Do.

- Download and install Rstudio from `https://posit.co/downloads/`
- Download and install Cyclone from `https://github.com/discretedynamics/`
- Familiarize yourself with Macaulay2 at

  `https://www.unimelb-macaulay2.cloud.edu.au/`

- Browse the Gene Intersection Network simulator (GINsim) website at

  `http://ginsim.org/home`

Exercise. Consider a Boolean model of the *lac* operon, based on five variables: mRNA (M), β-galactosidase (B), *lac* permease (P), allolactose (A), and intracellular lactose (L), and the following transition functions:

$$\begin{aligned} f_M &= A \\ f_B &= M \\ f_P &= M \\ f_A &= A \vee (L \wedge B) \\ f_L &= P \vee (L \wedge \overline{B}) \end{aligned}$$

(a) What other assumptions are made in this model? (E.g., presence or absense of extracellular sugars, time-steps, degredation, etc.)

(b) As we saw in class, the dynamics do not accurately reflect the behavior of the biological system it is meant to model. Therefore, something is wrong. Four of these functions are reasonable; justify each one in a single well-written sentence.

(c) Explain why one of these functions does not accurately reflect the underlying biology and/or the model assumptions. Propose a modification, aimed at eliminating the biologically infeasible fixed point, $(0, 0, 0, 1, 0)$. Give a rationale for your modification and specify the biological mechanism or model assumptions that justify the change.

(d) Use Macaulay2 to convert these Boolean functions into polynomials over $\mathbb{F}_2 = \{0, 1\}$. Then find the fixed points using a Gröbner basis of a particular polynomial ideal.

(e) Draw the wiring diagram of the old and new Boolean model.

(f) Use the BoolNet package in RStudio to find the attractors and plot the state space. Include a print-out or screenshot.

(g) Repeat the previous step, but with either Cyclone or GINsim.

(h) Justify why the long-term behavior of the system (fixed points) agrees with what we should expect biologically.