

1 **Title: Teaching systematic, reproducible model development using synthetic biology**

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61 **Abstract**

62 We present an educational unit to teach computational modeling, a vital part of chemical engineering
63 curricula, through the lens of synthetic biology. Lectures, code, and homework questions provide
64 conceptual and practical introductions to each computational method involved in the model development
65 process, along with perspectives on how methods can be iterated upon to arrive at a final model.
66 Ultimately, this content can be applied broadly to address questions in synthetic biology and classical
67 chemical engineering.

70 **Keywords**

71 Bioengineering, Computational Tools, Kinetics
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73

74 **INTRODUCTION**

75
76 Synthetic biology is an emerging technical discipline that applies engineering concepts to design
77 living systems to perform novel functions. One strategy for achieving this goal is using standard
78 biological parts, such as DNA sequences and proteins, which are first characterized and then composed
79 to create new functions such as genetically-encoded programs.^[1] When implemented in a cell or cell-free
80 system, such genetic programs can, as an example, direct the host to sense environmental or internal
81 cellular cues, process such inputs, and then respond via regulation of the expression of one or more target
82 genes. While synthetic biology employs concepts derived from electrical engineering, in which standard
83 electrical parts are composed to build circuits^[2], the origins, open challenges, and potential applications
84 of synthetic biology are closely aligned with chemical engineering^[3]. Specifically, there is a need to
85 develop systematic, scalable processes for the development, standardization, modularization, and
86 production of cell-based devices with applications ranging from bio-manufacturing to cell-based
87 therapies.^[3] Synthetic biology has matured towards a true engineering discipline by applying concepts
88 and practices established in mature technical fields^[4], including the incorporation of mathematical
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90

91 modeling to facilitate understanding and enable prediction^[1, 5]. Here we focus on models which employ
92 ordinary differential equations (ODEs) to describe system dynamics, incorporating fundamental concepts
93 taught in core chemical engineering subjects including mass balances and reaction kinetics.
94

95 Mathematical modeling is widely used in chemical engineering to understand and predict the
96 performance of chemical reactions and other complex processes, but new, holistic approaches are needed
97 to train students in the process of model development.^[6] This is a challenging goal, deriving in part from
98 the diversity of expertise and skills needed to model effectively, with topics including intuition-guided
99 iteration between model formulation and parameter estimation, investigation of multi-dimensional
100 design spaces with unconstrained parameters, and effectively comparing experiments to simulations.^[5]
101 In addition, the model development process is often opaque, as many publications incorporating
102 modeling focus on the final result while omitting description of the process used to arrive at the final
103 model. As a result, it is often not clear as to how choices made in the development process affect the final
104 model and how each computational task—such as model formulation, parameter estimation, parameter
105 identifiability analysis, and model selection—are inter-connected. Extensive prior work provides
106 strategies for teaching important modeling tasks, such as developing differential equation-based models
107 to describe systems of interest^[7-9], solving differential equations analytically and numerically^[9, 10],
108 utilizing various coding languages to solve differential equations^[9] [7, 11, 12], parameter estimation with
109 respect to experimental data^[8], and sensitivity analysis^[8]. Most prior work has been designed for use with
110 MATLAB, a commercially available programing and numerical analysis platform. While each of these
111 individual tasks is vital to the model development process, there exists a need for educational materials
112 focused on providing a holistic, conceptual framework of model development and analysis using an
113 accessible, open-source coding language. Such a framework could provide a theoretical roadmap for the
114 entire model development process by teaching both the theory behind each computational method^[9] in
115 the process and how methods can be iterated upon to arrive at a final model.
116

117 To address challenges in executing and communicating the model development process and to
118 lower the barrier to entry for new modelers, we recently published a tutorial describing a systematic
119 model development workflow for rigorous characterization of genetic programs, called GAMES (a
120 workflow for the Generation and Analysis of Models for Exploring Synthetic systems).^[5] GAMES
121 provides a conceptual framework for understanding, applying, and linking each computational method
122 involved in the model development process using example code written in an open-source coding
123 language, Python, and is therefore well-suited to be expanded to develop an educational unit designed to
124 teach the entire model development process. Further, GAMES represents a direct application of the
125 process-oriented thinking that is a key component of the chemical engineering curriculum, thus
126 complimenting existing undergraduate curriculum in chemical engineering and addressing the need for
127 teaching synthetic biology to “career chemical engineers” by incorporating synthetic biology concepts
128 into existing courses.^[13] Since GAMES applies concepts taught in core chemical engineering reaction
129 kinetics courses, the concepts and approaches employed could be used to develop and solve models
130 describing classical chemical engineering processes as well, which is a vital component of chemical
131 engineering education.^[10] Thus, GAMES can help students to understand and deploy systematic and
132 reproducible model development for any ODE-based model.
133

134 Our core thesis is that teaching a structured, systematic approach to the process of ODE model
135 development in synthetic biology will enable students to understand key concepts and apply these

136 concepts to new modeling problems. To this end, we developed an educational unit, consisting of a two-
137 day lecture series and a homework set, focused on an audience of advanced undergraduate and graduate
138 students. Following implementation of the unit in a computational biology course at Northwestern
139 University, we identified key areas for improvement for future iterations of the course. Overall, the goals
140 for this unit are to enable students to: (i) understand key steps and considerations in the model
141 development process at a conceptual level, rather than relying exclusively on automated model analysis
142 packages; (ii) practice implementing key methods and interpreting the results; and (iii) gain exposure to
143 diverse applications of chemical engineering thinking. These outcomes align with those which are known
144 to positively impact student experiences.^[14-16] By mapping core chemical engineering topics to new
145 application spaces, this tool may be especially useful when biology-focused chemical engineering
146 curriculum options are limited. This training also seeks to prepare students for future research
147 opportunities focused on mathematical modeling in synthetic biology. Here, we introduce instructors to
148 the GAMES workflow and describe strategies for implementing associated pedagogical tools in a core
149 or elective chemical engineering course.

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151

152 METHODS

153

154 GAMES Conceptual Workflow

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156 The GAMES workflow describes the model development process as a set of five interconnected
157 tasks, or modules (**Figure 1a**). After defining the system of interest, the modeler first initializes the model
158 development process in Module 0 by identifying a modeling objective, collecting or otherwise obtaining
159 training data, and formulating a base case model, which represents a series of biological, mechanistic
160 hypothesis proposed to describe how the system functions. Before estimating the values of the unknown
161 parameters (which are often kinetic rate constants), the modeler must first evaluate their parameter
162 estimation method in Module 1 to ensure that it is appropriate for their parameter estimation problem
163 (defined by the model equations, free parameters, and training data). After ensuring that the parameter
164 estimation method (PEM) is appropriate, the modeler can then use the PEM to estimate parameters using
165 training data in Module 2. Next, in Module 3, the modeler determines whether their parameters are well-
166 constrained, or identifiable. If any parameters are unidentifiable, they must be refined via either model
167 reduction or experimental design. Finally, in Module 4, the modeler compares any competing models
168 and selects the best option. Different iterations of the modules in the workflow can be used to accomplish
169 a variety of key modeling goals, such as parameter estimation, model refinement, experimental design,
170 model reduction, model selection, and model validation (**Figure 1b**).^[5]

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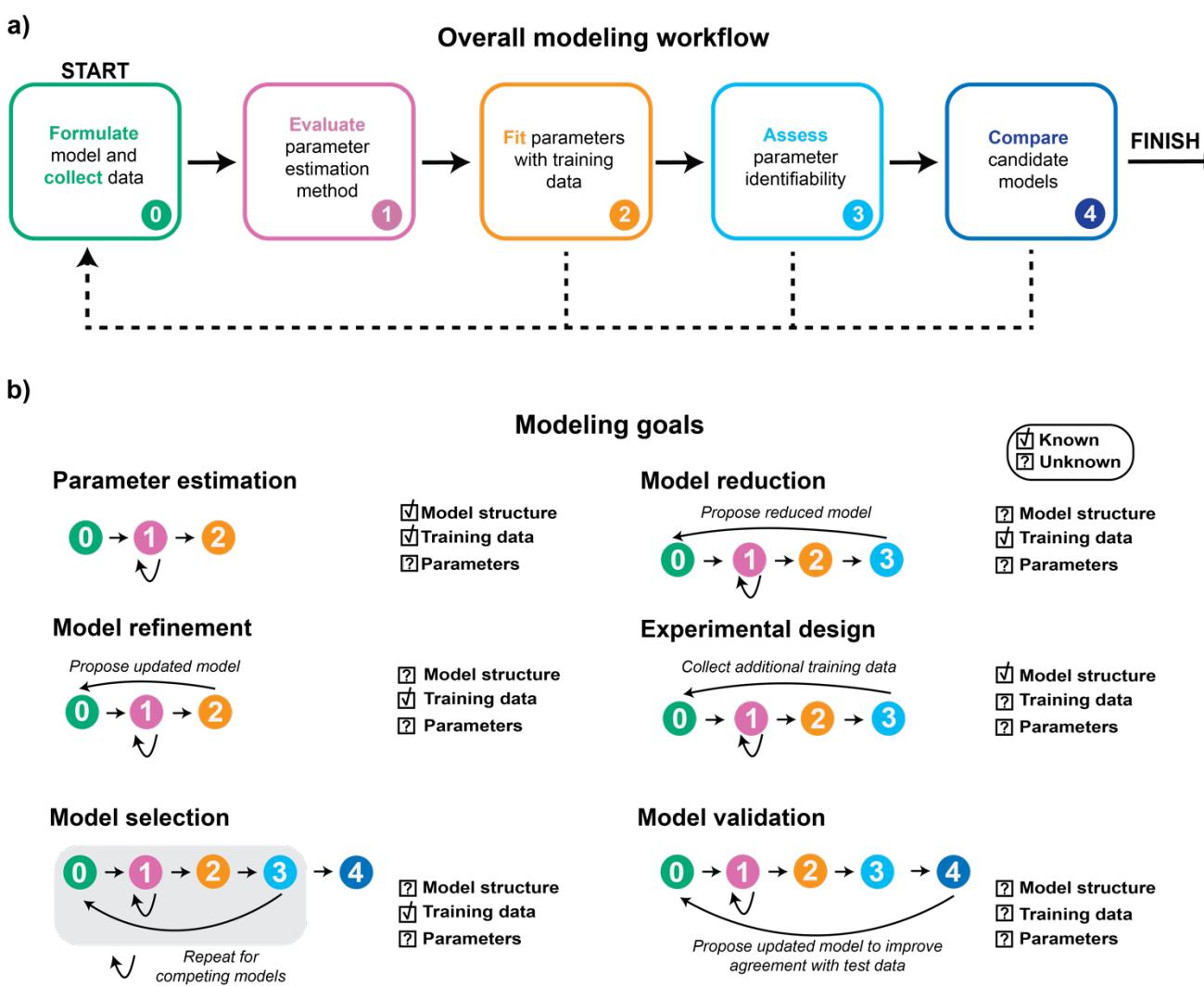
172

173 GAMES Software Package

174 To support the use of the GAMES, we developed a freely available Python-based software
175 package and deposited it on GitHub. This software manifests the concepts in each module through
176 practical implementations of each method. The software package is modular, such that the user must
177 simply modify only two files to run the workflow for any new system of interest: (1) the .py file, which
178 includes a problem-specific model class, containing information such as the ODEs, normalization
179 strategy, and plotting functions; and (2) the .json configuration file, which includes information related
180 to hyperparameters necessary for each method and defines free parameter values and bounds. The

181 software package is available on GitHub at <https://github.com/leonardlab/GAMES>. The specific version
182 of the GAMES software package necessary for the homework set presented here can be found at
183 https://github.com/leonardlab/GAMES_education.

184
185 Installation requires the use of various Python tools, including pyenv^[17] and Poetry^[18], to ensure
186 that the simulation environment and package dependencies are properly implemented, both of which are
187 vital for promoting code reproducibility, which is a major problem in computational modeling of
188 biological systems.^[19-21] As installation of software is a vital step in the use of any software package
189 obtained from GitHub, the installation of GAMES provides a useful opportunity for students to
190 understand Python environments and to practice execution of installation instructions. We highly
191 recommend that the instructor and/or teaching assistants for the course familiarize themselves with the
192 installation protocol before distributing the assignment and that an in-class or office hours session be
193 dedicated towards troubleshooting any installation roadblocks.
194



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196

197 **Figure 1:** Overview of the GAMES workflow. (a) GAMES describes the model development process as a
198 set of 5 interconnected tasks, or modules. The overall modeling workflow is iterative, as represented by
199 the dotted lines. (b) The modules described in GAMES can be iterated upon in different orders to
200 accomplish a variety of modeling goals, each of which is important in the development of mathematical
201 models. Reprinted with permission from Dray KE, Muldoon JJ, Mangan NM, Bagheri N, and Leonard
202 JN (2022) GAMES: A Dynamic Model Development Workflow for Rigorous Characterization of Synthetic
203 Genetic Systems. *ACS Synth Biol.* 11(2):1009-1029. DOI: 10.1021/acssynbio.1c00528. Copyright 2022
204 American Chemical Society.

EDUCATIONAL METHODOLOGY AND MATERIALS

Overview

The educational unit is structured to address overall learning objectives through an interconnected two-day lecture series and homework set. The overarching goal of the educational unit is to introduce model development concepts and to increase familiarity with modeling synthetic biological systems using both conceptual and experiential pedagogical materials. A key choice made in defining learning objectives was to focus on practicing interpretation and analysis of results in each step of the workflow, rather than on writing code or implementing computational methods. The unit was implemented in the spring 2022 iteration of the course “Computational Biology: Design and Analysis of Living Systems” at Northwestern University. Students in this course comprised 13 undergraduate and PhD students in both the Chemical Engineering and Integrated Biological Sciences departments. Incoming students were expected to have basic proficiency in Python (or some related programming language), along with a general knowledge of mass balances and reaction kinetics (which were introduced earlier in this course), such that students could understand how the ODEs in the GAMES tutorial were formulated from first principles. The amount of coding expertise required to complete the homework set is, by design, minimal. Instead, the assignment focuses on prompting thoughtful interpretation of GAMES-generated results. Similarly, the course instructor and/or teaching assistant should have sufficient proficiency in Python to facilitate resolution of difficulties with executing and modifying code, but *de novo* writing in Python is not required.

Lecture Series

The lectures provide a conceptual introduction to each module of the GAMES workflow^[5], using the same proof-of-principle example and topical sequence as the tutorial, to demonstrate each milestone in the process. The lectures were presented as two consecutive 50 minute class meetings. The lecture slides are freely available for download at Zenodo^[22]. Both lectures were held in-person with a Zoom option and were recorded. Learning objectives were provided at the beginning of each day (**Table 1**). The first lecture focused on introducing each module of GAMES in a linear, idealized manner such that iterations between modules was unnecessary. As model development is rarely linear in practice, the second lecture leveraged the students’ basic understanding of each module to elaborate the workflow to a more realistic, nonlinear form that incorporates the practically unavoidable iteration between modules. In the second lecture, additional practical information not included in the tutorial was presented. This information included a discussion of cross-validation methods for model validation along with a series

242 of lessons learned from applying GAMES to complex biological systems beyond the example presented
243 in the tutorial.
244

TABLE 1.
Learning objectives for the GAMES lecture series

Day 1	Day 2
Understand general challenges for developing models in synthetic biology	Analyze parameter profile likelihood results (PPL) and understand how results can motivate refinement of parameter identifiability
List the key steps in model development according to the GAMES workflow	Compare scenarios using model reduction or experimental design to refine parameter identifiability
Understand the importance of defining a modeling objective at the outset of a modeling quest	Define metrics for comparing competing models
Understand the importance of evaluating a parameter estimation method before interpreting parameter estimation results	Explain various nonlinear iterations between modules that may be necessary in practice
Explain the base case parameter estimation method used in the GAMES workflow	Understand challenges with applying the model development workflow to more complex synthetic biological systems
Understand the concept of parameter identifiability and why it is important for model development and analysis	

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246

247 Homework Set

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249 The homework set guides students through hands-on participation in the model development
250 process by introducing a new example designed to be explored using the GAMES code. Students were
251 given one week to complete the homework set, with extensions available if necessary. Learning
252 objectives were provided alongside each homework problem. Homework solutions are omitted from this
253 manuscript, but solutions are available to educators upon request via e-mail to the corresponding author.
254 Two, 1-hour office hour blocks with the course TA were offered to help students with this set.
255 Asynchronous help was available via the course Slack workspace. This version of the homework set has
256 been updated to use an improved, refactored version of the GAMES code and is therefore slightly
257 different than the homework set used in the spring 2022 implementation of our educational unit. The
258 differences relate only to the computational implementation of the GAMES workflow; all learning
259 objectives and conceptual framings remain the same. The text of the homework set is included in
260 **Supplementary Information**^[22]. The topics of each question are as follows:

261

- 262 1. Introduction to GAMES
- 263 2. Model formulation, normalization, and parameter estimation
- 264 3. Evaluation of parameter estimation method

265 4. Iteration between model development and parameter estimation
266 5. Parameter identifiability analysis and refinement

268
269 **IMPLEMENTATION AND OPPORTUNITIES FOR IMPROVEMENT**

270
271 Students who participated in our educational unit gained increased interest and understanding of
272 the model development process in synthetic biology. A core part of the curriculum of the course in which
273 this unit was implemented is guiding students through the process of proposing, reviewing, revising, and
274 executing an independent research project using methods and approaches introduced in this course. Some
275 students chose to incorporate ODE modeling via the GAMES framework, suggesting that our educational
276 unit provided students with the desire and ability to apply the concepts presented here to new problems
277 of interest. This material was successfully employed by both undergraduate and graduate students with
278 varying levels of computational and biological experience, suggesting that the educational unit could be
279 implemented for a range of different academic levels and proficiencies. While we implemented this unit
280 in a computational biology course, the unit could be implemented as part of the traditional chemical
281 engineering curriculum in a reaction kinetics class to expose students to computational modeling,
282 synthetic biology, and Python.

283
284 Through this initial offering, we identified several areas for improvement for the next iteration of
285 this education unit based on our own experience as course instructors (a formal evaluation of student
286 learning outcomes is planned for future offerings of this course). Students would likely benefit from
287 having more time to complete the homework assignment; two weeks would be a better timescale to
288 enable deeper engagement with several new and sophisticated topics. This recommendation is based
289 upon the general observation that students were more comfortable describing the general use of novel
290 concepts (e.g., parameter profile likelihood) than in applying these methods to interpret specific model
291 development scenarios. We see this as an opportunity to help students achieve deeper levels of learning
292 (i.e., moving from Understanding to Analyzing and Interpreting in the Revised Bloom's Taxonomy^[23]).
293 It would perhaps be useful to spread the GAMES lecture series content across three days to ensure more
294 time to present and probe understanding of core concepts introduced in this unit. Based on the questions
295 asked in office hours, we recommend a live demonstration of the code to prepare students to complete
296 the homework set. This could be completed either on the last day of lectures or interspersed throughout
297 the lecture series as each module is introduced. We suggest including a general introduction/refresher on
298 ODE model formulation focused on converting a biological hypothesis to a testable mathematical
299 implementation based on ODEs—this topic is not covered in the GAMES tutorial but is a central part of
300 the model development process. Depending on the course, such an introduction may already be included
301 in the curriculum. Otherwise, existing resources may help serve this role.^[24, 25]

302
303 **DIVERSITY, EQUITY, AND INCLUSION CONSIDERATIONS**

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305
306 A key shared goal of writing the GAMES tutorial^[5] and disseminating the educational materials
307 described here is to increase student access to the training and resources required to lead cutting-edge
308 research involving computational modeling in general, and particularly in synthetic biology. We
309 anticipate that these resources could make such training more accessible at institutions that currently

310 provide limited opportunities in computational biological modeling or synthetic biology. Since synthetic
311 biology curricula are most commonly implemented at large research institutions in the USA and the
312 EU^[13], this unit could help to overcome current limitations on access to such training for students who
313 do not attend these institutions. Implementing this educational unit may also increase student awareness
314 and interest in synthetic biology as an application of chemical engineering. We employed the freely
315 available Python language and disseminated these tools for free to reduce financial barriers that reduce
316 equity. Finally, the approaches embodied in these educational materials are designed to engage students
317 with a diversity of learning styles and to follow inclusive teaching best practices.^[26-28] Key choices
318 include using visual and audio presentation of step-by-step examples, communication of specific learning
319 objectives, integration of written self-directed instruction, distribution of slides to students in advance of
320 lectures, and recording of presented material for future reference. Overall, we hope that these resources
321 will help educators to engage a broader swath of students who might be interested in computational
322 biology and synthetic biology.

323

324

325 CONCLUSIONS

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327 Here, we present an educational unit focused on teaching systematic, reproducible model
328 development through the lens of synthetic biology. As a result of the unit, we anticipate that students will
329 become more aware of, interested in, and comfortable with synthetic biology, computational modeling,
330 and the intersection between the two. We expect that students will be able to apply the general skills and
331 concepts learned here to other parts of the chemical engineering curricula, including reaction kinetics,
332 process modeling, and engineering design courses. A key innovation of this educational unit vis-à-vis
333 prior work is the focus on providing a holistic, conceptual framework for the model development process.
334 Such a focus on process is vital in chemical engineering education and for building technical literacy as
335 to how modeling supports a variety of applications. As the field of chemical engineering evolves to keep
336 apace of new challenges and needs facing society^[29, 30], this educational unit exemplifies the opportunity
337 to integrate new and exciting applications, such as synthetic biology and computational modeling, into
338 the chemical engineering curriculum.

339

340

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342

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348 REFERENCES

349

- 350 1. Dray KE, Edelstein HI, Dreyer KS, and Leonard JN (2021) Control of mammalian cell-based
351 devices with genetic programming. *Curr Opin Syst Biol.* 28. DOI: 10.1016/j.coisb.2021.100372.
- 352 2. Purnick PE and Weiss R (2009) The second wave of synthetic biology: from modules to systems.
353 *Nat Rev Mol Cell Biol.* 10(6):410-22. DOI: 10.1038/nrm2698.

354 3. Luo Y, Lee JK, and Zhao H (2013) Challenges and opportunities in synthetic biology for chemical
355 engineers. *Chem Eng Sci.* 103. DOI: 10.1016/j.ces.2012.06.013.

356 4. Cheng AA and Lu TK (2012) Synthetic biology: an emerging engineering discipline. *Annu Rev
357 Biomed Eng.* 14:155-78. DOI: 10.1146/annurev-bioeng-071811-150118.

358 5. Dray KE, Muldoon JJ, Mangan NM, Bagheri N, and Leonard JN (2022) GAMES: A Dynamic
359 Model Development Workflow for Rigorous Characterization of Synthetic Genetic Systems. *ACS Synth
360 Biol.* 11(2):1009-1029. DOI: 10.1021/acssynbio.1c00528.

361 6. Elnashaie SSEH, Alhabdan FM, and Elshishini SS (1993) The vital role of mathematical
362 modelling in chemical engineering education. *Mathematical and Computer Modelling.* 17(3):3-11. DOI:
363 10.1016/0895-7177(93)90034-v.

364 7. Li X and Huang Z (2017) An inverted classroom approach to educate MATLAB in chemical
365 process control. *Education for Chemical Engineers.* 19:1-12. DOI: 10.1016/j.ece.2016.08.001.

366 8. Molina R, Orcajo G, and Martinez F (2019) KBR (Kinetics in Batch Reactors): a MATLAB-
367 based application with a friendly Graphical User Interface for chemical kinetic model simulation and
368 parameter estimation. *Education for Chemical Engineers.* 28:80-89. DOI: 10.1016/j.ece.2018.11.003.

369 9. Golman B (2016) Transient kinetic analysis of multipath reactions: An educational module using
370 the IPython software package. *Education for Chemical Engineers.* 15:1-18. DOI:
371 10.1016/j.ece.2015.12.002.

372 10. Gossage JL, Yaws CL, Chen DH, Li K, Ho TC, Hopper J, and Cocke DL (2001) Integrating best
373 practice pedagogy with computer-aided modeling and simulation to improve undergraduate chemical
374 engineering education *Proceedings Proceedings of the 2001 American Society for Engineering
375 Education Annual Conference & Exposition.* DOI:

376 11. Geng J, Chen K, Wang N, Ling S, Guo M, and Huang Z (2019) Comparison of R and Simulink
377 in Educating High School Students with ODE Modeling Skills. *Chemical Engineering Education.* 53(2).
378 DOI:

379 12. Inguva P, Bhute VJ, Cheng TNH, and Walker PJ (2021) Introducing students to research codes:
380 A short course on solving partial differential equations in Python. *Education for Chemical Engineers.*
381 36:1-11. DOI: 10.1016/j.ece.2021.01.011.

382 13. Hall GM and Howe J (2012) The impact of synthetic biology in chemical engineering—
383 Educational issues. *Education for Chemical Engineers.* 7(2):e51-e55. DOI: 10.1016/j.ece.2012.02.002.

384 14. Madan CaT, Braden (2013) The Benefits of Undergraduate Research: The Student's Perspective.
385 *The Mentor: An Academic Advising Journal.* DOI: <https://doi.org/10.26209/mj1561274>.

386 15. Russell SH, Hancock MP, and McCullough J (2007) The pipeline. Benefits of undergraduate
387 research experiences. *Science.* 316(5824):548-9. DOI: 10.1126/science.1140384.

388 16. Gillett JE (2001) Chemical Engineering Education in the Next Century. *Chemical Engineering &
389 Technology.* 24(6):561-570. DOI: 10.1002/1521-4125(200106)24:6<561::Aid-ceat561>3.0.co;2-x.

390 17. pyenv. <https://github.com/pyenv/pyenv> accessed November 30, 2022.

391 18. Poetry. <https://python-poetry.org/> accessed November 30, 2022.

392 19. Mukherjee S, Almanza A, and Rubio-González C (2021) Fixing dependency errors for Python
393 build reproducibility, *Proceedings 30th ACM SIGSOFT International Symposium on Software Testing
394 and*
395 *Analysis* DOI: <https://doi.org/10.1145/3460319.3464797>.

396 20. Papin JA, Mac Gabhann F, Sauro HM, Nickerson D, and Rampadarath A (2020) Improving
397 reproducibility in computational biology research. *PLoS Comput Biol.* 16(5):e1007881. DOI:
398 10.1371/journal.pcbi.1007881.

399 21. Tiwari K, Kananathan S, Roberts MG, Meyer JP, Sharif Shohan MU, Xavier A, Maire M, Zyoud
400 A, Men J, Ng S, Nguyen TVN, Glont M, Hermjakob H, and Malik-Sheriff RS (2021) Reproducibility in
401 systems biology modelling. *Mol Syst Biol.* 17(2):e9982. DOI: 10.15252/msb.20209982.

402 22. Dray KE, Dreyer KS, Lucks JB, and Leonard JN (2023) leonardlab/GAMES education:
403 supplementary material. *Zenodo*. DOI: 10.5281/zenodo.7935134.

404 23. Anderson LW and Krathwohl DR (2021) *A taxonomy for learning, teaching, and assessing: A
405 revision of Bloom's taxonomy of educational objectives*. Longman:

406 24. Endler L, Rodriguez N, Juty N, Chelliah V, Laibe C, Li C, and Le Novere N (2009) Designing
407 and encoding models for synthetic biology. *J R Soc Interface.* 6 Suppl 4:S405-17. DOI:
408 10.1098/rsif.2009.0035.focus.

409 25. Cedersund G and Roll J (2009) Systems biology: model based evaluation and comparison of
410 potential explanations for given biological data. *FEBS J.* 276(4):903-22. DOI: 10.1111/j.1742-
411 4658.2008.06845.x.

412 26. Keller J and Lyndgaard K (2017) A brief taxonomy of inclusive pedagogies: what faculty can do
413 differently to teach more inclusively. *Headwaters.* 30(1):64-82. DOI:

414 27. Zumbrunn S, McKim C, Buhs E, and Hawley LR (2014) Support, belonging, motivation, and
415 engagement in the college classroom: A mixed method study. *Instructional Science.* 42(5):661-684. DOI:

416 28. Lisa WPaB (2016) The future of engineering education - revisited. 50(1). DOI:

417 29. Th M, Schaer E, Abildskov J, Feise H, Glassey J, Liauw M, Ó'Súilleabháin C, and Wilk M (2022)
418 The importance/role of education in chemical engineering. *Chemical Engineering Research and Design.*
419 187:164-173. DOI: 10.1016/j.cherd.2022.08.061.

420 30. Engineering NAO, National Academies of Sciences E, and Medicine (2022) *New Directions for
421 Chemical Engineering*. The National Academies Press: Washington, DC.

422