

**Supplement: Conditional cooperativity of Toxin - Antitoxin regulation can mediate bistability between growth and dormancy**

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**Text S1: Correspondence of parameters with the growth rate dependence data of protein production rate in the steady state growth**

Klumpp et al. [1] reported that a decrease in cellular growth rate results in a global slow down of transcription, and provided the relative change of the transcription rate for steady state growth.

In our model equations,

$$\frac{dT}{dt} = \frac{\sigma_T}{\left(1 + \frac{[AT]}{K_O}\right) (1 + \beta_M [T_f])} - \frac{\Gamma_0}{1 + \beta_C [T_f]} \cdot T \quad (1)$$

$$\frac{dA}{dt} = \frac{\sigma_A}{\left(1 + \frac{[AT]}{K_O}\right) (1 + \beta_M [T_f])} - \Gamma_A \cdot A. \quad (2)$$

the growth rate slows down due to the free toxin, characterised by  $\beta_C$ , while the protein production rate is reduced at the same time, which is characterised by  $\beta_M$ . We can reproduce the relation in [1] when  $\beta_C$  and  $\beta_M$  satisfy a certain relation as follows.

In our model, the term  $\Gamma \equiv \frac{\Gamma_0}{1 + \beta_C [T_f]}$  in equation is the division rate. In ref. [1], cell division rate is measured in terms of doubling per hour, while our  $\Gamma_0$  is estimated to be 30 minutes doubling time [2]. Namely, we have

$$\Gamma = \frac{2\text{dbl}/\text{hour}}{1 + \beta_C [T_f]}, \quad (3)$$

and we get the amount of free toxin as a function of  $\Gamma$ [dbl/hour]:

$$[T_f] = \frac{2 - \Gamma}{\beta_C \cdot \Gamma}. \quad (4)$$

This gives the growth-rate dependent protein production change in our model to be

$$\tilde{\alpha}(\Gamma) = \frac{1}{1 + \beta_M [T_f]} = \frac{\Gamma/(2\beta)}{1 + \frac{1-\beta}{2\beta}\Gamma},$$

where  $\beta \equiv \beta_M/\beta_C$ .

In ref. [1], the growth-rate dependent change of the transcription rate  $\alpha_m(\Gamma)$  normalised by the value at  $\Gamma = 1$  and the gene copy number  $g(\Gamma)$  is given. In Fig. S1 left, we plotted  $\alpha_m(\Gamma)$  and fitted  $\beta$  so that normalised growth-dependent production rate

$$\alpha(\Gamma) = \frac{\tilde{\alpha}(\Gamma)}{\tilde{\alpha}(1)} = \frac{\frac{1+\beta}{2\beta} \cdot \Gamma}{1 + \frac{1-\beta}{2\beta} \cdot \Gamma} \quad (5)$$

agrees best with the data. With  $\beta \approx 0.4$ , we get a good fit to the data.

If we also take into account the change in the gene copy number, we should compare  $\alpha_m(\Gamma)$  with  $\alpha_m(\Gamma)g(\Gamma)/g(1)$ , which is shown in Fig. S1 right. In this case, we get  $\beta \approx 1.2$ .

In fig S2, we plotted the lines  $\beta = \frac{\beta_M}{\beta_C} = 0.4$  and  $\beta = \frac{\beta_M}{\beta_C} = 1.2$  in the phase diagram for the bistability with reference parameters, which demonstrate that we can get bistability with satisfying the relation from [1].

It should be noted that the growth-rate change in [1] is obtained by the steady state exponential growth, and the relation may not be the same if the growth rate is changed dynamically by the overproduction of toxin.

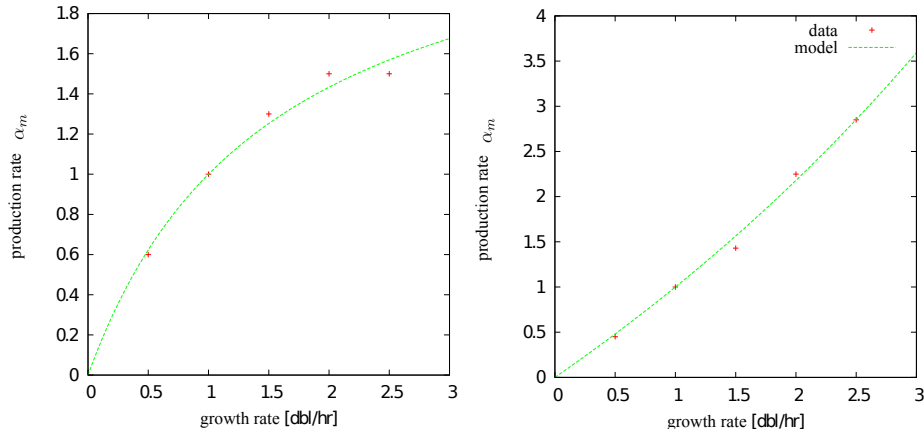


Figure S1: **Fit of the free toxin activity parameters to the grown-rate dependent global transcription rate.** Left: Red points: Global transcription rate  $\alpha_m(\Gamma)$  from Klumpp et al. [1]. Green Line: normalised production rate  $\alpha(\Gamma)$  from our model with  $\beta = 0.4$ . Right: Red points: Normalized global transcription rate multiplied by gene copy number,  $\alpha_m(\Gamma)g(\Gamma)/g(1)$  from Klumpp et al. [1]. Green Line: normalised production rate  $\alpha(\Gamma)$  from our model with  $\beta = 1.2$ .

## References

- [1] S. Klumpp, Z. Zhang, T. Hwa "Growth-rate dependent global effects on gene expression in bacteria" *Cell* **139(7)** 1366-1375 (2009)
- [2] I. Cataudella, A. Trusina, K. Sneppen, K. Gerdes and N. Mitarai "Conditional cooperativity in toxin antitoxin regulation prevents random toxin activation and promotes fast translational recovery" *Nucleic Acids Res.* **40** 6424-6434 (2012).

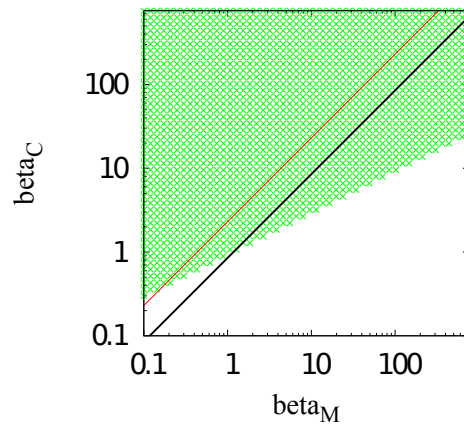


Figure S2:  $\beta_M/\beta_C$  fitted to the global transcription rate lies in the bistable region. Each green dot in the plot represents a combination of  $\beta_M$  and  $\beta_C$  that give bistable results. The red line represents  $\beta_M/\beta_C = 0.4$ , and the black line  $\beta_M/\beta_C = 1.2$ .