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The Need for Research-Grade Systems Modeling Technologies for Life Science Education

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Abstract

The coronavirus disease 2019 (COVID-19) pandemic not only challenged deeply-rooted daily patterns but also put a spotlight on the role of computational modeling in science and society. Amid the impromptu upheaval of in-person education across the world, this article aims to articulate the need to train students in computational and systems biology using research-grade technologies.

Importance of Computational Modeling in Biomedical Research

Nearly all biological processes are governed by complex nonlinear biochemical networks that span multiple biological organization layers, from molecular to cellular to organ and organismal levels. Computational modeling and systems biology have become integral parts of life sciences research to understand these systems' dynamics and mechanisms better. In biomedical research, computational modeling can decrease the time and cost of bringing new treatments to patients. Many recent events evidence the increasing role and importance of these tools and approaches. For example, in 2013, a pioneer of computational biology, Dr. Michael Levitt, won the Nobel Prize

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in Chemistry for the development of multiscale models for complex chemical systems. In 2018, the US Food and Drug Administration (FDA) launched the Model-Informed Drug Development (MIDD) pilot program. This program aims to increase the efficiency of new treatment development by expanding the use of computational modeling and simulations (e.g., in dose selection, clinical trial simulations, mechanistic safety predictions, or biomarker identification) (<https://www.fda.gov/drugs/development-resources/model-informed-drug-development-pilotprogram>). In 2020, the COVID-19 pandemic gave mainstream visibility to the importance computational modeling has on public health; epidemiological models have been essential to inform policy decision-making in real time [1]. Additionally, over 160 scientists from 25 countries launched a systems biology effort to map and model the systemic and dynamic impacts COVID-19 has on the human immune system and body. This comprehensive computational resource promises to provide tools to accelerate the identification of novel diagnostic and therapeutic options for the disease [2].

The Full Potential of Computational Modeling in Systems Biology Has Yet to Be Realized

With modern high-throughput -omics technologies, many of the parts of biological systems have been characterized. What we still lack is the infrastructure to allow scientists to easily integrate the many parts of the system into a coherent whole – a unified virtual biological system. A multiscale modeling infrastructure is thus needed to integrate and accelerate all scientists' (particularly experimentalists') research. Once created, the possibilities such a system will enable are immense and transformative. While the technological infrastructure for computational modeling and systems biology has grown to support model creation, exchange, and analyses [3,4], many tools require (complex) mathematics and computer programming skills, limiting their utility to those with extensive training in computational methods. This lack of usability hinders applying systems biology approaches to large-scale problems. It has further implications within education. With limited computational modeling infrastructure, educators are forced to cobble together mechanisms to achieve 21st century science standards. In

2011, the Vision and Change call to action released guidelines for postsecondary life sciences education, including dynamic modeling, systems biology, and simulations [5]. Simultaneously, the Next Generation Science Standards for primary and secondary education were released, also including computational modeling, simulations, and systems thinking as core competencies. [6] Another problem arises from the fact that the current computational modeling landscape is mostly limited to single-scale, single-approach models due to the lack of technological infrastructure for multiscale modeling. This further impedes systems-level biological discoveries and extends into education as educators and students have insufficient resources to teach and learn about systems as a whole. As a result, reductionist approaches in teaching are still commonplace [7].

Technological Opportunism for Life Sciences Education Amid the Pandemic

As the pandemic challenges in-person education, science educators have an opportunity to begin adopting and integrating not only technology-assisted active-learning and remote instruction pedagogical strategies but also computational modeling and simulation-based systems biology approaches. Computational systems modeling is in a unique position to serve as a means to learn biology. It can transform student learning of biology in any life sciences course from static and isolated parts lists to more realistic dynamic and complex systems. For example, in a biochemistry course, central metabolism should leverage computational modeling as the means for students to learn about the dynamics of and systemic behaviors of central metabolism. Simultaneously, computational modeling and simulations in the classroom can narrow the disconnect between how scientists study a question, for instance, human diseases, and how students learn about them. Dynamic systems modeling can provide a constructivist [8], active learning approach to enable students to acquire the quantitative, computational, and systems thinking skills they need in a data-driven world. Computational and systems modeling across content areas would help prepare all students for the challenges of the current society, not just those entering the field of computational biology.

Available Systems Modeling Technologies

One way to integrate computational systems biology into current life sciences curricula is to build onto the mathematics and computer science competencies students acquire in primary and secondary school. Many of the core competencies in computational modeling and systems biology are also foundational mathematics and computer science concepts. For example, as students learn discrete mathematics and Boolean logic, life sciences instructors can apply the logical modeling framework [10] to represent the causal and mechanistic relationships between components of a biological system. As students learn calculus and differential equations, life sciences instructors can apply these tools to teach biochemical kinetics [11]. As students learn a programming language, life sciences instructors can rely on it to teach them how to design and simulate biological networks. Research-grade technologies incorporated in the classroom (e.g., Matlab, R, Maple, and Mathematica) already support mathematics and computer science^{i-xviii} (**Figure 1**). However, requiring all biology and life sciences teachers to have interdisciplinary expertise in life sciences, computer programming, and computational modeling is a challenge.

Conversely, instructors may leverage resources such as PhET Models, CK12, Knowitall NASA Science Simulations, and Biointeractive by the Howard Hughes Medical Institute. These resources provide discrete content-based activities (e.g., short videos, short animations, and single-purpose pre-programmed simulations) that students can view or minimally interact with without specialized knowledge. These preconstructed curricular materials have become valuable resources for teachers to easily integrate into their instruction, especially as remote instruction became necessary overnight. However, the pre-constructed/programmed experience limits students' degree of freedom to change the models dynamically and learn by building. A few technologies are starting to emerge that support a constructivist approach to modeling and simulations without requiring prior experience in mathematics, programming, or modeling, such as MolecularWorkbench and SageModeler by Concordia Consortium.

The sheer amount of data to consider now for systems biology requires scientists, science educators, and future scientists to have access to appropriate (scientifically authentic) infrastructure that allows

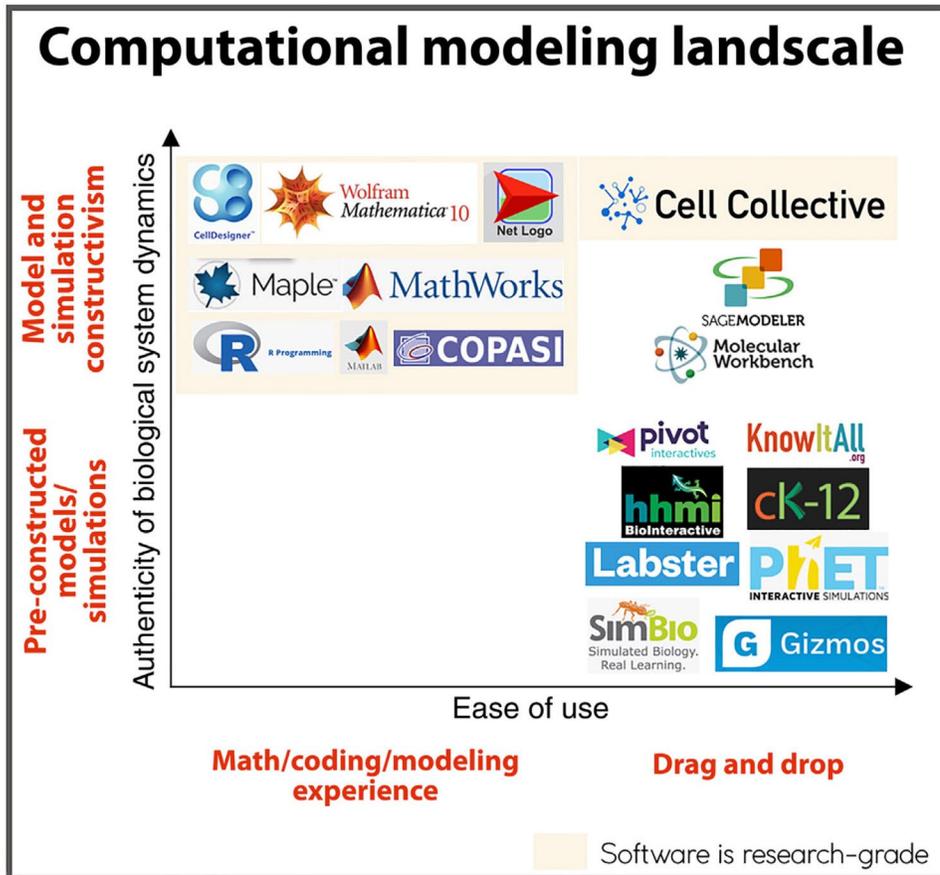


Figure 1. Landscape of Computational Systems Modeling Resources in Life Sciences.

users to interface with multiscale, data-driven biological systems. Cell Collective is an example of a tool attempting to remedy this situation. This research-grade computational modeling and simulation software was initially designed for scientists without prior training in computational modeling has since evolved to support education [12,13]. The software enables life sciences educators and students to teach/learn about biological processes in an experiential fashion by doing: by creating, simulating, and analyzing computational models of various biological systems. By design, the technology is accessible to students with a wide range of technical skills, including those with no prior training in modeling or computer science. Computational modeling lessons in Cell Collective cover various topics taught in traditional life sciences courses, including cell respiration, gene regulation, cell cycle, T cell differentiation, and glucose homeostasis

(<https://learn.cellcollective.org>). They guide students more accurately towards building/simulating/validating/revising models as scientists conduct research.

Expanding the Repertoire of Systems Modeling Education Technologies

Life sciences education needs multiple technical infrastructures explicitly designed to support this field's vast computational needs. Developing and sustaining effective, scientifically authentic educational technologies is not easy. It requires expertise in software development and the scientific domain as well as in education and education research. Discipline-based education research (DBER) is an emerging field defined as 'an empirical approach to investigating learning and teaching that is informed by an expert understanding of (STEM) disciplinary knowledge and practice' [14]. In life sciences education, DBER scientists, in particular, are focused on the integration of systems thinking concepts, computational modeling, and the use of new technologies. DBER scientists are exquisitely positioned to partner with computational systems biologists to increase the ease-of-use of existing, scientifically authentic technologies for postsecondary, secondary, and even primary educational purposes. They are also well-placed to design new research-grade technologies for life sciences education, and thus should be tasked with not only the intersection of deep disciplinary expertise and education but also codeveloping new technologies using the same tools and approaches as scientists to foster authentic competencies.

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Resources

i	Cell Collective:	https://cellcollective.org
ii	CellDesigner:	www.celldesigner.org/
iii	ck-12:	www.ck12.org/book/ck-12-biology/
iv	COPASI:	http://copasi.org/
v	Gizmos:	www.explorellearning.com/
vi	HHMI Biointeractive:	www.biointeractive.org/
vii	KnowItAll:	www.knowitall.org/
viii	Labster:	www.labster.com/simulations/
ix	Maple:	www.maplesoft.com/
x	MathWorks:	www.mathworks.com/
xi	Molecular Workbench:	http://mw.concord.org/modeler/
xii	NetLogo:	https://ccl.northwestern.edu/netlogo/
xiii	PhET:	https://phet.colorado.edu/
xiv	Pivot Interactives:	www.pivotinteractives.com/
xv	R:	https://rstudio.com/
xvi	Sage Modeler:	https://sagemodeler.concord.org/
xvii	SimBio:	https://simbio.com/
xviii	Wolfram Mathematica:	https://www.wolfram.com/education/

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