- **Article:** Speed, dissipation, and error in kinetic proofreading
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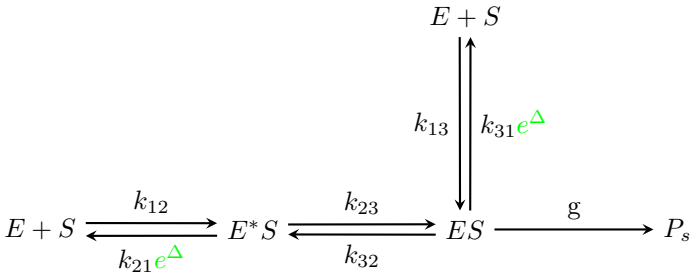
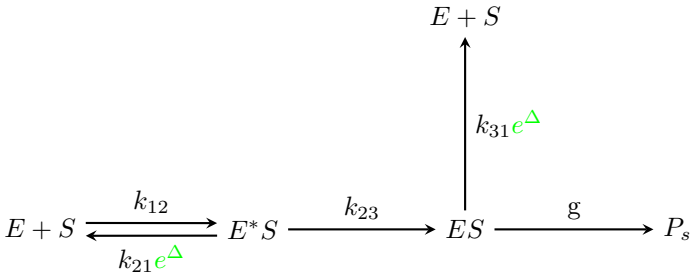
1 Brief introduction of kinetic proofreading

Hopfield's kinetic proofreading model provide a scheme for us to understand how biological circuits are designed to improve the accuracy of molecular recognition. The basic idea could be describe as follows:



- For simplification, we consider the case that there are two kinds of substates S. One is R, which stand for the right substates and another is W, which stands for wrong substates. The green part is an extra term for wrong substrates. The relatively higher rate for wrong substrates is driven by ATP hydrolysis.

If we take the limit that $k_{13} \ll 1$, $k_{32} \ll 1$, $e^{\Delta} \gg 1$, $k_{23}k_{31}e^{\Delta} \gg k_{13}k_{32}$, $k_{31} \gg g$. The reaction could be written as:



Simple calculation could show that when the system is in detail balance, the error rate(the ratio of the production rate of P_w to the production rate of P_r when the concentration of these two kinds of substrates are the same) is now $e^{-\Delta}$. But when we take the limit, the detail balance is broken and the error is now $e^{-2\Delta}$. Of course, the improvement of accuracy comes at the price. This circuit will consume more energy(ATP hydrolysis) and takes more time to produce the right production.

2 What is new

We can generalize the kinetic proofreading network to a ladder structure as showed in Fig 1.

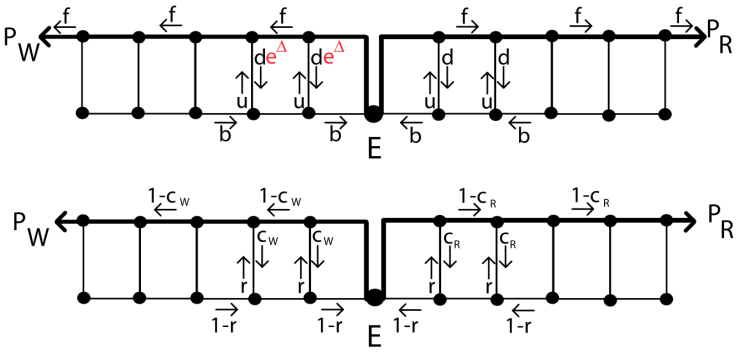


Figure 1: Ladder network

In the upper rail of ladder networks, the reactions can only move in 'forward direction', that is, moving towards the production of P_S. While in the lower rails, the process happens in opposite direction. We can consider an equivalent description of this as showed in the lower part of Fig 1: an enzyme-substrate complex processes along the upper rails towards to the final products or move along the lower rails away from the completion of the reaction. During both process, the complex may randomly switches to the other side of the ladder and thus move on opposite direction. The probability could be denoted as c_S and r separately. They satisfied the relationship:

$$c_R = \frac{d}{d+f} \qquad c_W = \frac{de^{\Delta}}{de^{\Delta}+f}$$

This process is a good analogue of instability of microtubules. Microtubules could be in "growth state" or "catastrophe state". In "growth state", the microtubules grows a the rate v_g while in "catastrophe state", the microtubules shrink at a rate v_s. Also, we use f_{res} and f_{cat} to describe the probability of the switch between this two states. When those parameters takes different values, the growth of microtubules could be bounded or unbounded as show in Fig 2 It is reasonable to ask if the reaction process in ladder network could exhibit the same dynamic property as the growth of microtubules. So both the right substrates and the wrong substrates c. There are four combination but one is impossible because if the wrong substrates are unbounded than the right substrates must be unbounded too. So we can discuss other three possibility:

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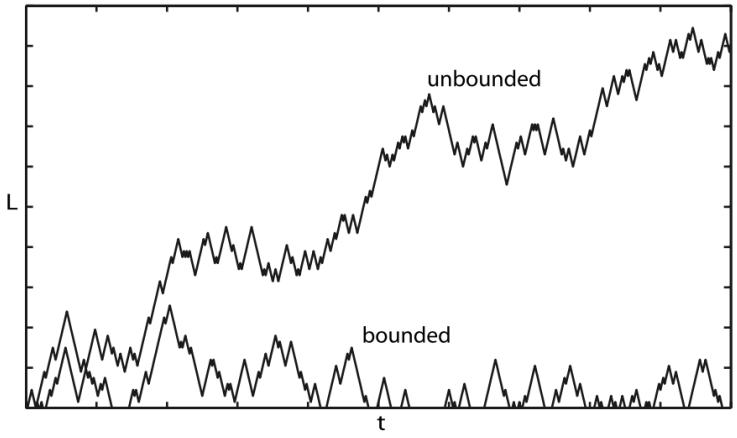

Figure 2: bounded and unbounded growth of microtubules