# BIQ 950 Bioinformatics II - Part 2

(May 24, 2019)

**Instructor:** Deniz Sezer (PhD Physics, Cornell University)
**E-mail:** dzsezer@gmail.com
**Office:** 25.02.02.25

**Teaching Assistant:** Tin Y. Pang (PhD Physics, SUNY Stony Brook)
**E-mail:** vvoorr@gmail.com

**Evaluation:** (Part 2 only)

| | | |
|---|---|---|
| Computer labs (in-class) | | 10 % |
| Midterm exam (take-home) | May 18 - 19 | 15 % |
| Final exam (take-home) | May 27 - 29 | 25 % |
| Total | | 50 % |

**Course Contents:**

| day | date | Lecture, Computer lab |
|---|---|---|
| | | Modeling population growth |
| 1 | May 15 | Bacterial growth. Models of exponential and logistic growth.<br>Lab1: Numerical solution of growth (differential) equations. |
| 2 | May 16 | Antibiotic resistance. Competition of two species.<br>Lab2: Antibiotic resistance under exponential and logistic growth. |
| | | Netwroks of chemical reactions |
| 3 | May 17 | What is inside a cell? Chemical reaction networks and the stoichiometry matrix.<br>Lab3: Closed and open reaction networks. Left and right null spaces. |
| | May 18 - 19 | **Midterm exam** (take-home) |
| 4 | May 20 | Enzyme-controlled reactions. Enzyme states and occupancy.<br>Lab4: Reaction network with enzymes. 3D structure of Phosphofructokinase. |
| | | Autosynthetic balanced growth |
| 5 | May 21 | Modeling the growth of an authosynthetic cell.<br>Lab5: The simplest self-replicating cell model. |
| 6 | May 22 | Bacterial growth laws. Growth time is additive.<br>Lab6: The simplest whole-cell model reproduces growth laws. |
| | | Optimization of cellular resources |
| 7 | May 23 | Is bacterial growth rate optimized? A mechanism of growth-rate optimization.<br>Lab7: Optimal composition of the simplest whole-cell model. |
| 8 | May 24 | Resource allocation and protein sectors. Constrained optimization.<br>Lab8: Cell kinetics naturally converge to optimal composition. |
| | May 27 - 29 | **Final exam** (take-home) |

**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.)
- Ingalls, *Mathematical Modeling in Systems Biology*, MIT Press, 2013. (Sec. 2.1.4 Numerical Simulation of Differential Equations.)

**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

- 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. (Ch. 2 Modeling of Chemical Reaction Networks, pp. 21–48.)

**Weekend 1** Farming mitochondria in fluctuating environment

- 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).
- Lane, *Power, Sex, Suicide*, Oxford University Press, 2005. (Ch. 1. The Deepest Evolutionary Chasm & Ch. 2. Quest for a Progenitor, pp. 27–50.)

**Day 4** More on the origin of eukaryotes. The stoichiometry matrix

- Lane, *Power, Sex, Suicide*, Oxford University Press, 2005. (Ch. 3. The Hydrogen Hypothesis, pp. 51–64.)
- Garg and Martin*, Asking endosymbionts to do an enzyme's job, *Proc. Natl. Acad. Sci. USA*, **115**, E4543–E4544 (2018).
- Ingalls, *Mathematical Modeling in Systems Biology*, MIT Press, 2013. (Sec. 5.4.1 Stoichiometric Network Analysis, pp. 150–160.)

**Day 5** Balanced growth. The simplest model of a whole cell

- Hagen, Exponential growth of bacteria: Constant multiplication through division, *Am. J. Phys.* **78**, 1290–1296 (2010). (First three sections only.)
- Jong*, ..., Mathematical modelling of microbes: metabolism, gene expression and growth, *J. R. Soc. Interface* **14**: 20170502 (2017).

**Day 6** Maximizing the growth rate. Bacterial growth laws

- Molenaar*, van Berlo, de Ridder, Teusink, Shifts in growth strategies reflect tradeoffs in cellular economics, *Molecular Systems Biology* **5**: 323 (2009).
- Scott, Gunderson, Mateescu, Zhang, Hwa*, Interdependence of cell growth and gene expression: Origins and consequences, *Science* **330**, 1099–1102 (2010).

**Day 7** Optimality of cell growth

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

**Day 8** Growth laws and protein sectors

- You, ..., Hwa*, Coordination of bacterial proteome with metabolism by cyclic AMP signalling, *Nature*, 301–306 (2013).