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SPECIAL ISSUE: MATHEMATICAL BIOLOGY EDUCATION

High School Internship Program in Integrated Mathematical Oncology (HIP IMO): Five-Year Experience at Moffitt Cancer Center

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Abstract
Modern cancer research, and the wealth of data across multiple spatial and temporal scales, has created the need for researchers that are well versed in the life sciences (cancer biology, developmental biology, immunology), medical sciences (oncology) and natural sciences (mathematics, physics, engineering, computer sciences). College undergraduate education traditionally occurs in disciplinary silos, which creates a steep learning curve at the graduate and postdoctoral levels that increasingly bridge multiple disciplines. Numerous colleges have begun to embrace interdisciplinary curricula, but students who double major in mathematics (or other quantitative sciences) and biology (or medicine) remain scarce. We identified the need to educate junior and senior high school students about integrating mathematical and biological skills, through the lens of mathematical oncology, to better prepare students for future careers at the interdisciplinary interface. The High school Internship Program in Integrated Mathematical Oncology (HIP IMO) at Moffitt Cancer Center has so far trained 59 students between 2015 and 2019. We report here on the program structure, training deliverables, curriculum and outcomes. We hope to promote interdisciplinary educational activities early in a student's career.

Keywords Mathematical modeling · Education · High school · Cancer · Oncology · Interdisciplinary

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1 Introduction

The H. Lee Moffitt Cancer Center (MCC) is a domestic, non-profit organization in Tampa, FL, USA. It is an independent institution and an NCI-designated comprehensive cancer center. The Center has over 7000 employees serving a population of over 21 million people. In 2008, MCC through the guidance of Robert Gatenby formed the Department of Integrated Mathematical Oncology, IMO. The central goal of the IMO is the integration of theoretical and computational modeling tools with experimental cancer research and clinical translation (Anderson and Quaranta 2008). By using a range of mathematical modeling approaches targeted at answering specific questions for different cancers, the IMO aids in the elucidation of aspects of basic cancer biology, involving complex, dynamics systems (such as interactions between multiple cell types and micro-environment in formation of bone metastases) as well as development and testing of treatment strategies. This multi-model, multi-scale approach allows for a diverse and rich interdisciplinary environment that has created many novel approaches for the treatment and understanding cancer (Poleszczuk et al. 2017; Walker et al. 2019; Altrock et al. 2015, 2018; Ferrall-Fairbanks et al. 2019; Andor et al. 2017, 2019; Araujo et al. 2014; Kaznatcheev et al. 2019; Zhang et al. 2017; Stanková et al. 2019; Gatenby et al. 2019a, b; Marusyk et al. 2014, 2016; Karolak et al. 2018, 2019a; Silva et al. 2017; Sudalagunta et al. 2018; Park et al. 2019; West et al. 2019; Enderling et al. 2019). Crucial to our success is the true integration of theoretical models with cancer growth, evolution and treatment data, which requires sophisticated imaging techniques and potentially new experimental and clinical protocols. To this end, the IMO is an interdisciplinary team of scientists incorporating experts in the field of mathematics, computer science, physics, genomics, evolutionary biology, ecology, imaging and visualization to name but a few. As of 2020, the IMO has eight faculty members, 14 postdoctoral fellows and six graduate students.

The *H*igh school *I*nternship *P*rogram in *I*ntegrated *M*athematical *O*ncology, HIP IMO, delivers interdisciplinary team science research experiences for high school students aged 16 or older by the time of the internship (http://www.moffitt.org/HIPIMO). Selected students spend 8 weeks during the Hillsborough County public schools summer break in the IMO department on the Moffitt Cancer Center campus. This mentored summer training program is designed for motivated aspiring scientists to help prepare them for interdisciplinary cancer research careers. Working under the direction and guidance of faculty/scientist mentors in Moffitt's IMO department, interns are involved in activities designed to foster the development of lifelong research skills. Students are assigned individual research projects appropriate to their interests and abilities. Applications are invited beginning November 1 for the following summer and close February 1, with enrollment decisions communicated by end of February of the internship year. Following a generous donation in 2017, HIP IMO students in the past 2 years received a $1000 scholarship. Support for accommodations and travel is provided for out of town students.

Students collaborate with their mentor to create a research project with achievable goals in the time allotted. They gain familiarity with standard methodologies

in a safe environment, participate in scheduled laboratory meetings, acquire necessary data through experimentation, computation, surveys or other means and document findings in an appropriate format (laboratory journal, audiovisual recording or digital databases). Students review and discuss their findings with research mentors, draw conclusions and make new plans. Students gain experience by designing and delivering a 15-min presentation to department members, Moffitt leadership, parents, teachers and patients at the HIP IMO research day. At the end of the program, they write a three-page scientific report.

2 Advertisement, Application and Student Selection

The program is advertised as one of the research training programs at MCC on the MCC website. Additionally, in collaboration with administrators of Hillsborough County Public Schools, program announcements are distributed to local schools. A large proportion of students learn about the program by word of mouth, from friends and from relatives of past participants. We advertise the program on social media (Twitter and LinkedIn). Applications can be downloaded in Word and pdf format from the HIP IMO website. Student information includes school contact details as well as voluntary reporting of demographics. After discussions with high school students and teachers, we decided to not request transcripts. Transcripts do not necessarily correlate with students' performance in a hands-on internship setting and may discourage students without perfect grades especially from underrepresented racial and ethnic groups from applying to the program. Rather, each applicant must answer three questions that help gauge their experience, passion and future goals:

(1) Which, if any, college level biology, mathematics or computer programming classes have you completed?
(2) What research skills and expertise can you apply to the program? Please emphasize any cancer biology, mathematics or computer programming experience that you may have.
(3) What are your career interests/goals and how may the HIP IMO program help your career?

Applications require a letter of recommendation from a teacher. IMO faculty members select students based on the match between a student's skill and the mentor's research objectives. We want the student's career goals to align with the mentor's projects and focus of the various IMO research groups.

3 Curriculum

After selection in the spring, the assigned faculty mentors communicate with their mentees on relevant literature and prerequisites for successful completion of the summer internship. Each student is required to create a LinkedIn account and to join

the HIP IMO group on LinkedIn. This helps us track the students' career paths after completing HIP IMO. The first week of HIP IMO comprises various boot camps to prepare the students for the hands-on modeling and simulation tasks of their projects. In the *cancer biology* and *cancer immunology* boot camps, students learn the molecular basis of cancer and immunology, the hallmarks of cancer (Hanahan and Weinberg 2000, 2011) and the various cancer treatment strategies, including radiotherapy, chemotherapy, targeted therapy and immunotherapy. Students get to visit research wet laboratories and observe different cell types and experimental conditions under the microscope. With the establishment of the Center of Excellence for Evolutionary Therapy at Moffitt, students also receive training in adaptive cancer therapy (Basanta et al. 2012; Basanta and Anderson 2013; Enriquez-Navas et al. 2016; Gatenby and Brown 2017). In the *mathematical modeling in cancer*, boot camp students learn the seven steps to modeling a biological problem [formulate question, determine basic model ingredients, describe system qualitatively, describe system quantitatively, analyze equations, checks and balances, relate results back to question; (Otto and Day 2007)], how to develop a flow diagram and construct a mathematical model from verbal descriptions of biological interactions, and how to analyze such models.

As part of the boot camp, we discuss different growth laws in oncology [linear, exponential, logistic, Gompertz (Gerlee 2013; Benzekry et al. 2014)], predator–prey models in ecology and cancer (Wilkie and Hahnfeldt 2013), carcinogenesis and cancer therapy (Enderling and Chaplain 2014; Walker and Enderling 2016). The students also learn about the rigorous modeling pipeline of model calibration, validation and prediction performance evaluation (Brady and Enderling 2019). To facilitate the programming core of HIP IMO, MATLAB and Hybrid Automata Library (HAL) (Bravo et al. 2018), boot camps are provided. During these boot camps, instructors teach the use of the different programming languages and syntax and demonstrate simple modeling projects using hands-on exercises. Students get programming exercises and homework to become proficient in the different programming environments. Boot camp instructors are available throughout the program to help individual students with programming and debugging. Additional classes include biostatistics, medical physics and intellectual property and licensing. After the one week of boot camps, students perform individual mentored research in their assigned research group. Students are provided with a MacBook pro laptop with required software to execute and document their research. To facilitate networking and community building, every Friday we host a student–mentor luncheon where lunch is provided for all program participants.

Weeks two through eight feature predominantly individual project work. Students meet daily with their mentor to discuss the research question, research project and progress. Projects are developed such that the student is the main researcher on the project. The role of the mentors and peers is to facilitate the research and guide the student in a successful internship. Most projects aim to answer a distinct research question that adds to bigger projects that are currently ongoing. As such, essential computer code, software and expertise are established to guide the student. Students also participate in weekly department research-in-progress meetings, weekly group meetings and department and institution-wide research seminars including basic,

clinical and quantitative sciences Grand Rounds. This provides insights into a variety of research projects at different development stages from scientists at different career stages.

In week two, students participate in a journal club and present a peer-reviewed publication that is relevant to their research project (5–10 min). Often this includes a paper authored by the faculty mentor. Students receive no guidance for the journal club presentation, to assess a variety of presentation styles. After all presentations, students select their favorite presentation and identify for themselves styles to adopt for their future presentations. Mentors help evaluate the individual presentations in their research groups. After 4 weeks, students present their research question and preliminary results in a midterm project presentation (5–10 min each).

The final highlight of the program is the HIP IMO research day on the last day of the internship (Friday of week eight). Each intern gives an oral presentation of their research project, with length dependent on the number of enrolled students. We aim to keep the total presentations under 4 h. Each student can invite up to four family members to the research day. The program administration invites the teachers that provided the recommendation letter, as well as the school principals. The presentations are attended by all members of the IMO department, as well as MCC leadership and researchers. As with all presentations at the IMO, we extend a warm welcome to patient advocates to share their perspective and comment on the impact of each research project. After all presentations, the program provides a reception and dinner for students, families and researchers to network and to reflect upon the program.

4 Outcomes

Since 2015, HIP IMO has enrolled 59 students (average 12/year) with an average enrollment rate of 27% (Table 1). Twenty-eight male (47%) and 31 female (53%) HIP IMO interns have graduated from the program, including six students (10%) from racial and ethnic groups identified by the National Institutes of Health (NIH) to be underrepresented in biomedical research (3 Blacks or African Americans, 3

Table 1 HIP IMO demographics 2015—2019

	2015	2016	2017	2018	2019	Total
HIP IMO scholars	7	9	12	14	17	59
Applications	15	25	43	65	70	218
Enrollment rate	46%	36%	28%	21%	24%	27%
Male	6 (86%)	3 (30%)	5 (42%)	7 (50%)	7 (41%)	28 (47%)
Female	1 (14%)	6 (60%)	7 (58%)	7 (50%)	10 (59%)	31 (53%)
Underrepresented racial and ethnic groups	–	1 (11%)	1 (8%)	1 (7%)	3 (18%)	6 (10%)
Out of state students	1 (MN)	1 (CA)	2 (CA, NJ)	3 (CA, OH, PA)	3 (NC, OH, VA)	10 (17%)

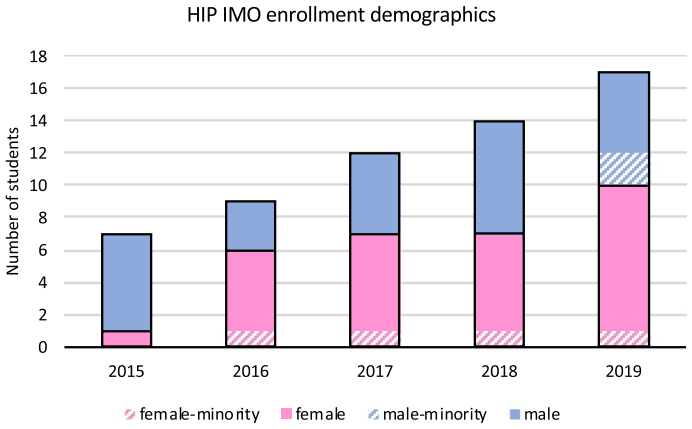

Fig. 1 HIP IMO enrollment demographics. Minority identifies students from racial and ethnic groups underrepresented in biomedical research (3 Blacks or African Americans, 3 Hispanics or Latinos)

Hispanics or Latinos; Fig. 1). The majority of students (83%) came from Hillsborough County and other counties in Florida. Ten students (17%) came from out of state, including California (3), Ohio (2), Minnesota (1), New Jersey (1), Pennsylvania (1), North Carolina (1), Virginia (1). All students (26) who have graduated from high school since participation in HIP IMO continued onto college, including Duke University (2), Columbia University (2), Rutgers University (2), University of Florida (UF, 3), University of South Florida (USF, 3), Georgia Tech (1), University of Missouri (1), University of Michigan (1), New York University (1), Vanderbilt University (1), Stanford University (1), UC Berkeley (1), UC Santa Barbara (1), The Ohio State University (1), Harvey Mudd College (1), Saint Louis University (1), Johns Hopkins University (1), Northwestern University (1), University of Miami (1). Seven students (35%) have pursued a double major in the quantitative and life sciences, with computer sciences being the primary major (6; 30%). Two students (10%) have pursued medical degrees, and two students have graduated and continued onto graduate school at the time of this report (Computer Science, Engineering). Two students (10%) have co-founded companies while in college. Two students have graduated from college and work as software engineers.

HIP IMO has defined a set of learning objectives that are assessed through entry and exit surveys. Students rate their skills on a scale from one to ten (where one is the lowest and ten is the highest) in computer programming, mathematics, cancer biology, mathematical oncology, scientific research, literature review, oral presentation and interdisciplinary team science. The average self-assessed skill level across all questions at the beginning of the program was 4.9 ± 1.7 ($n = 59$). By the end of the HIP IMO, the average response increased by 22% (6.0 ± 1.8; $n = 49$). The largest skill improvements were recorded in mathematical oncology (4.3–7.2, 69% increase, $p < 0.001$ [Mann–Whitney U test]), computer programming (4.1–6.2, 52%, $p < 0.001$), cancer biology (5.1–7.2, 42%, $p < 0.001$) and mathematics (5–6.9, 38%, $p < 0.001$; Fig. 2). After HIP IMO, students strongly agreed (1) to have a network

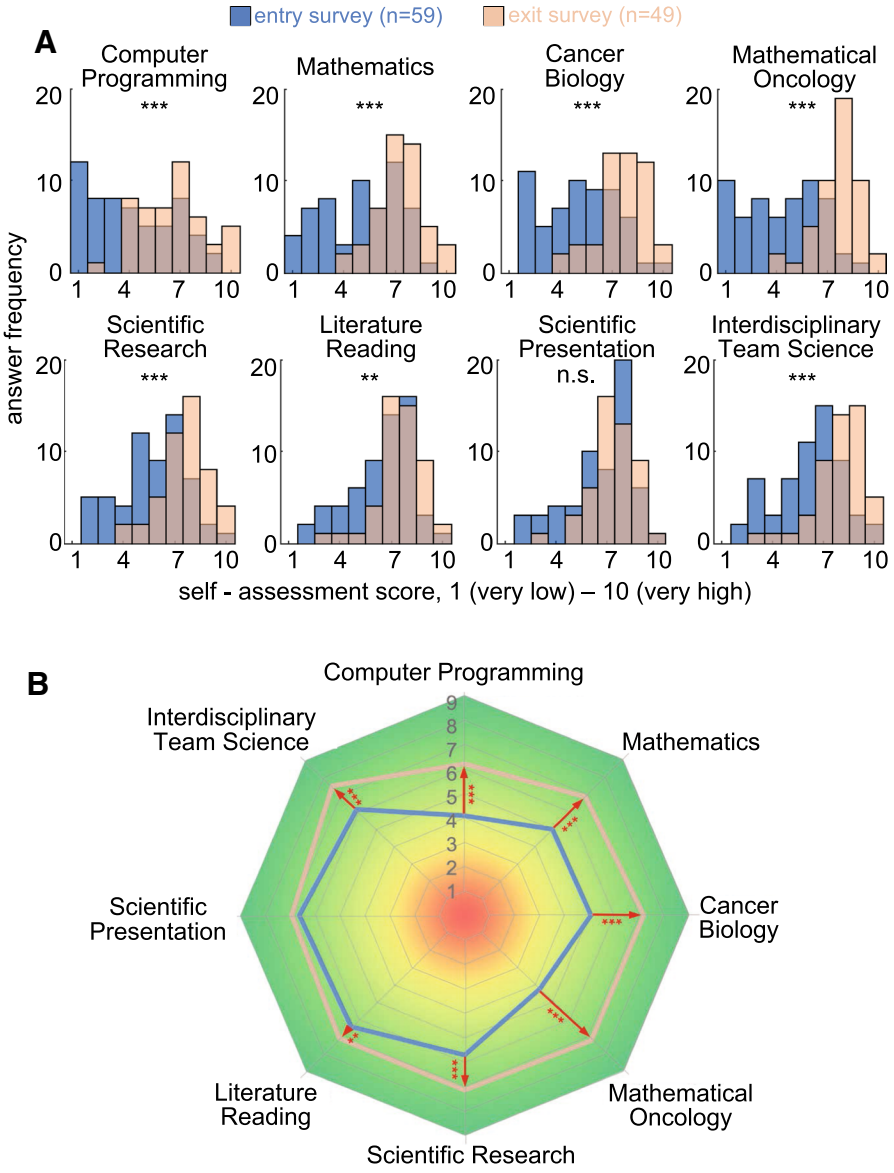

Fig. 2 Self-reported skill assessment of students before (blue, $n=59$) and after HIP IMO (orange, $n=49$). **a** Distributions of answers to surveys of self-assessment of different skills. Answers between 1 and 10 (very low–very high). Statistical analysis of difference in response distributions using Mann–Whitney U test; ***indicate $p<0.001$; **indicate $p<0.01$; n.s. not significant. **b** Radar plot of entry and exit survey average responses to the self-evaluated skills demonstrating meeting of HIP IMO learning objectives

Fig. 3 Word cloud of three adjectives students used to describe the program ($n = 49$). Font size represents answer frequency

of peers and mentors that will help advance their careers (4.4/5) and (2) to pursue a career in science (4.4/5). The majority of students expressed interest in an interdisciplinary career in cancer research or medicine, which is reflected in the high proportion of double majors among the students enrolled in college (35%). When asked to describe HIP IMO with three adjectives, the most common responses were fun (10), challenging (9), innovative (7), enlightening (7) and engaging (5) (Fig. 3).

Student projects have contributed to a number of peer-reviewed and published articles and book chapters in topical and interdisciplinary journals including PLoS Computational Biology (Howard et al. 2019a), Scientific Reports (Yagawa et al. 2017), International Journal of Radiation Biology (Sunassee et al. 2019), Games (Warman et al. 2018), Annals of Epidemiology (Howard et al. 2019b) and Encyclopedia of Biomedical Engineering (Karolak et al. 2019b), as well as several BioRxiv preprints (Warman et al. 2015; Kandru and Desai 2019; Vitos et al. 2019; Bhatt et al. 2019).

5 Discussion and Conclusion

The first five years' experience of the High school Internship Program in Integrated Mathematical Oncology at Moffitt Cancer Center has shown that junior and senior high school students of diverse demographic and socioeconomic backgrounds can perform excellent hands-on research in mathematical oncology. As demonstrated by the outcome analysis, learning objectives are clearly met under the guidance of dedicated faculty mentors and postdoctoral fellows. While the program has been able to teach six students (10%) from racial and ethnic groups identified by the National Institutes of Health (NIH) to be underrepresented in biomedical research, future work in collaboration with our new office of Community Outreach, Engagement and Equity will include stronger advertisement, dialog and inclusion of students from title 1 schools.

The increasing number of interested students and outstanding applicants emphasizes the need to educate high school students about interdisciplinary team science at the interface of mathematics and biology. The opportunity to explore career opportunities in the life sciences, and cancer research in particular, for students with a strong background and interest in mathematics, physics or computer science offers new interdisciplinary career trajectories for students before choosing college degrees in traditional disciplines. Due to the strong commitment of faculty mentors, students can deliver quality research that may contribute to publications and grant

proposals—clearly demonstrating a benefit to the teaching faculty as well. We hope that programs such as HIP IMO serve as motivation and blueprint for the development of similar programs. These programs would enable more students to get engaged in and excited about cutting edge mathematical biology research that can directly influence and promote their future academic careers.

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