

*Read:* Chapter 1: Mechanisms of gene regulation: Boolean network models of the lactose operon in *Escherichia coli*, by R. Robeva, B. Kirkwood, and R. Davis, pages 1–35.

*Do:* Create an account on the Sage Math Cloud (<https://cloud.sagemath.org>).

1. Consider the following system of polynomial equations:

$$\begin{aligned}x^2 + y^2 + xyz &= 1 \\x^2 + y + z^2 &= 0 \\x - z &= 0\end{aligned}$$

To compute a Gröbner basis for this system over  $\mathbb{Q}$ , type the following commands into Sage, one-by-one, and press Shift+Enter after each one:

```
P.<x,y,z> = PolynomialRing(QQ, 3, order='lex'); P
I = ideal(x^2+y^2+x*y*z-1, x^2+y+z^2, x-z); I
B = I.groebner_basis(); B
```

- (a) For the system above, use the Gröbner basis you just computed to write a simpler system of polynomial equations that has the same set of solutions. Solve that system *by hand* (it's not hard) to find all *real-valued* solutions to the original system.
  - (b) Next, solve the original system but over the binary field,  $\mathbb{F}_2 = \{0, 1\}$ . For this, you need to replace `RR` with `GF(2)` in the Sage code.
  - (c) Now, solve the original system but over the ternary field,  $\mathbb{F}_3 = \{0, 1, 2\}$ .
2. Repeat the previous problem for this system of polynomial equations:

$$\begin{aligned}x^2y - z^3 &= 0 \\2xy - 4z &= 1 \\z - y^2 &= 0 \\x^3 - 4yz &= 0\end{aligned}$$

3. Consider the following simple model of the *lac* operon:

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

For this problem, make the convention that  $(x_1, x_2, x_3, x_4, x_5, x_6) = (M, P, B, R, A, L)$ .

- (a) Justify each function in a single sentence. What other assumptions are made in this model? (E.g., presence or absence of external lactose and glucose?)

- (b) Write each function as a polynomial over  $\mathbb{F}_2 = \{0, 1\}$ . Then, write out the system of equations  $\{f_i + x_i = 0, i = 1, \dots, 6\}$ , whose solutions are the fixed points of the Boolean network.
- (c) Go into Sage and type the following command:

```
P.<x1,x2,x3,x4,x5,x6> = PolynomialRing(GF(2), 6, order='lex'); P
```

Now, define an ideal  $I$  generated by the six polynomials,  $f_i + x_i$ , from Part (b). Use Sage to compute the Gröbner basis of this ideal, and include a print-out of a screenshot.

- (d) The Gröbner basis describes a simpler system of equations with the same solutions as the original. Write out this system and then solve it by hand to determine the fixed points of the Boolean network.
- (e) Compute the entire phase space of your model with the help of either the *Analysis of Dynamic Algebraic Models* (ADAM) toolbox, at <http://adam.plantsimlab.org/>, or *TURING: Algorithms for computation with finite dynamical systems*, at <http://www.discretedynamics.org>. Include a print-out of a screenshot. Are there any periodic points that are not fixed points?