

1. **Fixed points.** Consider the following 10-variable model of the *lac* operon, from class, where the 3 parameters are added with “frozen” update functions.

$$\begin{array}{ll}
 f_M = \overline{R} \wedge \overline{R_m} \wedge C & f_{A_m} = L \vee L_m \\
 f_B = M & f_L = \overline{G_e} \wedge P \wedge L_e \\
 f_P = M & f_{L_m} = \overline{G_e} \wedge ((L_{em} \wedge P) \vee L_e) \\
 f_C = \overline{G_e} & f_{L_e} = L_e \\
 f_R = \overline{A} \wedge \overline{A_m} & f_{L_{em}} = L_{em} \\
 f_{R_m} = (\overline{A} \wedge \overline{A_m}) \vee R & f_{G_e} = G_e \\
 f_A = L \wedge B &
 \end{array}$$

Use Macaulay2 to compute a Gröbner basis of the ideal $I = (f_{x_1} + x_1, \dots, f_{x_{13}} + x_{13})$, in the quotient ring $\mathbb{F}_2[x_1, \dots, x_{13}]/(x_i^2 - x_i)$. Solve the resulting system by hand to find all fixed points of the original Boolean model. Code is provided on the course website.

2. **Bistability.** Consider the following model of the tryptophanase (*tna*) operon in E. coli:

$$\begin{array}{ll}
 f_A = M \wedge \overline{\gamma} & f_P = \overline{W} \wedge \overline{W_m} \\
 f_B = M & f_W = \omega_e \wedge B \\
 f_C = \overline{\gamma} & f_{W_m} = (\omega_{em} \wedge B) \vee \omega_e \vee W \\
 f_M = C \wedge \overline{P} &
 \end{array}$$

There are three parameters: γ is glucose, ω_e is high levels of extracellular tryptophan, and ω_{em} represents (at least) medium levels of extracellular tryptophan.

- (a) Let γ , ω_e , and ω_{em} be “frozen” variables, making this a 10-variable model. Use Cyclone to find the attractors. Code is provided on the course website.
- (b) Fix $(\gamma, \omega_e, \omega_{em}) = (0, 0, 1)$ as constants to get a 7-variable model, which assumes no glucose and medium levels of extracellular tryptophan. Use BoolNet to find the attractors under an asynchronous update, and summarize your findings. This can be done with the command

```
> getAttractors(tnaModel, type="asynchronous", startStates=256)
```

How does this compare to the synchronous state space?

- (c) Explain how/why this model exhibits bistability.