In class Lecture 21 - Dynamical Systems and the Lambda Switch

Tuesday, April 5, 2022 8:48 AM

Lattice model vs. chemical potential

"Canonical ensemble"

STATES	ENERGY	MULTIPLICITIES	BOLTZMANN WEIGHT
(empty)	$L \cdot \varepsilon_{sol}$	$\frac{\Omega^L}{L!}$	$\frac{\Omega^L}{L!} e^{-\beta \varepsilon_{sol} L}$
(bound)	$(L-1)\varepsilon_{sol} + \varepsilon_b$	$\frac{\Omega^{L-1}}{(L-1)!}$	$\frac{\Omega^{L-1}}{L!} e^{-\beta(\varepsilon_{sol}(L-1)+\varepsilon_b)}$

$$p_{bound} = \frac{\frac{L}{\Omega} e^{-\beta \Delta\varepsilon}}{1 + \frac{L}{\Omega} e^{-\beta\Delta\varepsilon}}, \quad \Delta\varepsilon = \varepsilon_b - \varepsilon_{sol}$$

Consider μ: "grand-canonical ensemble"

STATES	ENERGY	BOLTZMANN WEIGHT
(empty)	$\varnothing$	$e^{0\beta} = 1$
(bound)	$\varepsilon_b - \mu$	$e^{-\beta(\varepsilon_b + \mu)}$

we calculated $\mu(L)$ for an ideal gas using a lattice model

(L → # in reservoir)

$$\mu(L) = \mu_0 + k_B T \ln\left(\frac{c}{c_0}\right)$$

$$p_{bound} = \frac{e^{-\beta(\varepsilon - \mu)}}{1 + e^{-\beta(\varepsilon-\mu)}}$$

$$e^{-\beta(\varepsilon-\mu)} \rightarrow e^{-\beta\varepsilon} \cdot e^{\beta(\mu_0 + k_B T \ln\frac{c}{c_0})}$$

$$= e^{-\beta\varepsilon} \cdot e^{\beta\mu_0} \cdot e^{\ln c/c_0}$$

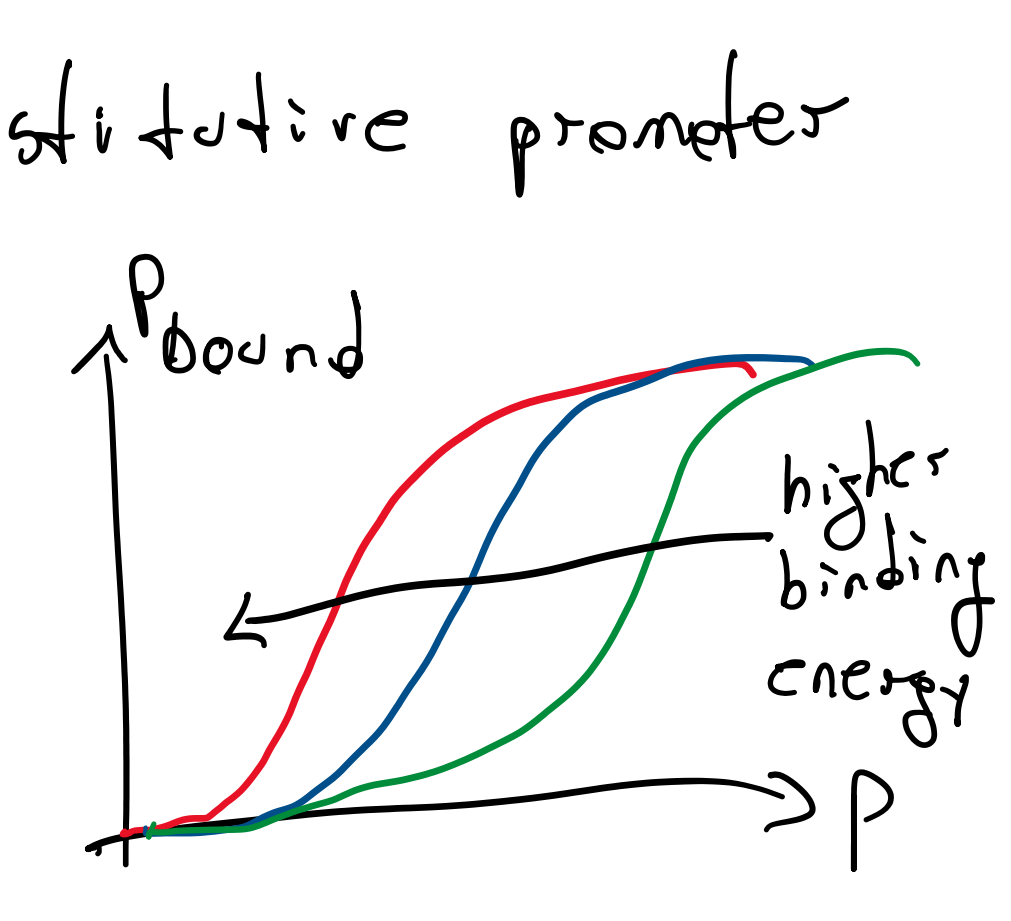
$$= e^{-\beta(\varepsilon-\mu_0)} \frac{c}{c_0}$$

$$= e^{-\beta(\varepsilon-\mu_0)} \frac{L}{\Omega v}$$

($\frac{L}{\Omega v}$ → c, v → $1/c_0$)

$$= \frac{L}{\Omega} e^{-\beta\Delta\varepsilon}$$

From constitutive promoter



Revisiting cooperativity:

Remember simple repression:

$$\text{fold-change} = \frac{1}{1 + \frac{R}{N_{NS}} e^{-\beta\Delta\varepsilon_{rd}}} \quad \text{(in weak promoter approx.)}$$

$$= \frac{1}{1 + \frac{[R]}{K_d}}$$

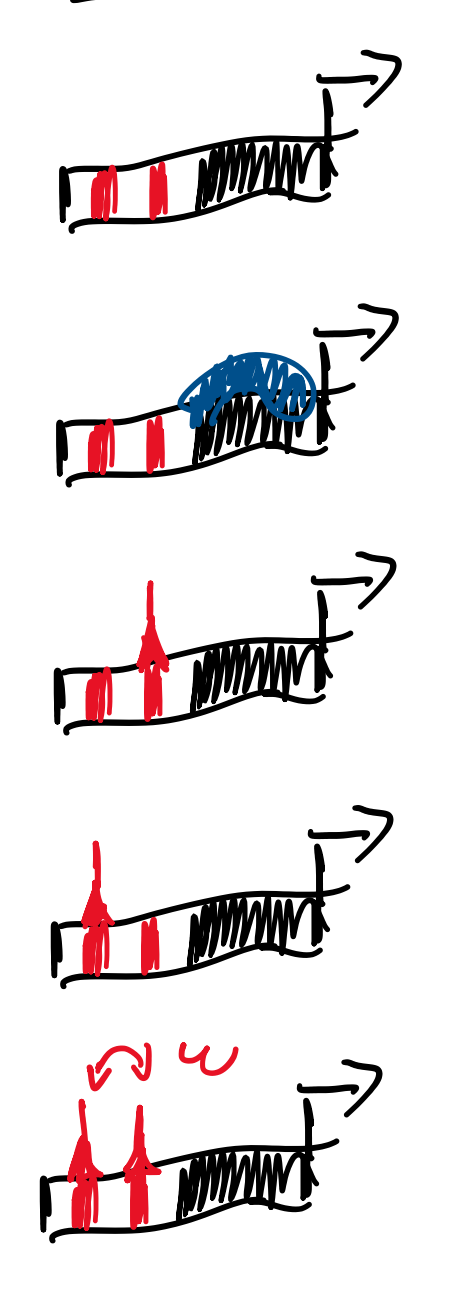
because

$$\frac{R}{N_{NS}} e^{-\beta\Delta\varepsilon_{rd}} = \frac{[R]}{K_d}$$

$$\frac{R}{v\Omega} \frac{v}{N_{NS}} e^{-\beta\Delta\varepsilon_{rd}} = \frac{[R]}{K_d}$$

$$K_d = \frac{N_{NS}}{v} e^{\beta\Delta\varepsilon_{rd}}$$

Think of cI:



STATE	RATE	BIOCHEMICAL WEIGHT
(empty)	$\varnothing$	1
(polymerase bound)	r	$[P]/K_p = p$
(one repressor)	$\varnothing$	$[R]/K_R = r$
(one repressor)	$\varnothing$	$[R]/K_R = r$
(two repressors, ω)	$\varnothing$	$\frac{[R]}{K_R} \cdot \frac{[R]}{K_R} \cdot \omega = r^2\omega$

$$p_{bound} = \frac{p}{1 + p + 2r + r^2\omega}$$

$$\text{fold change} = \frac{p_{bound}(R \neq 0)}{p_{bound}(R = 0)} = \frac{p}{1+p+2r+r^2\omega} \cdot \frac{1+p}{p}$$

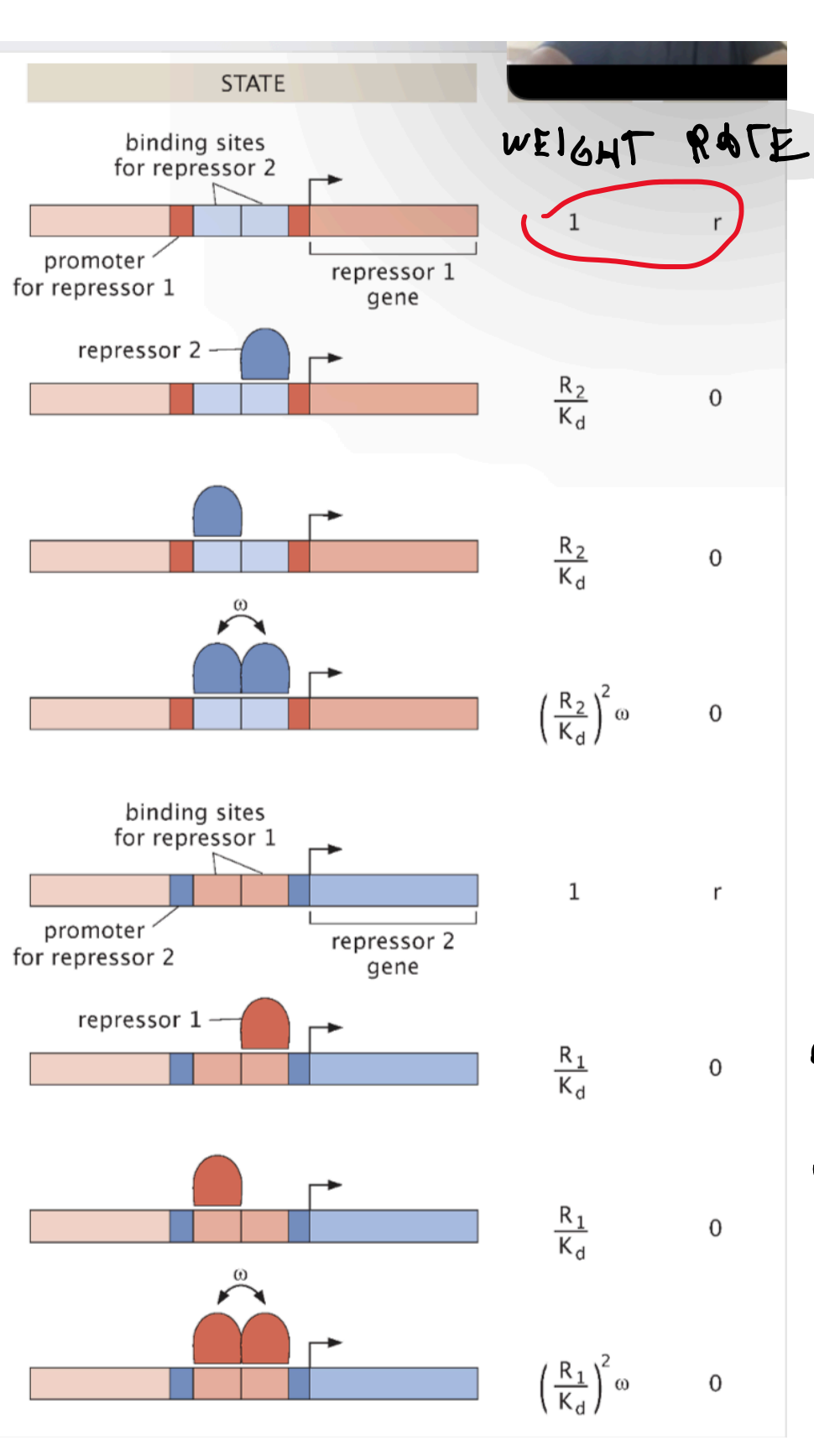
$$= \frac{1+p}{1+p+2r+r^2\omega} \simeq \frac{1}{1+2r+r^2\omega}$$

($p \ll 1$ (weak promoter approx.))

what if I have no coop? $\omega = 1$

$$\text{fold change} = \frac{1}{1+2r+r^2} = \frac{1}{(1+r)(1+r)}$$

Mutual repression gene switch



states of system

$$\frac{dR_1}{dt} = \sum_i r_i p_i - \gamma R_1$$

$$= r \cdot \frac{1}{1 + 2 R_2/K_d + \left(\frac{R_2}{K_d}\right)^2 \omega} - \gamma R_1$$

$$\frac{dR_2}{dt} = r \frac{1}{1 + 2\frac{R_1}{K_d} + \left(\frac{R_1}{K_d}\right)^2 \omega} - \gamma R_2$$

$$\frac{dR_1}{dt} = r \cdot \frac{1}{1 + 2 R_2/K_d + \left(\frac{R_2}{K_d}\right)^2 \omega} - \gamma R_1$$

Parameters: (1) r, (2) K_d, (3) ω, (4) γ

To make the analysis simpler, I'm going to write these equations in non-dimensional form

(1) multiply both sides by $\frac{1}{\gamma}$

$$\frac{1}{\gamma}\frac{dR_1}{dt} = \frac{\frac{1}{\gamma} r}{1 + 2 R_2/K_d + \left(\frac{R_2}{K_d}\right)^2 \omega} - \gamma R_1 \frac{1}{\gamma}$$

($\frac{r}{\gamma} = r'$; $\gamma t = \tau$ (unitless))

(2) Measure all concentrations in units of K_d

$$\frac{1}{K_d}\frac{dR_1}{d\tau} = \frac{\frac{1}{K_d} r'}{1 + 2\frac{R_2}{K_d} + \left(\frac{R_2}{K_d}\right)^2 \omega} - R_1 \frac{1}{K_d}$$

($\frac{R_1}{K_d} = \tilde{r}_1$, $\frac{r'}{K_d} = \tilde{r}$, $\frac{R_2}{K_d} = \tilde{r}_2$)

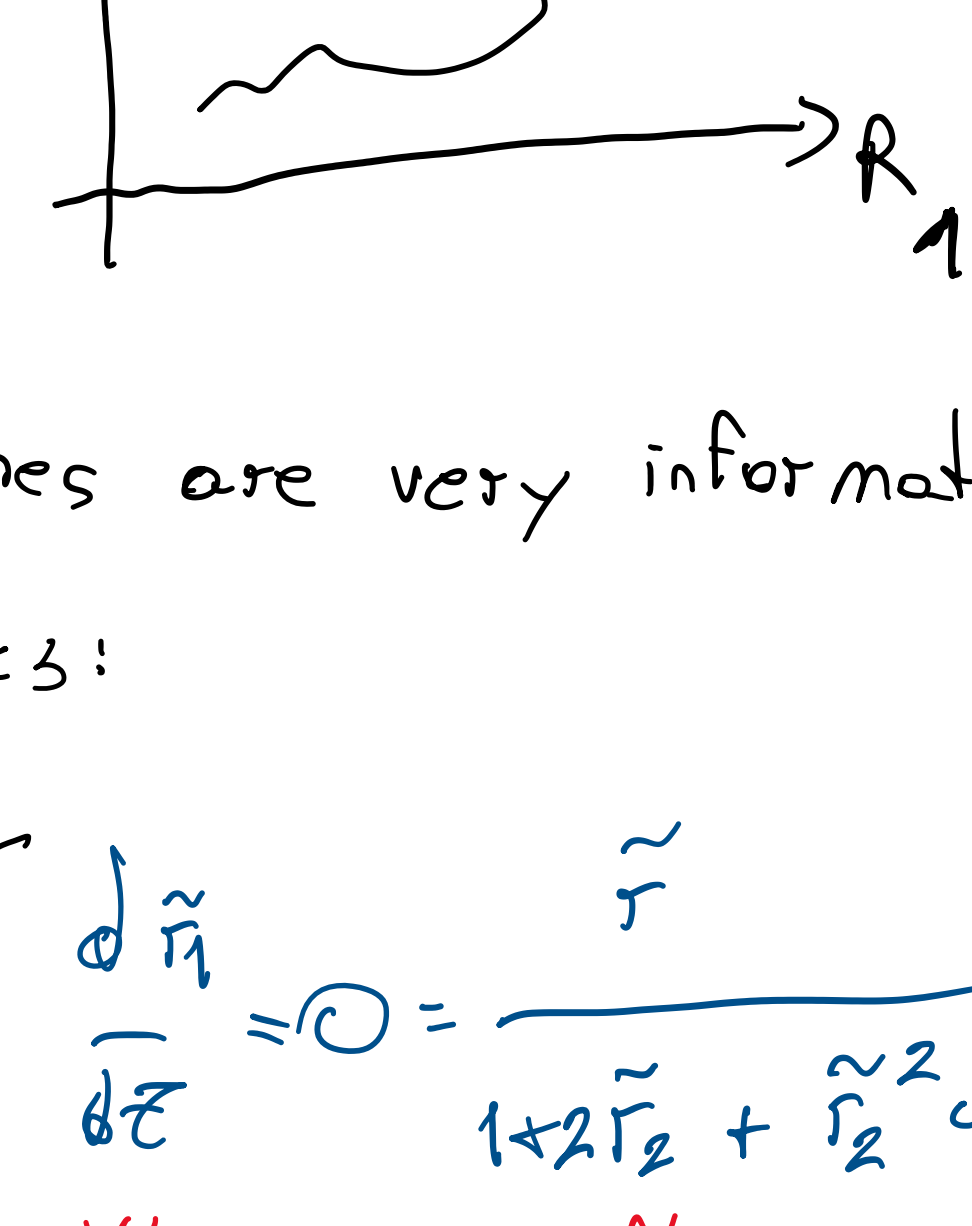
$$\Rightarrow \frac{d\tilde{r}_1}{d\tau} = \frac{\tilde{r}}{1 + 2\tilde{r}_2 + \tilde{r}_2^2 \omega} - \tilde{r}_1$$

(1 parameter: ω)

similarly

$$\frac{d\tilde{r}_2}{d\tau} = \frac{\tilde{r}}{1 + 2\tilde{r}_1 + \tilde{r}_1^2\omega} - \tilde{r}_2$$

Phase diagram



Two lines are very informative about the system's dynamics:

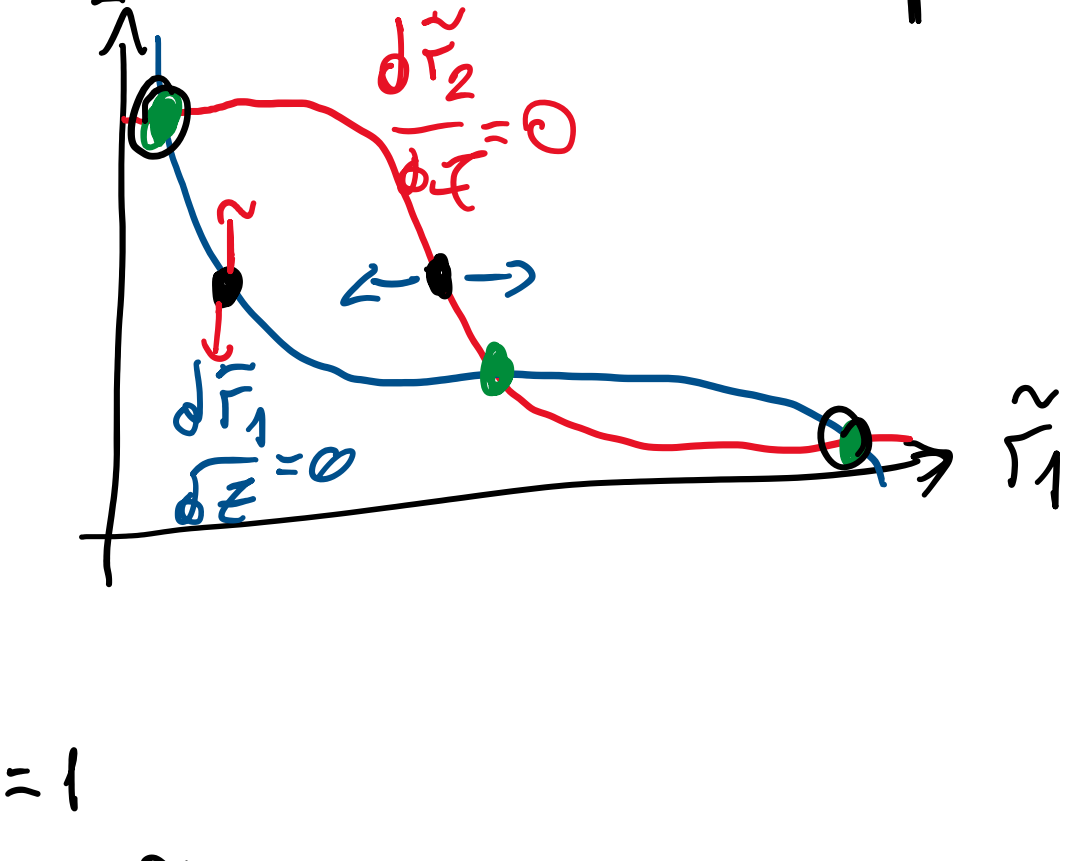
nullclines

$$\frac{d\tilde{r}_1}{d\tau} = 0 = \frac{\tilde{r}}{1 + 2\tilde{r}_2 + \tilde{r}_2^2\omega} - \tilde{r}_1$$

$$\frac{d\tilde{r}_2}{d\tau} = 0 = \frac{\tilde{r}}{1 + 2\tilde{r}_1 + \tilde{r}_1^2\omega} - \tilde{r}_2$$

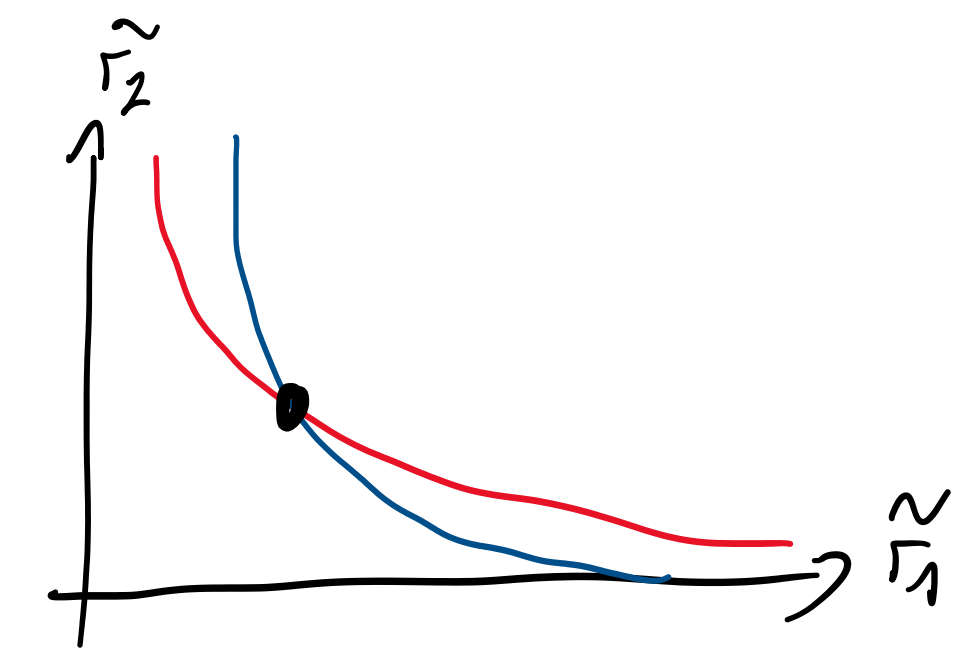
$$\Downarrow$$

$$\tilde{r}_2 = \frac{\tilde{r}}{1 + 2\tilde{r}_1 + \tilde{r}_1^2\omega}$$



BISTABILITY

if $\omega = 1$



MONOSTABILITY