Emergence of robust growth laws from optimal regulation of ribosome synthesis

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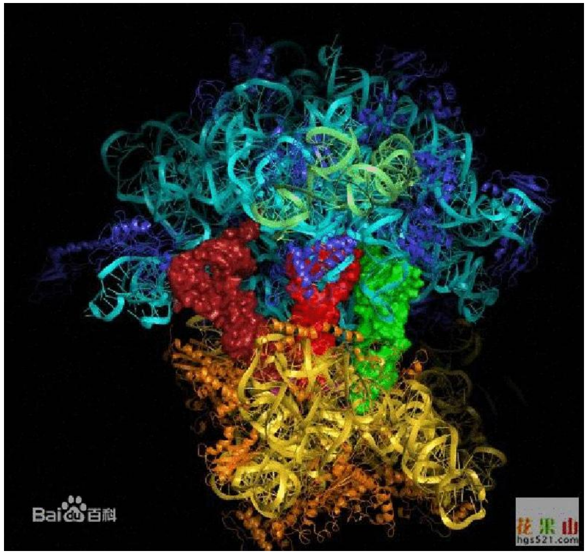
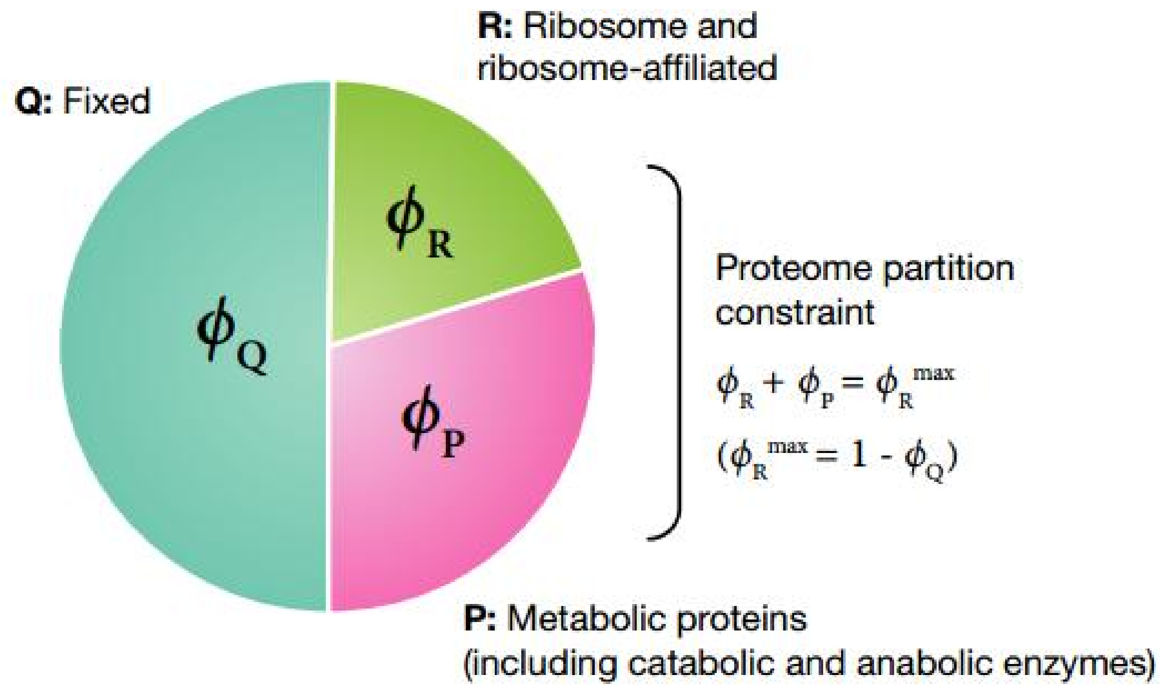
Background

- 核糖体蛋白质对rRNA有很强的结合作用，当没有rRNA结合时，它就会在细胞质中积累并结合到mRNA上抑制翻译

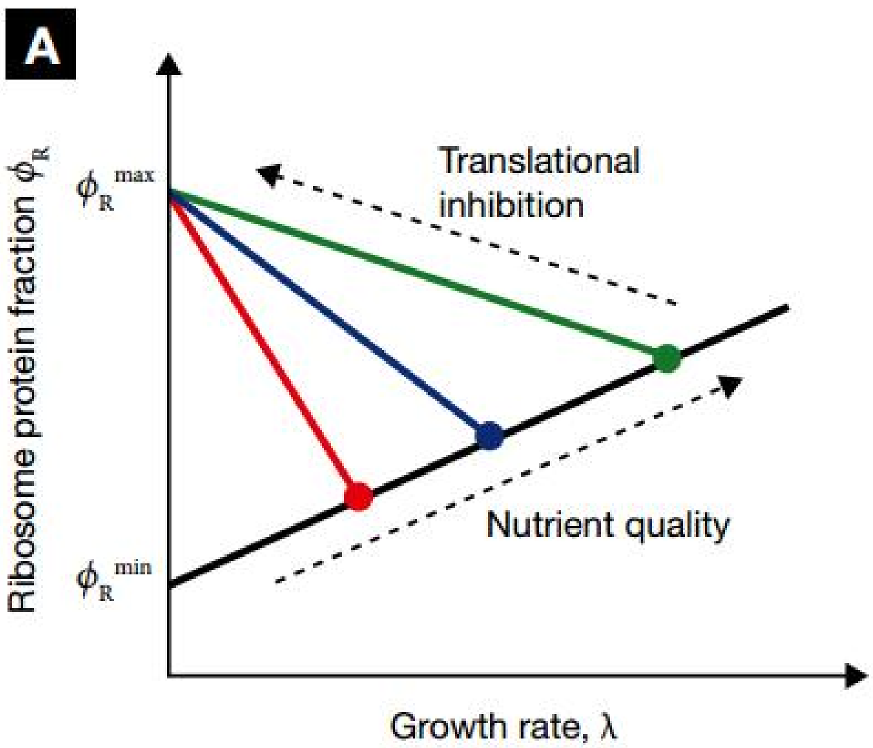
- 蛋白质的合成包括氨酰-tRNA合成，肽链合成的启示、延伸及终止。部分抗生素能与氨基酰-tRNA合成酶特异性结合从而使该类酶失去催化氨基酸与tRNA结合的能力部分；部分抑制肽链延伸的主要分为四环素类抗生素、酰胺醇类抗生素、大环内酯类抗生素





- The growth rate dependence of the ribosome and metabolic proteins are constrained by the partitioning

- Q:a growth rate-independent fraction

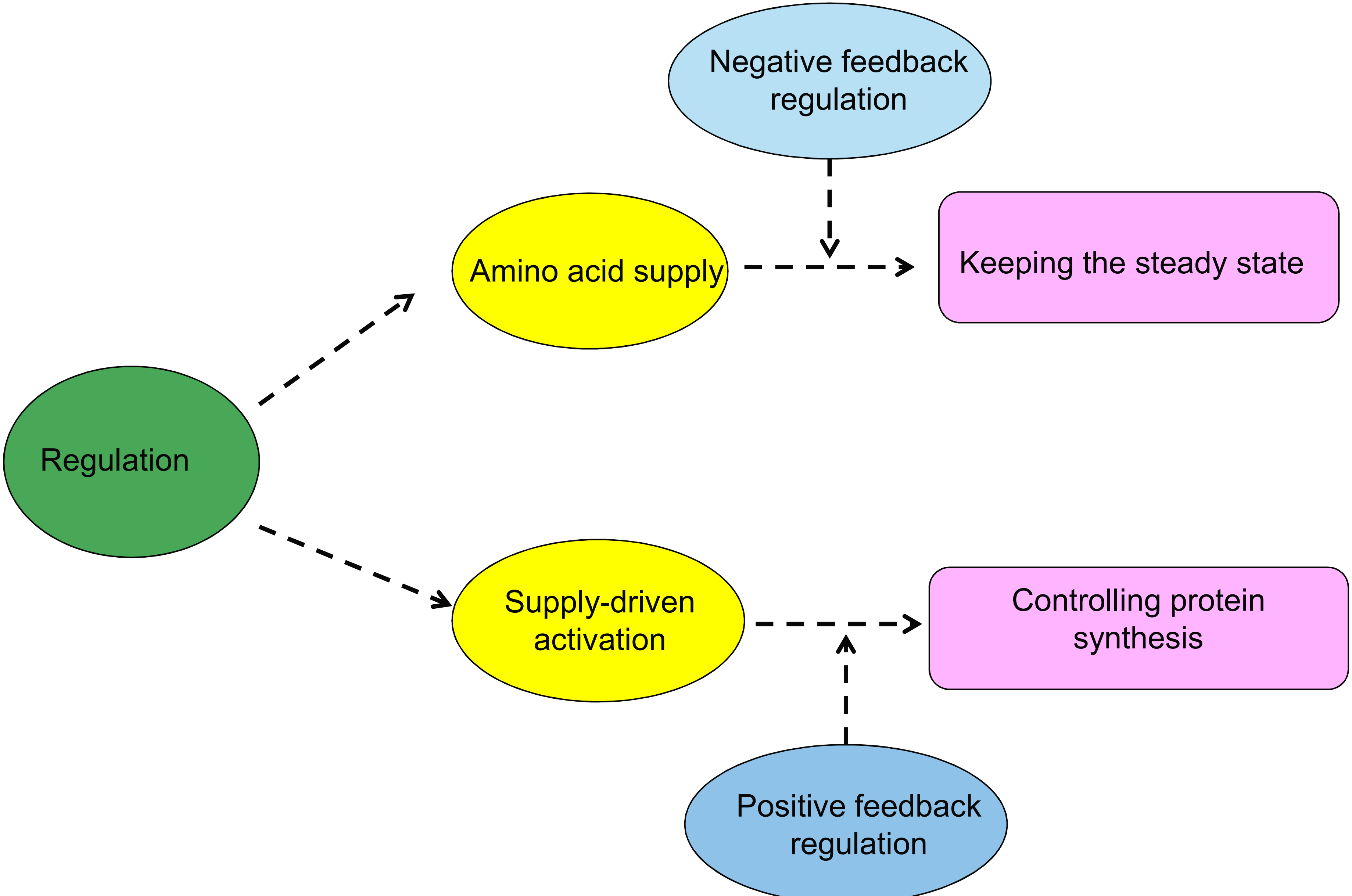


$$\phi_R = \phi_R^{min} + \frac{\lambda}{\gamma},$$

$$\phi_R = \phi_R^{max} - \frac{\lambda}{\nu},$$

γ :protein translation rate

ν :nutritional efficiency


Negative feedback regulation
Amino acid supply
Keeping the steady state
Regulation
Supply-driven activation
Controlling protein synthesis
Positive feedback regulation

Protein synthesis

$$\frac{dM}{dt} = \lambda M$$

λ :the growth rate

M:the total protein mass

$$\frac{dM}{dt} = \lambda M = k N_R^{Act}.$$

N_R^{Act} :number of active ribosome

$$\lambda M = k\left(N_R - N_R^{min}\right).$$

$M_R = N_R m_R$

m_R : the mass per ribosome

$\phi_R = M_R/M,$

$\gamma = k/m_R$

$$\lambda = \gamma\left(\phi_R - \phi_R^{min}\right),$$

Amino acid flux

$$\frac{dM_a}{dt} = J_a^{in} - \beta \frac{dM}{dt}$$

$a = M_a/M$
Amino acid level

J_a^{in} :amino acid influx rate
β:the fraction of translation

$$\frac{da}{dt} = \frac{J_a^{in}}{M} - \frac{1}{M}\frac{dM}{dt}(\beta + a)$$

$$\frac{dM}{dt} = \lambda M$$

$$da/dt = 0$$

$$\frac{J_a^{in}}{\beta M} = \lambda$$

$$\lambda = \frac{k_a \eta_a}{\beta} \phi_P.$$

$$J_a^{in} = k_a \eta_a M_P$$

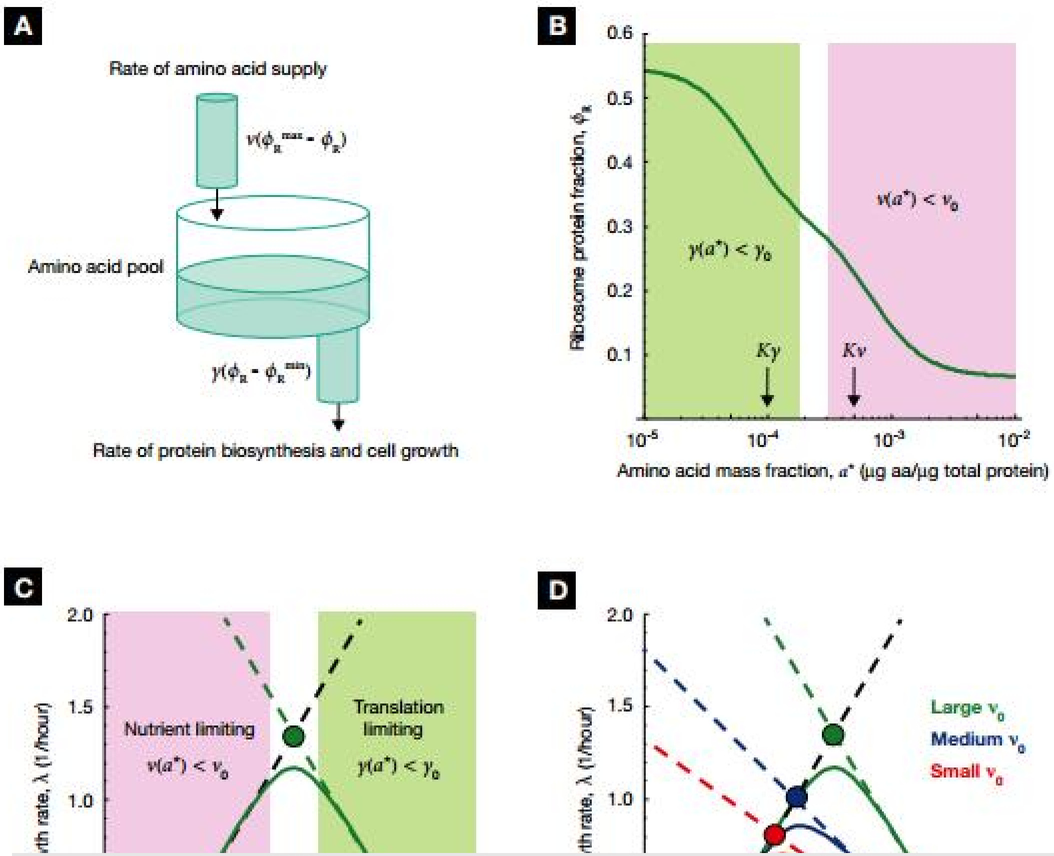
$$\frac{J_a^{in}}{M} = k_a \eta_a \phi_P$$

$$\lambda = \frac{k_a \eta_a}{\beta} (\phi_R^{max} - \phi_R).$$

$$\nu = \frac{k_a \eta_a}{\beta}$$

$$\lambda = \nu (\phi_R^{max} - \phi_R).$$

Growth rate maximization

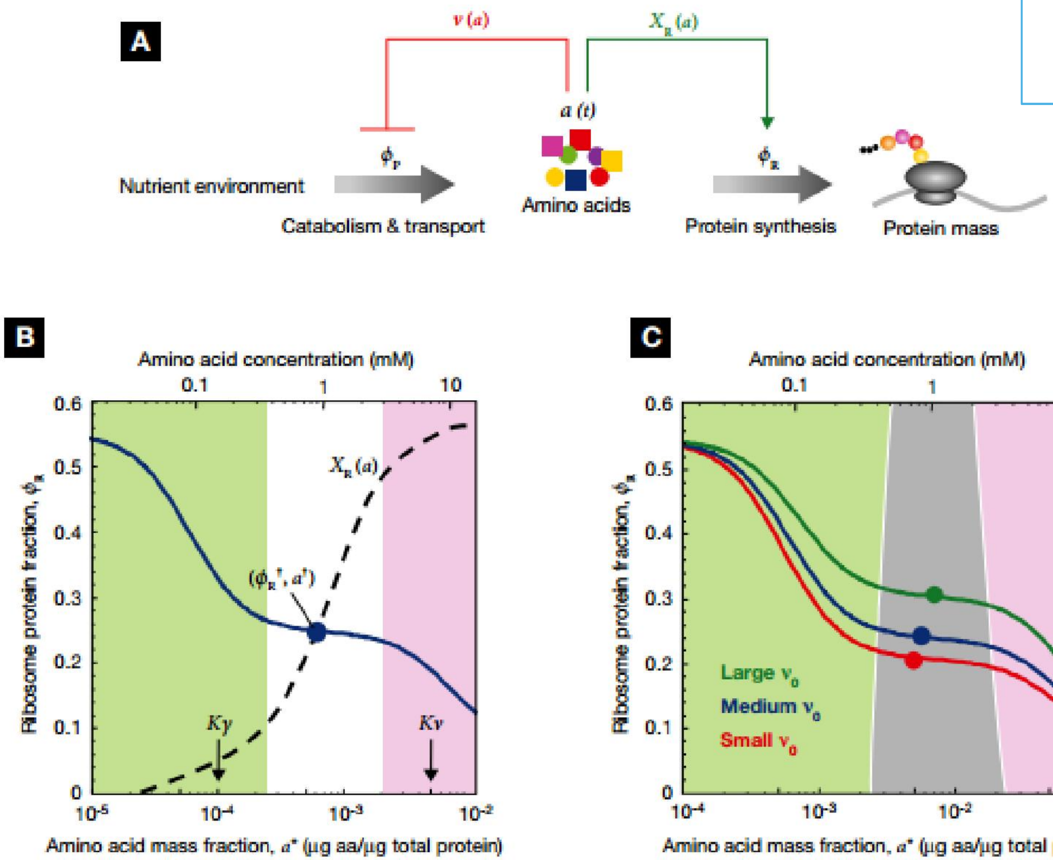


$$\phi_R = \phi_R^{min} + \left(\phi_R^{max} - \phi_R^{min}\right) \frac{\nu(a^*)}{\gamma(a^*) + \nu(a^*)}$$

$$\lambda = \gamma(a^*)\left[\phi_R - \phi_R^{min}\right]$$

Amino acid flux balance and growth rate maximization

Control of ribosome synthesis



$$\frac{dM_R}{dt} = \chi_R(a)\left[kN_R^{Act}\right] = \chi_R(a)\left[k\left(N_R - N_R^{min}\right)\right]$$

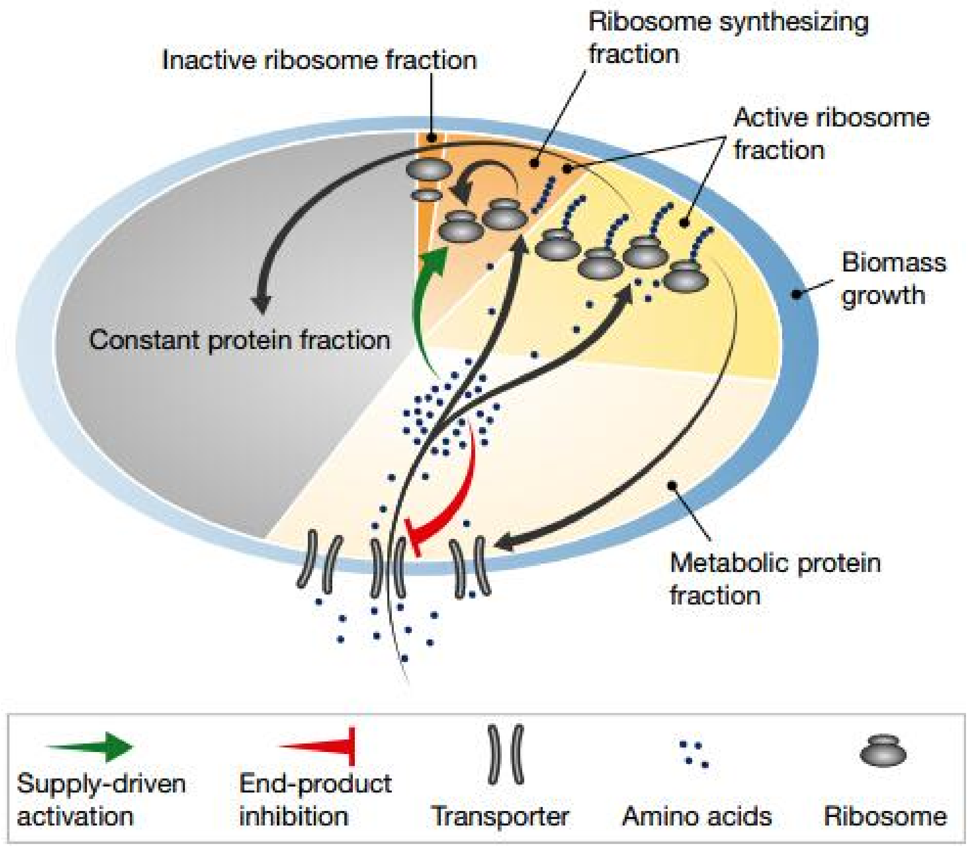
↓

$$\lambda\phi_R = \chi_R(a^*)\left[\gamma\left(\phi_R - \phi_R^{min}\right)\right]$$

↓

$$\phi_R = \chi_R(a^*)$$

Conclusion



Ribosome synthesizing fraction
Inactive ribosome fraction
Active ribosome fraction
Biomass growth
Constant protein fraction
Metabolic protein fraction
Supply-driven activation
End-product inhibition
Transporter
Amino acids
Ribosome

亮点

- 从表面的现象到分子机制的研究,深入了解稳定的生长规律

改进

- 考虑除指数增长以外的生长方式，更深入的了解控制稳健生长规律的分子机制

Thank You !