctoral scientists completing their training, and 90% engaged in research careers.

Cooperation, Interactions and Collaboration. A major strength of the QCB training faculty is the extensive degree of collaboration and interaction that characterizes the group (***Table D***). These interactions range from informal arrangements to full-scale collaborations involving joint co-authorship on papers (73 among the current group, ***Table D***) to collaborator or PI status on an MPI grant application,

Table D. Collaborations among the QCB TP Preceptors

Collaborators	Project	Co-mentor/ co-authorship/co-PI[1]
Douglas-Dragnea	Molecular assembly models of immature HIV-1	No/Yes/No
Douglas-Thielges	Self-assembly of biomolecular catalysts	No/Yes/No
Dragnea-Setayeshgar	Synthesis and biophysical properties of a bacterial bioadhesive	Yes/Yes (2)/**Yes**
Dragnea-Setayeshgar	Experimental and computational studies of optical interactions in bioinspired lattices.	Yes/No/No
Dragnea-Zlotnick	HBV and hepadnovirus stability and assembly	No/Yes (2)/No
Giedroc-Clemmer	Ion mobility-MS of metal sensor proteins	Yes/Yes (2)/No
Giedroc-Dann	Crystallography of CoV nucleocapsid protein	Yes/Yes/No
Giedroc-Dann	Crystallography of metalloregulatory proteins	Yes/Yes (4)/No
Giedroc-Winkler	Cell biology of transition metal homeostasis in *Streptococcus pneumoniae*	Yes (2)/Yes (7)/No
Giedroc-Zlotnick	NMR studies of the HBC core protein dimer	No/No/Yes
Jacobson-Zlotnick	Resistive pulse-sensing of single virus particles	Yes/Yes (7)/**Yes**
Mackie-Hohmann	Pharmacology of cannabinoid receptor signaling: agonists and allosteric modulators	No/Yes (10)/**Yes** (3)
Mackie-Lu	Cannabinoid and endocannabinoid signaling	No/Yes (6)/ **Yes** (2)
Mukhopadhyay-Clemmer	Structural determinants of S-palmitoylation	No/Yes (2)/No
Mukhopadhyay-Dragnea	Alphaviruses as bioinspired templates for imaging and cargo delivery	No/Yes (3)/**Yes**
Mukhopadhyay-Fuqua-Setayeshgar	Bacterial pseudotaxis through a porous environment	No/Yes (2)/No
Mukhopadhyay-Zlotnick	Alphavirus assembly mechanisms	No/Yes (5)/No
Pohl-Clemmer	New MS fragmentation approaches of complex oligosaccharides	No/Yes/Yes
Schlebach-Flood	Chloride-selective fluorescent probes for cystic fibrosis therapies	No/No/No
Schlebach-Mukopadhyay	Impact of viral membrane protein biogenesis on ribosomal frameshifting	No/No/Yes
Schlebach-Ziarek	Bicelle size and bacteriorhodopsin folding	No/Yes/No
Shaw-Walczak	Spindle microtubule organization and dynamics	No/Yes (6)/No
Shaw-Winkler	Superresolution microscopy of penicillin-binding proteins in pneumococcus	Yes/Yes (2)/No
Thielges-Clemmer	Cooperative formation of icosahedral Pro clusters	No/Yes/No
Thiegles-Cook	Evaluation of extended timescale 2D IR probes	No/ Yes/No
VanNieuwenhze-Winkler	Mechanism of action of new cell well antibiotics	No/No/**Yes**
VanNieuwenhze-Winkler	Analysis of peptidoglycan synthesis in bacterial growth and shape determination	Yes/Yes (3)/**Yes**
Winkler-Giedroc	NMR studies of peptidylglycan biosynthesis and chemokine killing in the pneumococcus	Yes/Yes (2)/No
Zlotnick-VanNieuwenhze	Assembly inhibitors of Hepatitis B Virus	No/Yes/**Yes**

[1]Co-mentor: jointly supervised a student well beyond service on an advisory committee; Co-authorship: joint authorship on publications (number of publications, if more than 1); co- PI, co-PI or Key Person on a submitted grant application (**bold-face** type if funded).

which currently numbers 11 funded proposals to date. As a result, true joint mentorship of students and QCB trainees is not uncommon, with 11 co-mentored students thus far, a number we believe will increase in the upcoming project period, catalyzed by a growing cohesion among the trainee cohort and trainers alike. The close physical proximity of trainer laboratories, core instrumentation laboratories and multiple conference rooms facilitates daily interactions and spontaneous exchanges between QCB groups via trainees or preceptors alike (see **Facilities and Environment**).

VII. Trainee Positions, Recruitment and Retention

Positions. The QCB training program was initiated with internal funding by the College of Arts and Sciences over four years (July 1, 2010-June 30, 2014) and is currently supported by an NIGMS award (July 1, 2014-June 30, 2019) at a fellowship slot allocation of 2/4/4/4/6 in years 01-05. The QCB Steering Committee annually solicits fellowship applications on April 15 from rising second- and third-year students in QCB preceptor laboratories, who apply for two-year and one-year fellowships, respectively. A letter of solicitation that outlines trainee application and appointment criteria is provided (**Appendix E.1**). The Steering Committee has evaluated 38 applications over four rounds of competition (2014-2017), which was used to support 17 trainees (28 slots) advised by 14 different PIs (41% of the current trainers). Four (4) of these 17 trainees (23%) are underrepresented minorities (URM), while 8 (45%) are female. Our year-05 competition has just been completed, and continues this trend in student demographics, but also includes the appointment of a female US military veteran.

In the upcoming project period, we request support for 34 NRSA-funded slots over five years, allocated 6/6/6/8/8 in years 01-05. We justify this request on the following basis: ***1)*** *We are the only NIGMS-funded, interdisciplinary training program on the Bloomington campus*, and thus can aggressively recruit the best students interested in chemical and physical biology to our program; ***2)*** *The depth, strong TGE-eligibility and quality of the applicant pool to our six feeder programs.* We receive an average of 714 applications per year (average UG GPA 3.5), and all applicants have significant undergraduate research experience (*e.g.,* 10.9 months, for new eligible entrants to the Chemistry and Biochemistry Ph.D. programs in Fall 2017) (**Table 6A**), an important predictor of success in graduate school. This results in the matriculation of 73 new training grant-eligible students (from 104 total entrants; 70% TGE) (**Table 6A**). ***3)*** *A sizable fraction of TGE entrants in our feeder programs join QCB trainer laboratories.* Of these 73 new TGE entrants per year, ≈21 (29%) join QCB trainer groups [given 117 current TGE students in trainer labs (**Table 1**), and ≈5.5 years, time-to-degree]. An NIGMS award of 6 slots allocated as 3 2-year appointments per year therefore represents ≤15% NIGMS-derived support of all TGE students in QCB trainer laboratories in a typical year. This ensures a highly competitive annual fellowship competition historically involving ≈10 applicants, *but one also based on past admissions statistics*. ***4)*** *We anticipate that the number of new TGE entrants and fellowship applications will rise significantly over the course of the next award period.* Of the 34 current QCB trainers, 10 have been added since 2016 and 7 since Spring 2018, all of whom are either new to Indiana University or are senior investigators who add strategic strengths in molecular neuroscience and receptor signaling, membrane protein structure, chloride channels and membrane protein proteostasis (***Fig. 2***). Furthermore, applications and new entrants to our newly created (2016) Cell, Molecular and Cancer Biology (CMCB) graduate program are trending sharply upward (Fall 2018 admissions are 6 new students, 4 TGE), and are now on par with other smaller QCB TP feeder programs. This reorganization was driven by QCB Steering Committee member Walczak, and is now managed by QCB trainer Hundley, as CMCB DGS, with support of this training program a major motivation for doing so. These two factors alone justify an increase to 8 slots in years 04-05. ***5)*** *A strong record of support of URM students relative to the pool of eligible entrants to our programs.*

Selection and Recruitment. The steering committee selects trainees for fellowship support by considering the application as a whole. We carefully review the standard metrics (undergraduate GPA, GRE scores) and like to see all applicants reach a minimum “metrics” threshold (**Appendix E.2**). However, we also strongly weigh undergraduate research experience and any co-authored publications, and the research summary itself. We tend to favor qualified applicants who present innovative and interdisciplinary projects that involve collaboration, and point toward a significant extension of current advisor-funded research. We also make a deliberate effort to diversify the existing trainee cohort, both in terms of research activity, QCB trainer laboratory and degree-granting program, but also with respect to gender and racial

diversity, giving strong consideration to applicants from underrepresented groups. These fellowship appointments priorities are consistent with ongoing and future efforts to increase the diversity of the *applicant pool* to our programs (see **Recruitment Plan**). The percentage of new URM entrants to our programs overall is 9.2% (2013-2017; range 5-13%) of new entrants eligible for support by this program (**Table 6A**). We believe that we can do better, considering that our current trainee cohort is far more diverse than the applicant pool. We have refocused the charge of the Recruitment Committee to proactively pursue applicants to *all* QCB feeder graduate programs; in addition, we plan to more strongly leverage the success of the APS Bridge program in recruiting a larger number of URM biophysics students (see **Recruitment Plan**). Another innovative feature of enhancing student diversity in our cohort is an emerging partnership with our SACNAS chapter, the President-elect of which is Perla Peña Palimino, a Biochemistry Ph.D. student. SACNAS, in collaboration with The Graduate Mentoring Center (see **Retention Plan**), has developed a visiting faculty speaker series, and plans to host an inaugural SACNAS Minority Alumni Speaker Series, supported by a Richard N. McKaig Leadership Award. This will allow our SACNAS student *cohort* to connect with URM faculty at other institutions, thus helping the QCB TP catalyze increased diversity of the applicant pool.

Retention. The training program has outlined a series of specific measures to ensure that all QCB trainees thrive in the research laboratory and consistently engage in professional development activities that lead to career success (see **Retention Plan**). These include a degree of oversight by the Steering Committee, including bi-annual (second-year) and annual (third-year and beyond) trainee reporting requirements that collectively ensure that the objectives of the QCB training program are being met. This same reporting tool will also be used to justify re-appointment to a second year of support for those students who receive a two-year fellowship. Major criteria for re-appointment are documented progress in the research laboratory, satisfactory performance in didactic courses, participation in QCB TP-sponsored activities, and a commitment to career development, including participation in the Career Development Symposium, and plans to attend a regional, national or international conference. Grounds for revocation of fellowship support are a failure to pass the 5th semester candidacy examinations, the desire to transfer to a non-QCB trainer laboratory, or to switch to the M.S. program. We also outline specific strategies in which the training program leverages its partnership with the University Graduate School, which provides fellowship support specifically targeted to a URM student (see **Retention Plan**). This has rapidly increased the diversity of the QCB trainee cohort beyond that of participating departments, thus creating critical mass and synergies among relatively small numbers of students; this in turn, fosters URM trainee success.

VIII. Training Outcomes

Graduate training outcomes for predoctoral students associated with all 34 QCB preceptor groups are summarized in **Table 5A**, which lists publications for all current and past (graduated in 2008 or later) training grant-eligible (TGE) students, and in **Table 8A**, which summarizes information on the effectiveness of our program in preparing students for their careers. **Table 5A** lists 742 publications from 252 eligible students from 32 of 34 QCB trainer groups (Asst. Profs. Schlebach and Ziarek have not yet published). Of these 253 students, 43 are considered new entrants to the program; thus, 210 past or more senior current students in QCB trainer groups have co-authored 741 papers, or ≈3.5 papers per student, an outstanding record of accomplishment. These 742 publications include *31 co-authored publications by 17 current or recently graduated QCB trainees supported by current NIGMS support (2014-2018), 13 of which derive from URM trainees (Perez, Ramos and Sanchez).*

Table 8A lists outcomes for all 81 recent TGE graduates from QCB trainer groups who took their degrees in or after 2013. 61 of these 81 graduates earned the Ph.D., yielding an M.S. attrition rate of 25%, a level consistent with major feeder program averages for overall attrition (2008-2012: Biochemistry, 18%; Biology, 21%; Chemistry, 41%). Of these 81 students, 8 are from underrepresented groups (10%), and 7 of these 8 students earned the Ph.D. (12% M.S. attrition). These graduates include one URM student (L. Weaver) who trained with QCB Steering Committee member Walczak, and has won both F32 and K99 awards as a postdoctoral researcher at Johns Hopkins University. Dr. Weaver plans to return to Indiana University this summer to participate in the Hudson Holland Summer Program (see **Recruitment Plan**). Mean time-to-degree among all 61 Ph.D. students is 5.7 years (**Table 8A**) and 6.3 years for the 7 URM graduates. Given the statistics of small numbers, we consider these numbers largely comparable, a

conclusion consistent with time-to-degree and attrition statistics available for QCB feeder programs overall. For example, considering 2008-2012 entrants, in Chemistry, the average time-to-degree is 5.5 years for all students (163) and 6.1 years for 19 URM students (12% of total); this average falls to 5.7 years with the elimination of a single student (among 18 URM graduates). The same figures in Biology are 5.9 (98 students) and 6.2 years (10 students: 10%), respectively. In Biochemistry, CMCB and Neuroscience, the time-to-degree is 5.9, 5.9 and 5.0 years, respectively, and includes two URM graduates total. In Physics, there were 71 total graduates with an average time-to-degree of 6.4 years, which includes 9 URM graduates (13%) at 6.6 years, time-to-degree. The rate at which URM students complete their Ph.D. degree programs, relative to all students overall, is also not significantly different, *e.g.,* 25% URM attrition vs. 21% for all students in Biology. This is consistent with the fact that the average percentage of URM students that enter our six programs (9.2%, **Table 6A**) is comparable to that percentage that completes the Ph.D. (10-13%). Thus, QCB TP graduate feeder programs are collectively characterized by an excellent overall track record of ensuring the success of students from underrepresented groups.

Examination of outcomes data over a longer 15-year timeframe reveals 232 graduates (TGE and non-TGE students) from 28 QCB trainer groups, with 19% finishing with M.S. degrees, thus painting a picture that is not substantially different from that described above. While many of these 61 Ph.D. graduates (**Table 8A**) are working in postdoctoral positions and pursuing further training, others are already engaged in a wide range of research-intensive or research-related careers in industry and academia, the latter including that of staff scientist, lecturer (3) and tenure-track Assistant Professor (5).

IX. Program Evaluation

The QCB TP leadership plans to distribute annual surveys to all preceptors (**Appendix C.2**) and current trainees (**Appendix C.3**) in the Fall semester of every year, and to alumni of the training program one, two and five years following graduation to determine if the training program is meeting its training mission and achieving our specific objectives (**Appendix C.4**). Complete contact information and current and previous position title of all former trainees will also be requested during this time. It is our direct experience that these survey instruments provide valuable feedback, not only on the mechanics of the program, but more importantly, the degree to which participation in the QCB training program has catalyzed the development or appreciation of new interdisciplinary research directions (for both current trainers and trainees). For alumni, we wish to learn the extent to which the program has prepared them for their current careers, leading to professional satisfaction. We are currently broadly publicizing trainee and career outcomes of current and former trainees on our program website (iuqcb.indiana.edu) by posting News regularly on the front page and via social media (Twitter @iuqcb), and by keeping the “Current Trainees” and “Alumni” pages of the website up to date. The PD and co-Director will continue to meet with the trainee cohort periodically, at least once annually, typically early in the Spring semester, to discuss the results of the previous Fall trainee survey and to broadly discuss both curricular and extracurricular components of the program so that its effectiveness as a cross-disciplinary training program can be evaluated *in real time*, and to seek suggestions as to what the program could be doing better. This meeting is meant to complement more regular (≈quarterly) meetings of the trainee cohort, called by our two rotating QCB Ambassadors, to implement and otherwise further engage members of the trainee cohort to lead student-run activities and implement any mid-course corrections as the program continues to mature. It was exactly this kind of meeting that early on led to the idea and potential content of Topics-based e-learning modules, which students themselves ultimately created to increase the potential for educating students from disparate backgrounds (**Section I.D.a**). At a more recent trainee cohort meeting, a wide-ranging discussion of our QCB TP extracurricular events in the context of a discussion of recent trainee and alumni surveys, led directly to a discussion of career development activities (**Section II**), and changes in the implementation of QCB Evenings, coupled by a transformation of the QCB Seminar Series into a true QCB trainee-invited seminar series (**Section I.D.g**). This “hands-on” continuous approach to program evaluation maintains the optimal value of the QCB training experience, while driving ownership of the program by the trainees, the desired outcome.

Plan for Instruction in the Responsible Conduct of Research

Responsible conduct of research (RCR) training, previously conducted as a course managed by the Poynter center at IUB, was fully integrated into the CHEM C689, Quantitative and Chemical Biology (QCB) Journal Club in Fall 2016 and Fall 2017, by Course Director and QCB trainer Charles Dann. In this context, all trainees participated in *eight hours of RCR instruction in four sessions*.

Topics in each session, presented in a guided discussion format are:

1) Ethics in peer review and authorship (case studies)

2) Mentor-mentee responsibilities and relationships (invited discussion and case studies) and data acquisition, management, sharing and ownership (case studies)

3) Research misconduct and policies for handling misconduct (case studies and discussion of procedures for reporting and subsequent actions from the Office of Research Integrity at IU)

4) Scientists as responsible members of society, contemporary ethical issues in biomedical research and policies regarding human subjects, *e.g.*, informed consent and study design (case studies).

As can be seen, these four intensive discussion sessions cover six primary topics of primary interest to trainees in our program. To enhance trainee engagement, specific cases for topics were chosen with trainee input, and the discussions were led by graduate students and moderated by Prof. Dann to ensure active participation, critical thinking about perspectives, and relevant dialogue. The first two of the RCR sessions were held in a conference room that allowed everyone to sit at a single table for discussions. The final two sessions were held off-campus over dinner, providing a different context that generally promoted a more deliberate style of discussion in a relaxed setting. These off-site sessions, despite being scheduled for two hours, generally lasted three hours or more with significantly more active engagement by trainees.

While understanding each RCR topic via example case studies, trainees were continually asked to relate cases to their own research experiences and to bring up additional questions that expand the discussion beyond the cases presented. Students were challenged to speak to the motivation for choices that were made, many that were ultimately deemed unethical, so that they could foresee and prevent themselves or others from making misguided choices. While online resources for RCR case studies were used to identify some examples for discussion, additional materials from primary literature, news outlets, and readings from nonfiction books were also utilized, *e.g.*, *The Secret Life of Henrietta Lacks* by Rebecca Skloot, *Radium Girls* by Kate Moore, to present a myriad of viewpoints and enhance trainee engagement. While learning outcomes are admittedly difficult to gauge in an open discussion course, every effort was made to ensure that all students participated. Based on dynamic conversations throughout the course and the manageable cohort size (10-12 students), we believe strongly that our trainees could serve as RCR liaisons among their graduate student peers upon completion of this QCB-associated RCR requirements.

Although QCB trainees only take this course once, this training is supplemented in a number of different ways throughout a trainee's graduate student career. We require that all QCB trainees complete the online Collaborative Institutional Training Initiative (CITI) training course (students select biomedical or physical science emphasis area) offered by Research Ethics, Education & Policy (REEP) at http://researchcompliance.iu.edu/eo/eo_citi.html after completion of the C689 RCR requirement, as a way to reinforce trainee knowledge of the material. In addition, the Office of Research Administration (ORA) sponsors a Responsible Conduct of Research Seminar series, which also meets NIH requirements, in the form of two 2-hr workshops each semester, which are jointly lead by research-active faculty and representatives of the Office of Research Compliance. Other department or program-specific discussions of material related to RCR are available to students. For example, QCB training faculty in Chemistry, including PD Giedroc and trainer Schlebach in 2017, routinely participate in a panel discussion of various aspects of research integrity, including authorship and data fabrication, during CHEM C500, Introduction to Research, that all graduate students take as part of their first-year research experience in the department (see Training Plan).

Finally, all QCB training faculty employ group-specific conventions that are used to continuously reinforce fundamental concepts of research integrity to trainees, particularly those related to data management, collaborative research, conflicts of interest, authorship and peer review. We find that a discussion of these topics is most effective when integrated into weekly laboratory group meetings, where a discussion of primary research data that they, the trainees, have generated takes place. This leads naturally to the core concepts of reproducibility and statistical significance, biological replicates, and the importance of well-designed control experiments, to support a particular hypothesis.

Plan for the Instruction in the Methods for Enhancing Reproducibility

Our QCB training program seeks to engage graduate students in cross-disciplinary training, research experience and classroom instruction in chemical and physical biology. As such, instruction in methods for enhancing rigor and reproducibility designed to teach trainees how to reach evidence-based conclusions and to solidify quantitative reasoning skills are organic to the objectives of our program (**Section I.C**), and are broadly distributed in a number of formats throughout a trainee's curriculum and graduate career trajectory.

These instructional plans begin with a research orientation exercise at the beginning of the first year, exemplified by CHEM C500, Introduction to Research, organized by the Chemistry DGS and QCB trainer A. Flood. The first six weeks of this course, through October 5 (the remainder is devoted to independent research; **Section I.D**), consists of twice-per-week panel discussions hosted by Chemistry faculty, many of whom of which are QCB trainers. Although this short-course covers many topics, including "successful habits of achieving a 5-year Ph.D.", *e.g.*, time management, and other topics that touch on research conduct and ethics, including conflicts of interest, policies with human subjects, mentor/mentee responsibilities and relationships, peer review and collaborative research (see **Plan for Instruction in Responsible Conduct of Research**), the course highlights the central importance of scholarship, and understanding the scientific underpinnings of a specific research project. We emphasize to students that it is *their responsibility* to identify and evaluate prior research that makes a project viable, and that the first year in graduate school is the ideal time to develop robust literature reading skills, a central scholarly attribute. This ability to read the literature is reinforced by QCB preceptors in their own research laboratories, as students are required to write a first-year C500 report that includes sufficient background material that *motivates* the experiments that were carried out in that first year.

There is also explicit discussion of how to collect and record data, and what constitutes "good" and "bad" data in C500. The concepts of the experimental design and the importance of control experiments, biological vs. technical replicates, are also discussed briefly, as are best practices of data management and data interpretation. Since other QCB feeder programs do not have a formal C500-like panel discussion of these topics, we propose to open up this course to second- and third-year QCB fellowship winners from other feeder graduate programs to audit, facilitated by the fact that the course meets in the evenings early in the Fall semester. It is important to recognize, however, that a C500 or similar classroom experience cannot substitute for the individual efforts of QCB trainers, who train students in rigor and reproducibility according to specific conventions of their own groups. To ensure that this happens, we plan to emphasize the importance of best practices for enhancing reproducibility, alongside RCR as currently done, to trainers in our annual (August-September) meeting of the QCB training faculty.

These early first-year plans are reinforced by deliberate efforts of QCB trainers who teach in the QCB curriculum to further relay these core concepts in enhancing reproducibility to trainees (**Section I.D**). We propose to develop a topics-based e-learning module in CHEM C681 that provides for basic instruction in the statistical analysis of data (from biological vs. technical replicates, *p*-values, various tests of statistical significance, variance, confidence intervals and propagation of errors, etc.) that will bring all trainees up-to-date on commonly used statistical approaches (**Section I.D.a,b**). This instruction is again reinforced by one-on-one trainee mentoring in QCB preceptor laboratories as part of their thesis projects. We have also incorporated specific reference to statistical criteria in the course content of CHEM C680, Introduction to Quantitative Biology and Measurement (**Section I.D.c**), particularly in the context of single-molecule methods, NMR dynamics and ligand binding models. Finally, QCB Journal Club, CHEM C689 (**Section I.D.d**), like many other graduate program-specific journal clubs and student seminar series, is also used to raise recognition of statistical significance and reproducibility, but using a different approach. During these activities, much like literature group meetings we regularly host in our own research groups, the speaker presents the results of recently published research; however, it is our experience that many students naturally gravitate to a broader discussion of the significance of one finding or another, based on error bars or other measure of uncertainty of the published data. Then, as trainees write manuscripts themselves, all of these "once-theoretical" concepts become very real. Here, trainees are instructed to ensure that the statistical tools, numbers of replicates, and methods used to establish "pair-wise" significance, for example, used to analyze the primary data are spelled out clearly in the "Materials and Methods" (or equivalent)

section of their manuscripts. Certainly, most journals now require a comprehensive description of any statistical analyses used, often prior to submission of the manuscript for publication. In addition, an important aspect of the peer review process and a trainee's successful revision of a manuscript for publication is often focused on questions of statistical significance and reproducibility. These examples illustrate that a natural consequence of preparing work for publication (**Table 5A**) is the process of "putting into practice" key elements of instruction in methods for enhancing reproducibility.

Finally, although not the major focus of the course, there are elements of instruction for enhancing reproducibility in MSCI M509, Basics of Scientific Communication, required of all QCB trainees (**Section II**). One part of this course (**Appendix B.8**) explicitly discusses making requests from colleagues for materials and reagents, and joint responsibilities that derive from the sharing of materials. Another part of this course discusses figure preparation for manuscripts, which touches on statistical significance and presenting "representative" data derived from multiple datasets. This discussion goes hand-in-hand with discussion, via examples, of the importance of a clear and concise "Materials and Methods" section of a manuscript. The standard that QCB trainers teach to trainees is that there should be sufficient detail that enables another investigator to "completely replicate" the experiments. This now involves a description of what was done to ensure authentication of both biological and chemical sources, and is something trainers in this program take very seriously. To illustrate, a current QCB trainee, B. Rued, was first author on a recent (2017) *Mol Microbiol* paper that was, in part, able to trace disparate biological findings on her target protein (GpsB) in the literature to distinct genetic backgrounds of *S. pneumoniae* strains. A MicroCommentary that appeared with her paper (Lewis, **2017**, *Mol Microbiol 103*, 913) advocated for a policy in which an author provides strain validation in the form of complete genomic sequence as part of the biological authentication of the findings and possibly, manuscript submission. This would bring the quantifiable principles of rigor and reproducibility to microbiology, much like publically available statistical databases of structural coordinates and NMR data are used routinely now. This paper was previously publicized on our website and discussed in C680 as an excellent illustration of pan-training program efforts to enhance reproducibility at the *chemistry-biology interface*.

In addition to the formal coursework-associated efforts detailed above, we plan to experiment with the introduction of topics pertaining to enhancing reproducibility to QCB trainee-organized quarterly meetings of the trainee cohort, in the upcoming project period. Here, a QCB trainer could lead a brief, informal discussion of a specific case study with trainees, *e.g.,* an example of a poorly written Materials and Methods, discussion of a specific figure/figure legend that details shortcomings in statistical analyses, or the implications of small number of animals to establish biological relevance, etc., while at the same time making trainees aware of the various web-based tools that are available to reinforce these concepts. This would allow QCB trainers to reiterate or enhance key elements of reproducibility that directly impact trainee development over the course of their graduate careers.