The Biophysicist

INSPIRE: Development of an Interdisciplinary Science Program in Research and Entrepreneurship

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ABSTRACT We developed the *Interdisciplinary Science Program in Research and Entrepreneurship* (INSPIRE) to address the changing career landscape that students with an interest in Biophysics, Physical Chemistry, and Biochemistry face. Third and fourth-year undergraduate Chemistry and Physics students participated in a 4-week, hands-on program that introduced applications of biophysical and biochemical techniques to drug discovery, while simultaneously engaging in a crash course on entrepreneurship and pharma. The principal objective of this inaugural, pilot program was to introduce undergraduate students interested in pursuing a PhD to the interdisciplinary nature of Chemistry and Physics research in the Life Sciences, while simultaneously introducing the idea of translating their future graduate work into a career in biotechnology.

KEY WORDS drug discovery; biophysical techniques; biotechnology; interdisciplinary learning; undergraduate education; hands-on learning; entrepreneurship training; research translation

I. INTRODUCTION

An education within science, technology, engineering, and mathematics (STEM)-associated fields such as chemistry and physics provides a critical advantage to students competing within a 21st century job market. According to the U.S. Bureau of Labor Statistics, STEM occupations have grown 79% over the past 3 decades and are projected to grow an additional 11% from 2020 to 2030 (1). Perhaps more important than the technical skills a STEM education provides are the critical thinking and innovation skills. Companies often cite these career-readiness skills as the most desirable asset in an employee, with a special emphasis on the need for employees who can work on a diverse variety of tasks. This need for graduates with an interdisciplinary skill set should be considered in contrast to most university curricula, which tend to segregate the sciences into distinct silos with labels such as physics, chemistry, and biology, but fail to show the students how these disciplines interrelate.

This segregation of the disciplines extends from undergraduate to graduate school. There are many reasons for this, but in part, it is because most PhD programs are still overly focused on developing the next generation of academics, while being, typically, much less concerned with providing the necessary training to PhDs targeting

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careers outside of academia. However, this approach is getting increasingly difficult to defend as the number of PhD students who are interested in ultimately landing a faculty position decrease each year (2). A *Nature* survey of graduate students in STEM fields around the globe found that only 56% picked academia as their first choice of a career (3). This number, which has been trending downward, is still highly inflated compared to the number of those students who will actually obtain a faculty position, with an even smaller fraction achieving a tenure track appointment (4). So long as we continue to frame graduate school, primarily, as a path to becoming a professor, it will get increasingly difficult to convince undergraduate students to enroll in chemistry and physics graduate programs. This recruitment challenge is only compounded by the prospect of an additional 3–5-year postdoc upon graduation with a PhD.

Recent research shows that many PhDs prefer non-academic careers upon graduation (5, 6). While many may consider an industrial career, it is not clear how many PhDs have truly considered starting their own companies, perhaps through translation of technology developed during their graduate research. And while some universities have a culture of promoting start-up companies (e.g., Stanford and MIT), most chemistry and physics students will attain a PhD without any training in entrepreneurship or innovation. Why then do we not introduce chemistry and physics students to the concept of translational research or seed the idea of starting their own companies at the start of their graduate studies, or even earlier, so they recognize that the pursuit of a PhD could be a pathway to an entrepreneurial career?

Introducing undergraduate students to translational research and innovation, before they begin their PhD, has other benefits. For instance, it gets students acquainted with and thinking about intellectual property early on. Similarly, students familiar with the challenges of translating research into a marketable product may choose to address these challenges as the research develops, not solely at the end of their PhD. This would better position them for spinning out a company at an earlier date, perhaps even before completing their PhD. Finally, business skills such as networking, people management, and presentation skills all translate to the research environment, but are generally not emphasized in an undergraduate STEM education.

One area of the innovation economy where chemistry and physics PhDs with a cross-disciplinary interest in the life sciences can uniquely contribute is within biotechnology and pharma. The primary driver of innovation and growth within the biotechnology ecosystem are start-up companies. In fact, in 2018 start-ups were responsible for some 80% of the total biopharma drug development pipeline (7).

Technologies from the physical sciences, developed by chemists and physicists, have had significant impact on advancing medicine. Nuclear magnetic resonance spectroscopy (NMR) and X-ray crystallography play a central role in drug discovery within many pharmaceutical companies, while advances in cryo-electron microscopy, super-resolved and single-molecule imaging are just beginning to reveal their full potential (8). As an example, the unprecedented speed at which scientists revealed the structure of the severe acute respiratory syndrome coronavirus 2 virus's spike protein was a major breakthrough in the COVID-19 pandemic. This structural determination was made possible by recent advances in biotechnologies, accelerated vaccine development, and enabled scientists to develop small molecules, antibodies, and other therapeutics to disrupt the proteins' function.

Quantitative chemical and physical insight enable rational, design-oriented approaches to the early phases of drug discovery. High-resolution biophysical and biochemical measurements provide detailed mechanistic, kinetic, and structural information on compound–target interactions. They may reveal binding kinetics, identify challenging targets associated with protein-protein interactions, and provide the foundation for fragment-based drug discovery. These techniques yield information on aggregation, solubility, and cell permeability and accelerate hit-to-lead drug discovery, prioritization, and optimization.

In recent years, a consensus has been growing for the need to develop interdisciplinary, STEM focused programming at the undergraduate level (9–13). Many of these programs focus on assembling teams of students to tackle interdisciplinary or transdisciplinary subjects while developing interpersonal and teamwork skills that are often not part of the pedagogy within a more classical, undergraduate science laboratory course. For example, Jeffery (14) developed a collaborative framework, centered around extending a database on protein function and structure, which linked undergraduates from different universities as well as high school students. This online, collaborative research experience in biophysics was largely motivated by the restrictions imposed during the COVID-19 pandemic. To provide hands-on experience in the experimental biosciences, however, requires students to be physically present within a research laboratory. A helpful reference is provided by Whittikar and Nunemaker (15) who have provided a series of reflections and recommendations for mentoring undergraduate researchers and for motivating these students to consider a future career in the STEM fields. Relatedly, Muzzio et al. (16) have emphasized the need to integrate knowledge across disciplinary boundaries to confer students with the behavioral skills that enable them to work well with others via developing skills in communication, time management, teamwork, etc. Their work established the importance of early exposure of undergraduate students from various STEM majors to the interdisciplinary field of biophysics, through a well-structured research plan.

The Interdisciplinary Science Program in Research and Entrepreneurship (INSPIRE) program was designed to expand upon these efforts by providing undergraduate students with a more holistic exposure to both the academic and industrial sides of biophysical research, and to help them make an informed decision about their choice of career paths in the future. It is also noteworthy that these programs underscore the importance of components such as: interdisciplinary training, collaborative participation, a need for experienced researchers at universities/industries to improve communication with students at all levels, adding content to improve behavioral/professional skills, etc. These components are all aspects incorporated into our program.

We developed the INSPIRE program as an intensive, hands-on introduction to the role of interdisciplinary biophysical and biochemical techniques in drug discovery, as well as a crash-course in entrepreneurship and innovation. The program explicitly targeted 3rd and 4th year undergraduate chemistry and physics students with aspirations for attending graduate school, framing the pursuit of a PhD as an on-ramp to the innovation economy. In this first-year pilot study, INSPIRE consisted of a 4-week summer curriculum including modules on bioinformatics, fragment-based drug discovery, protein expression and purification, biophysical assays, the pharmaceutical industry, and an introduction to innovation and entrepreneurship. The overall theme of this program has been illustrated in Fig 1.

In this inaugural year of the program, the theme was G-protein coupled receptor (GPCR) pharmacology. GPCRs constitute the largest family of membrane proteins in eukaryotes and are intimately involved in cellular signaling (17, 18). As such, they play a pivotal role in a variety of cellular processes from controlling neuronal and hormonal signaling to regulating cell homeostasis. Around 35% of all pharmaceuticals target GPCRs, and because only ∼12% of GPCRs have been subjected to large-scale drug screens, they hold enormous potential for the development of new drugs (19). Heterotrimeric G proteins connect GPCRs to intracellular signaling networks enabling them to receive and process extracellular signals. Students focused primarily on the Go protein, which is the most abundant heterotrimeric G-protein in the central nervous system (20). As such, alterations in signaling by the Go protein is implicated in neurodegenerative conditions such as Parkinson's and Alzheimer's disease. This served as an ideal system for achieving the pedagogic goals of the INSPIRE program.

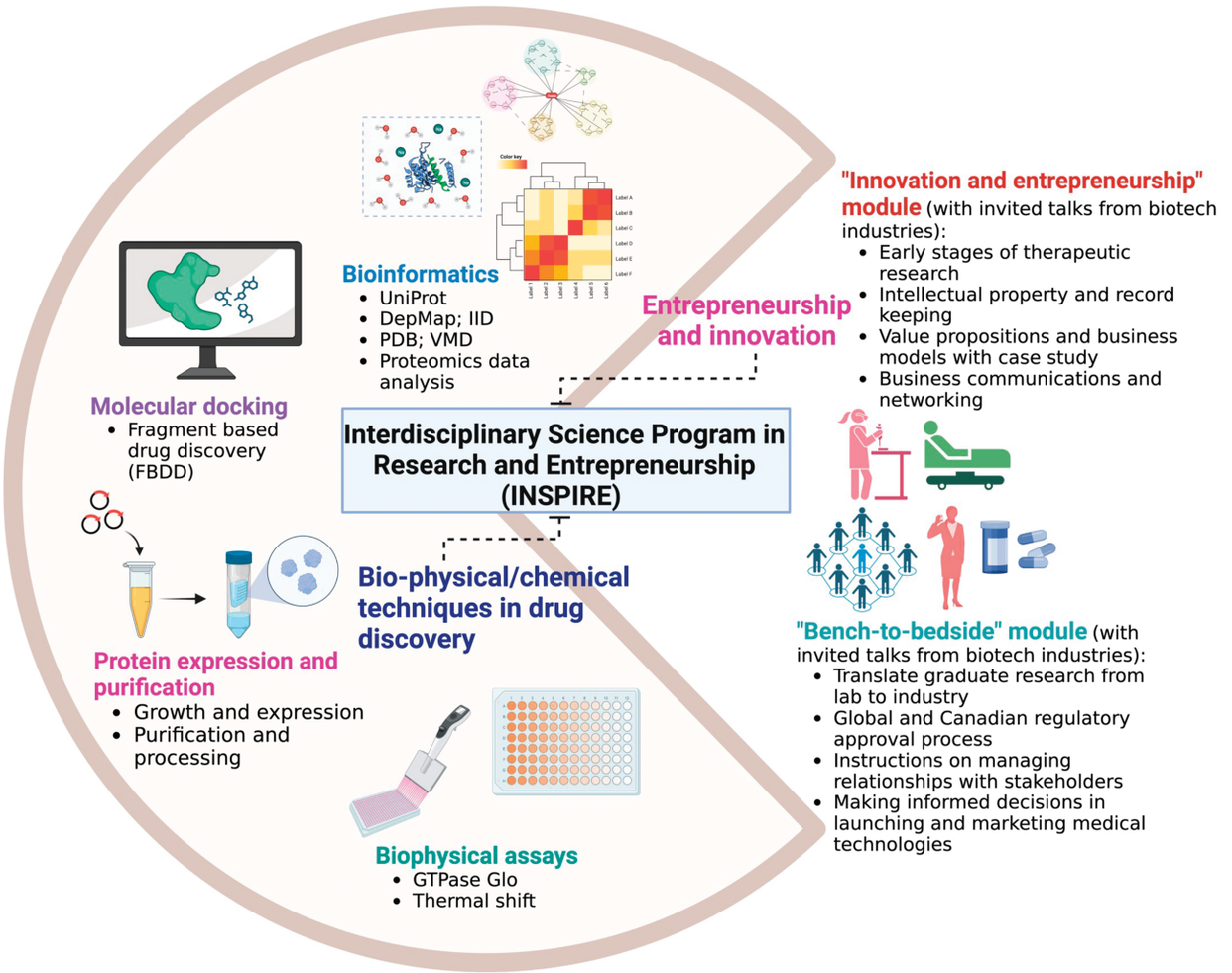

Fig 1. Illustration showing the components of the INSPIRE training program in drug discovery.

II. SCIENTIFIC AND PEDAGOGICAL BACKGROUND

The INSPIRE training modules were designed to familiarize students with all the stages of drug discovery, from early research through translation. With a combination of interactive lectures and hands-on activities, students were introduced to the various available tools and methods employed at different stages of the drug discovery pipeline. The 4 key learning goals for this program were

1. Students will be able to explain the various steps involved in drug discovery, from the early stages of therapeutic research through to translation of a discovery.
2. Students will be able to identify and apply a range of interdisciplinary approaches in modern medicinal/life-science research.
3. Students will be able to identify career opportunities in the life-sciences/biotechnology economy and evaluate how their skills and interests align with these potential career paths.
4. Students will leave the program with the recognition that discoveries they make in graduate school can be translated into a career path in the life-sciences/biotechnology economy.

To attain these learning goals students participated in a series of 4 scientific training modules and 2 industrial and entrepreneurship modules.

The scientific training modules allowed the students to develop a therapeutic strategy while exploring a biological target (see Table 1 for a summary of the tools/methods). In the Protein Analysis module, students learned how to make the pivotal

Table 1. Summary of tools/methods in the research training modules.

Module	Tools/methods	Description	Application
Protein Analysis	DepMap	Free online database	Selection of protein target and the model cell line
	Perseus	Open-source software	Analysis of proteomics data to explore biological processes and pathways implicated in diseases
	Uniprot	Free online database	Obtaining information about protein sequence, structure, and function
	IID	Free online tool/database	Obtaining protein-protein interaction (PPI) information
Fragment Based Drug Discovery (FBDD)	Enamine	Free online tool	Selection and filtering of compound libraries
	ChimeraX	Open-source software	Interactive visualization and analysis of molecular models
	Maestro	Commercial software (Free for educational purposes)	Molecular docking and high-throughput library screening
Protein Expression and Purification	GenSmart Design	Free online tool	Design of DNA plasmid for bacterial transfection
	Bacterial transformation	Biochemical method	For protein expression
	Protein extraction	Biochemical method	For protein extraction
	Affinity Chromatography	Biochemical method	For protein purification
	SDS-PAGE	Biochemical method	For protein quantification
Biophysical Assays	GTPase Glo-Sensor Assay	Biophysical assay	Evaluation of protein function
	Thermal shift analysis	Biophysical assay	Evaluation of protein stability and binding

decision of selecting a therapeutic target (e.g., protein/signaling pathways implicated in the disease, protein-protein interactions, protein structural/functional information, etc.) with the aid of online resources/open-source software. The next step was to then identify "hit" molecules capable of binding to the target protein. FBDD, a common hit identification approach in drug discovery, was introduced as the second module. Students learned how to obtain and refine protein crystal structures, select a desired binding site on the protein, select a fragment library and use molecular docking to screen the library against the protein and identify potential hit fragments. The next step was to prepare a recombinant version of the target protein in the Protein Expression and Purification module. In this third module, students expressed the GPCR Goα in bacterial cells and purified it by using immobilized metal affinity chromatography. In the last module on Biophysical Assays, 2 assays were introduced that evaluate compound binding based on protein stability and function. The thermal shift assay measures the change of protein stability upon binding and the GTPase Glo-sensor assay evaluates the effect of binding on GTPase activity of the protein. Consequently, as these scientific training components were intended to educate the students in pharmaceutical research by combining knowledge from various disciplines such as bioinformatics and molecular biology, we believe it fits well within the purview of achieving learning goals 1 and 2.

The industrial and entrepreneurship modules supplemented the scientific program with the aim of introducing the students to the life-sciences/biotechnology economy. The Innovation and Entrepreneurship module was designed to educate science students on the translation of scientific discoveries from the lab to the marketplace through the founding of a start-up venture. Students also participated in the From Bench to Bedside module, which led students through the initial stages of research and development at a pharmaceutical company to the launch and marketing of medicines in Canada. It is commonly seen that graduate students often lack any practical knowledge about research translation, which is something that should be rectified starting at an early stage—supporting achievement

of learning goals 3 and 4. Similarly, the students were provided with opportunities to understand the business aspects of drug discovery directly from some of the experts driving this field via lectures and integrated short activities.

A. Classroom format

Training modules were designed to be highly interactive and collaborative. The bioinformatics-based modules (i.e., Protein Analysis and FBDD modules) were held in a computer lab, while experimental modules (i.e., Protein Expression and Purification and Biophysical Assays modules) were held in chemistry teaching labs. Sessions started with a 10-min presentation by TAs to provide instructions on the module and class activities. The students were divided into groups of 4-5 and specific tasks were assigned to each group. During these sessions, students were encouraged to raise questions and problem solve for potential solutions among the group. Course instructors and teaching assistants facilitated and directed these discussions at the tables of each group. At the end of the sessions, students recorded their data according to the instructions provided.

B. Group presentations

At the end of each module, each student group independently presented their findings to the class. For each module, student groups collaboratively prepared a presentation in a separate session. Presentations included a module introduction, learning objectives, results, and suggested modifications to improve the module. Presentations were jointly presented by all group members for 10 minutes followed by 5 minutes of questions and discussion from the rest of the cohort and instructors.

III. METHODS

The inaugural INSPIRE program ran from June 13 to July 8, 2022. A pool of 25 undergraduate students from STEM fields were selected through an open application process without holding any biases towards their primary specialization subject other than fulfilling the general requirements of the INSPIRE program (i.e., having a desire to pursue interdisciplinary graduate research in the physical and life sciences). However, both the theme of the program along with the scientific relevance to pharmaceutical research and entrepreneurship were clearly emphasized.

Of the 25 students admitted, all expressed an interest in attending graduate school. We queried participants for their preferred graduate program with the top choices being either biochemistry/chemistry, biology (any field), or physics (indicated by 13, 6, and 4 students, respectively). Over half the participants self-identified as women. These numbers correlated with undergraduate degree in the application pool (unexpectedly, we attracted a lot of interest from biology students). We did not explicitly ask if students were interested in biophysics, which is data we hope to collect in the future.

Details pertaining to the components covered under the Scientific Training and Industrial and Entrepreneurial modules are presented below.

A. Scientific training modules

1. Module 1, Protein Analysis

The Protein Analysis module aimed to introduce students to various bioinformatics methods for identifying and analyzing disease-related target proteins using model proteins from the GPCR family. Throughout the module, students utilized a range of online tools and resources, including: DepMap (21), UniProt (https://www.uniprot.org/), IID (22), VMD (visual molecular dynamics) (23), and Perseus (24) to gain hands-on experience in acquiring and analyzing protein data.

The DepMap module was designed to help students understand the role of genes in cancer progression by utilizing the database's genetic and pharmacological blueprint of $>$2,000 different cancer cell types. Students explored gene essentiality, target tractability, and mutation effects using GPRC5A as a model protein and analyzed correlations between specific genes and treatments across 600 cancer cell lines using the data explorer tool. Each student group was also assigned a unique protein from the GPCR family and explored its interactions with various drug molecules.

The objective of the UniProt module was to teach students how to use the UniProt database to study and extract basic information about the structure and function of proteins with a focus on protein annotations, subcellular localization, sequence search, 3D structures, mutagenesis, and disease characteristics. Students used the same protein assigned to each group in the DepMap module to now determine its functional and pathological properties.

The IID database module aimed to teach students about PPI and their significance in biological processes. Using 2 members of the GPCR family, CXCR2 and CXCR1, students learned how PPI data can be used to identify alternative pathways and to explore various search methods available in IID. The module included an exploration of interaction topology using degree and clustering coefficient concepts, and groups were assigned multiple genes and asked to map their interactions across the interactome, identifying context-specific interactions and topology.

To further enhance the students' understanding of protein structure and function, the VMD tool was introduced in the next module, allowing them to browse and select protein crystal structures from the Protein Database Bank (https://www.rcsb.org/) and investigate their 3D properties. Using the 6KPC protein as a model for visualization, students were able to explore the protein's hydrophobic and hydrophilic surfaces and residues, its various domains, and interactions between residues that form secondary structures, ultimately applying their newfound skills to investigate key characteristics of their assigned protein.

To help students understand how to analyze and process proteomics data, the final section of the course introduced the software tool Perseus. Students used a case study of a proteomics dataset produced by Geiger et al. (25) with the Stable Isotope Labeling by Amino Acids in Cell Culture (SILAC) method. Through the module, students learned various types of proteomics data analysis using Perseus, including data filtering, normalization techniques, and intuitive representations using scatter plots, histograms, volcano plots, and intensity curves. Additionally, the module introduced Perseus-based statistical techniques such as Student *t* tests, principal component analysis, hierarchical clustering, network enrichment, and correlation analysis. Students were given the freedom to explore disease biology and investigate potential drug targets. This more open-ended, exploration-focused module introduced students to the initial phase of drug discovery where you find a patient need and a druggable protein/pathway that could potentially address it. This also encouraged discussion and collaboration among students allowing them to become comfortable with each other and the instructors.

2. Module 2, FBDD

FBDD is a method for finding new pharmacologically active medicines and exploring potential new therapeutic targets (26). This module's objective was to inform students about the rational drug design process by using FBDD and several computational tools for drug screening such as Enamine (https://enamine.net/), ChimeraX (27), and Maestro (28). This module taught students how to use their knowledge of medicinal chemistry to develop rational drug designs and find potential hit fragments to target the heterotrimeric G protein subunit alpha (Goα) protein.

A brief introduction was given at the beginning of the module to inform students about the history and evolution of FBDD, its influence on drug discovery, and its progressive departure from conventional drug research. Each group of 5 students was given the chance to rationally select their target binding site of interest. In this phase, students discussed in groups how they planned to target the Goα protein (i.e., allosterically, orthosterically, etc.). A fragment library appropriate for their suggested targeting technique was then chosen using Enamine. The fragments were then docked onto the chosen binding site on Go utilizing high throughput virtual screening (HTVS) with Maestro Schrödinger (the software licenses for Maestro were generously donated by Schrödinger). The interactive viewing and analysis of computational molecular models were made possible by the software ChimeraX. Students

spoke about their protein targeting strategy, library and hit selection criteria, interpretation of the structure-activity connections of hit fragments, and their proposed hit optimization utilizing rational drug design during their final presentation.

3. Module 3, Protein Expression and Purification

After identification using FBDD, the hit compounds must be screened against a recombinant form of the target protein using a biophysical assay. In this module, students prepared recombinant Goα protein with an N-terminal 6xHis and Maltose Binding Protein (MBP) tag with a Tobacco Etch Virus cleavage site, which was overexpressed in *Escherichia coli* BL21 (DE3) cells. The *E. coli* cultures were harvested the following day after sufficient growth and induction with isopropyl-D-1-thiogalactopyranoside (IPTG).

Students prepared 1-liter bacterial cultures to overexpress recombinant Goα protein, induced the cultures with IPTG, and harvested the cells the following day. Protein purification was performed in pairs, with students given 20 mL of lysed cells to filter and load in a Ni-NTA column. They purified His-MBP-GOα and subsequently removed the tag to isolate GOα. Quality was assessed by electrophoresis and intact mass analysis. At the end of the module, students learned to perform a protein concentration assay, analyze data, and create figures in Microsoft Excel. They also analyzed gels on Image Lab (https://www.bio-rad.com/fr-ca/product/image-lab-software). At the end of the purification module, a discussion was held to reinforce concepts and foster a collaborative workspace. Students presented their purification results and discussed pitfalls during expression and/or purification. Instructors presented potential scenarios and questions on protein expression and purification to assess students' ability to catch mistakes and to suggest viable solutions. This allowed students to communicate and apply the materials they learned.

4. Module 4, Biophysical Assays

The final training module aimed to provide students with a hands-on experience in evaluating the impact of compound binding on the stability and functional attributes of target proteins. To achieve this, 2 biophysical assays were included in the module. The first was the thermal shift assay, which measures changes in the thermal denaturation temperature (melting temperature) of a protein to determine its stability, a property that is often altered by drug binding. The second assay was the GTPase Glo-Sensor Assay, a bioluminescent assay that monitors the activities of GTPases and their immediate regulators. This assay was used to track the effect of compound binding on the GTPase activity of the GOα protein.

To ensure that students had a firm grasp of the background theory and experimental procedures, these were thoroughly explained and reviewed prior to conducting the assays. This approach proved effective in providing students with direction and confidence as they performed the assays. The class was divided into 5 groups, each investigating the effects of different regulators or components of the reaction. This encouraged meaningful discussions among students about the numerous factors affecting the signaling pathway and how to activate or inhibit certain effects. The students presented their findings and faced questions from their instructors and peers. Communication between and among groups was critical to their teamwork development and successful experimentation. The students learned how to operate instruments, collect raw data, and process it through Excel to create figures for their final presentation.

In addition to the hands-on component of the module, a series of lectures were delivered by expert faculty members introducing students to modern biophysical techniques with concrete examples of how the techniques can be used to further a drug discovery program. Table 2 provides a list of the lecture titles and their relevance to drug discovery.

B. Industrial and entrepreneurship modules

1. Module 1, Innovation and Entrepreneurship

The Innovation and Entrepreneurship module was intended for students in the physical,

Table 2. Biophysical lectures.

Lecture topic	Drug discovery relevance
Single-molecule Imaging	Quantify GPCR oligomerization, interactions, and spatial organization
NMR I	Combinatorial screening to quickly generate a high-affinity region-specific hit molecule
Molecular dynamics	Predict drug-induced protein conformational changes
Ultrasensitive protein detection	Detect low-abundance biomarkers in patients in response to drug treatment
NMR II	Identification of druggable allosteric pathways
Single-molecule spectroscopy	Investigate dynamics induced by the local environment or structural orientation that may be hidden within ensemble averages
Intrinsically disordered proteins	Improve rational drug design on novel molecular targets
Crystallography	Observe angstrom-level protein-drug interactions to guide compound development
EPR	Observe drug-induced dynamic rearrangements within a protein

chemical, and life sciences, and served as an overview of the process of translating scientific research into practical applications with societal impact. This module aimed to educate science students on the transition from science to the marketplace and direct those who express an interest in entrepreneurship to further resources. The format consisted mainly of lectures with integrated short activities and real-world examples drawn from scientific research and technology.

The following topics were covered during the module:

- Introduction to the course and overview of innovation within the context of university research, including a case study.
- Exploration of the sources of ideas, the origins of companies, the innovation gap, and the distinction between invention and innovation, followed by a brainstorming session using design thinking.
- Overview of intellectual property and strategy, including record keeping.
- Introduction to value propositions and business models, including a case study of science-based companies.
- Overview of business communications and networking, with a practical component.
- Discussion of the steps to be taken when one has an invention, including working with the university, co-inventors, and supervisor.

In addition to the lectures, a networking lunch was held featuring invited guests from newly founded life-science companies, industry, and academic research groups. This event provided students with an opportunity to apply the skills acquired during the module and foster connections among peers and with the invited guests.

2. Module 2, From Bench to Bedside

The objective of this module was to provide an overall understanding of the entire drug discovery process, from the initial stage of research and development to the launch and marketing of medicines in Canada (See Table 3). The module was provided in an interactive lecture format.

The module covered topics such as:

- Transforming medicine from the laboratory to large-scale production.
- Navigating the global and Canadian regulatory approval processes.
- Career opportunities in regulatory affairs, market access, and best practices for launching a medicine in Canada.
- How to effectively negotiate and manage relationships with stakeholders.
- How to make informed decisions when launching, marketing, and selling medicines.

In addition, 2 guest speakers from pharmaceutical companies within the Greater Toronto Area visited, participated in presenting the material, and interacted with students after the class lecture.

Table 3. From bench to bedside sessions.

Session title	Topics
Introduction to pharma R&D: Clinical trials and manufacturing	• An overview of the global drug discovery process • Transforming the medicine from lab to factory-scale • Navigating the global and Canadian regulatory approval processes
Regulatory affairs: getting the drug approved	• Overview of the Canadian healthcare system • Summary of Canada's pharmaceutical environment • Effectively navigating the systems • Effectively negotiating and managing relationships with stakeholders • Career opportunities in Regulatory Affairs
Market access: getting medicines reimbursed	• Best practices for launching a medicine in Canada • Understanding the market access processes and stakeholders • The importance of multichannel promotion • Introduction to Pharmaceutical Sales • Changing behavior through persuasion and influence
Launching, marketing and selling medicines in Canada	• Introduction to the Canadian life sciences ecosystem • An overview of the generic and biosimilars industry in Canada • An overview of vaccines • The emergence and importance of biologics

C. Demographics and survey data

On the last day of the program (July 8, 2022) we surveyed participants asking for both feedback on what they found most useful/informative and on areas in which they felt the program could improve (survey design adapted from Piunno et al. (13)). Participants were informed by the course instructors that the surveys were voluntary and would be used both to inform the program and be integrated into pedagogical research that may result in a published study. Oral consent to use the surveys for these stated purposes, in the presence of the program instructors, was provided by all participants. The surveys were anonymous, and we could not identify individual participants during or after data collection (this information was conveyed to all participants). Student numerical survey results were analyzed through a weighted average of the student's responses where the weight was the proportion of students who selected that score. The number of students who responded to the survey is accounted for in the error associated with each average.

III. RESULTS AND DISCUSSION

Overall, we received positive and reassuring feedback from this first cohort of students (See Table 4 for a summary of responses. For access to the full survey responses, see the Supplemental Material). Many students said the program gave them the chance to learn about novel biophysical techniques while also improving their awareness of the academic and corporate world of drug development. The program's value in terms of networking with other students and professors was also noted. Many students stressed the value of the hands-on experience the curriculum offered, both in the lab and in computational contexts, facilitated by the absence of pressure to produce results. Additionally, several students pointed out that the lab experience was particularly beneficial because it was uncommon for undergraduate programs to offer something similar. The program received praise for its balance of computational and wet lab experience, as well as for providing students with a chance to collaborate and work with students from different backgrounds. Students were encouraged to ask questions and engage in discussions during the lectures. To maximize their chances of interacting with the faculty presenters, and to provide an opportunity to discuss the concepts learned, we asked the presenters to keep their lectures short (20–30 minutes) to allow for more time to interact with the students. Many students favorably commented on the interactive nature of the lectures.

Table 4. Participant survey responses (1, *strongly disagree*; 2, *disagree*; 3, *somewhat disagree*; 4, *neither agree nor disagree*; 5, *somewhat agree*; 6, *agree*; 7, *strongly agree*).

Survey statements	Avg.[a] score	Std. dev.
What was your level of interest in the lab portion of the program (*i.e., When you first learned about it)*?	6.6	0.7
The laboratory manual provided information required to conduct the experiments effectively.	5.9	1.1
The laboratory module activities stimulated my interest in the subjects.	6.4	0.8
The difficulty level of the laboratory modules was appropriate.	6.1	0.5
The pace of the program was appropriate.	5.7	1.2
I have more of an understanding of how interdisciplinary science promotes drug discovery.	6.7	0.5
I feel more confident in my understanding of modern biophysical techniques.	6.3	0.6
I encountered new concepts I had not been exposed to during my formal academic courses.	6.6	0.6
The instructors were helpful.	6.9	0.3
The instructors were well prepared.	6.9	0.4
The teaching assistants were helpful.	6.7	0.5
The teaching assistants were well prepared.	6.6	0.5
I feel more confident in my ability to perform biophysical assays.	6.2	0.7
I feel more confident in my ability to find the disease relevance of a protein.	6.4	0.5
I feel more confident in my ability to dock fragments to a protein.	6.2	1.1
I feel more confident in my ability to visualize proteins.	6.1	0.9
I feel more confident in my ability to express and purify proteins.	6.1	0.9
I acquired a better understanding of how innovation happens in a university research context.	6.5	0.5
I better understand the various aspects of the pharma industry.	6.4	0.6
I would recommend this program to other undergraduate students.	6.9	0.3

[a] Avg., average; Std. dev., standard deviation.

While participants had a mostly favorable impression of the program, we received a number of suggestions for how to improve the program moving forward. For instance, some students felt that the step-by-step, guided instruction we provided on computational tools such as Maestro and VMD would have benefitted from more of an overview of the algorithms. This was a balance we had to navigate throughout development of the program, that is, weighing the need to provide background content with the desire to get the students working with the tools. Similarly, a few students commented that some modules were a bit rushed and suggested that we lengthen the duration of the program. Some students felt that because activities in the computer lab and the wet lab could be done by only one person at a time, due to limited materials and bench space, this restricted the learning opportunities. Again, here we are balancing 2 needs, one is the cost of running the program, in terms of hardware and consumables, and the other is a desire to provide each student with a sufficient level of hands-on experience. Finally, we noted a mix of responses in regard to the translational biotech modules. Many of the students really appreciated being exposed to this aspect of the science, while many others were uninterested and would have preferred more talks on the actual science. These responses reveal a challenge faced by any program of this nature, that is, pitting a desire to expose students to the practical/pragmatic aspects of a career in science, against the pure enthusiasm most young scientists have at such an early stage of their career.

We next relate information gained through the survey responses directly to the primary learning outcomes for the program:

1. *Students will be able to explain the various steps involved in drug discovery, from the early stages of therapeutic research through to translation of a discovery.*

Students got hands-on experience with early stage in-silico docking, bioinformatics, and biochemical research. Several students reported a more nuanced understanding of the drug discovery process beyond just learning individual concepts in their coursework. One student identified "the practical experience to be the most valuable aspect" of the program. Students also noted that the entrepreneurial and translational aspects were mostly consumed via lecture. In future years, an interactive case study focused around strategic translational and business decisions could provide students with a more concrete grasp on later-stage drug discovery. We are also planning to enable students to spend one day with a start-up company housed within an incubator space on campus.

2. *Students will be able to identify and apply a range of interdisciplinary approaches in modern medicinal/life-science research.*
   Between the diverse entourage of instructors, faculty lecturers, university leadership, and industrial partners, the interdisciplinary nature of drug discovery was on full display. Several students identified the lecture series on biophysical techniques to be "highly valuable." However, some students felt overwhelmed by the breadth of material or felt more enthusiastic about some modules/topics while less so about others. In future years, we are planning on allowing students to enroll in a subset of modules that most pique their interest. This will enable us to develop longer modules of more depth while better tailoring the program to the varied academic backgrounds of the students.
3. *Students will be able to identify career opportunities in the life-sciences/biotechnology economy and evaluate how their skills and interests align with these potential career paths.*
   Driven by speakers largely from outside of academia, entrepreneurship focused modules provided students with an entry-level understanding of the life-sciences/biotechnology economy. Several students identified the "networking opportunities in the program to be highly valuable," but they reported less enthusiasm about the business aspect of the program and were significantly more excited about the science or career aspects. This might be partially rectified by better motivating these sessions, perhaps, by providing statistics on the actual career paths of PhDs and inviting recent graduates who found employment within industry and/or at a start-up.
4. *Students will leave the program with the recognition that discoveries they make in graduate school can be translated into a career path in the life-sciences/biotechnology economy.*
   Students were introduced to a diverse network of future academic collaborators, industrial partners, entrepreneurial mentors, and fellow entrepreneurs. This network will likely have a far greater impact on their success than any one individual technique ever could. Still, overall, the students reported less satisfaction, or perceived personal relevance, with the translational discussions. To connect better with the participants, we intend to invite to speak, and/or hold a round table with, actual graduates who went on to translate their research into a business.

IV. CONCLUSION

We intend to follow up with all participants in the 2022 INSPIRE program over the summer to ask if they did indeed apply to a graduate program, or if they instead pursued a job in industry or elsewhere. It will be of interest to collect these metrics in all future years over the summer one-year post completion of the program in which the students participated. This will be done by sending a survey link over email, and we will indicate that their responses to the survey will be anonymous. This follow-up survey will provide one indication of the success of the INSPIRE program in steering students toward a career in interdisciplinary science.

We hope that the lessons learned through development of the INSPIRE program will inform the creation of similar programs at other institutions. With the changing landscape of a career in

chemistry and physics, it is becoming increasingly important to help students chart their future course. By exposing students early on to the idea that options exist beyond academia, and that the research they undertake may one day translate into a company or business of their own design, programs like the INSPIRE program described here are better preparing our students for the challenging and exciting road ahead.

USE OF HUMAN SUBJECTS

A Human Participants Ethics Protocol was approved by the University of Toronto (RIS Human Protocol Number 42854).

SUPPLEMENTAL MATERIAL

The full survey responses as well as a program manual with all scientific module assays are available at: https://doi.org/10.35459/tbp.2023.000248.

AUTHOR CONTRIBUTIONS

JNM was responsible for conceptualization, funding, and project administration; TS and TR were responsible for supervision, methodology and data analysis; and QFA, BK, EJQ, and RR developed all scientific modules. All authors contributed to writing and editing the manuscript.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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