Heinrich Heine University, Düsseldorf | Program in Quantitative Biology

BIQ 940 Mathematical Modeling of Biological Systems

(June 5, 2020)

Instructor: Deniz Sezer (PhD Physics, Cornell University) dzsezer@gmail.com
Teaching Assistant: Käthe Weit kaethe.weit@yahoo.de

Evaluation:

Computer labs (×9)		25 %
Midterm exam (take-home)	May 30 - June 1	35 %
Final exam (take-home)	June 8 - 11	40 %
Total		100 %

Course Contents:

Day	Date	Lecture, Computer lab
		I. Modeling population growth
1	May 25	General information about the course. Cell division and exponential growth. Lab1: Numerical integration of exponential and logistic growth.
2	May 26	Antibiotic resistance. Competition of two species. Lab2: Antibiotic resistance under exponential and logistic growth.
		II. Modeling netwroks of chemical reactions
3	May 27	What is inside a cell? Chemical reaction networks. Lab3: Closed and open reaction networks.
4	May 28	Enzyme controlled reactions. Balanced exponential growth. Lab4: Autosynthetic network with enzyme-catalyzed reactions.
		III. Modeling autosynthetic cell growth
5	May 29	The simplest model of an autosynthetic cell. Lab5: Balanced growth and optimal growth rate of the simplest cell model.
	May 30	**Midterm exam**
	June 1	Pfingstmontag
6	June 2	Maximizing the cell growth rate. *E. coli* eats lactose. Lab6: Autosynthetic cell model of lactose consumption.
		IV. Modeling transcription regulation
7	June 3	Control of protein expression: transcription factors and operons. Lab7: Glycerol utilization with induced lac operon.
8	June 4	Growth time is a sum of the individual enzyme work times. Lab8: Optimal protein composition does not depend on the k_{cat}'s.
9	June 5	Is bacterial growth rate optimized? Optimization through kinetics. Lab9: On-the-fly optimization of the growth rate.
	June 8-11	**Final exam**

Supplementary readings:

Day 1 Exponential and logistic growth

- Phillips, Kondev, Theriot, Garcia, Orme, *Physical Biology of the Cell*, 2nd ed., Garland Science, 2013. (Computational Exploration: Growth Curves and the Logistic Equation, pp. 103–105.)

Day 2 Antibiotic resistance

- Gullberg, Cao, . . . , Andersson*, Selection of resistant bacteria at very low antibiotic concentrations, *PLoS Pathogens* **7**: e1002158 (2011).

Day 3 What is inside a cell? Chemical reaction networks

- Liebermeister, Noor, Flamholz, Davidi, Bernhardt*, Milo*, Visual account of protein investment in cellular functions, *Proc. Natl. Acad. Sci. USA* **111**, 8488–8493 (2014).
- Ingalls, *Mathematical Modeling in Systems Biology*, MIT Press, 2013.
  (Sec. 2.1 Chemical Reaction Networks, pp. 21–25 and pp. 35–39.)
- Palsson, *Systems Biology: Properties of Reconstructed Networks*, Cambridge University Press, 2006.
  (Ch. 6 Basic Features of the Stoichiometry Matrix, pp. 89–95.)

Day 4 Enzyme rate laws. Balanced growth

- Ingalls, *Mathematical Modeling in Systems Biology*, MIT Press, 2013.
  (Sec. 3.1 Enzyme Kinetics, pp. 55–64.)
- Hagen, Exponential growth of bacteria: Constant multiplication through division, *Am. J. Phys.* **78**, 1290–1296 (2010). (First three sections only.)

Day 5 The simplest model of an autosynthetic cell

- Jong*, . . . , Mathematical modelling of microbes: metabolism, gene expression and growth, *J. R. Soc. Interface* **14**: 20170502 (2017).

Exam 1 Bacterial growth laws. The origin of eukaryotes

- Scott, Gunderson, Mateescu, Zhang, Hwa*, Interdependence of cell growth and gene expression: Origins and consequences, *Science* **330**, 1099–1102 (2010).
- Zachar, Szilágyi, Szamádó, Szathmáry*, Farming the mitochondrial ancestor as a model of endosymbiotic establishment by natural selection, *Proc. Natl. Acad. Sci. USA*, **115**, E1504–E1510 (2018).

Day 6 Maximizing the cell growth rate

- Molenaar*, van Berlo, de Ridder, Teusink, Shifts in growth strategies reflect tradeoffs in cellular economics, *Molecular Systems Biology* **5**: 323 (2009).

Day 7 The *lac* operon

- Kirschner and Gerhart, *The Plausibility of Life*, Yale University Press, 2005.
  (Ch. 4: Weak Regulatory Linkage, pp. 112-121.)
- You, . . . , Hwa*, Coordination of bacterial proteome with metabolism by cyclic AMP signalling, *Nature*, *Nature* **500**, 301–306 (2013).

Days 8 & 9 Optimality of cell growth

- Towbin, Korem, Bren, Doron, Sorek, Alon*, Optimality and sub-optimality in a bacterial growth law, *Nature Communications* **8**: 14123 (2017).