10/22/10

MODEL FOR sRNA INHIBITION:
(E. LEVINE ET AL. PLOS BIOLOGY 5, e229 (2007))

$\xrightarrow{\alpha_m} m \xrightarrow{\gamma_m} \emptyset$ m: mRNA

$\xrightarrow{\alpha_s} s \xrightarrow{\gamma_s} \emptyset$ s: sRNA

$m + s \xrightarrow{k} \emptyset$

$m \xrightarrow{\alpha_p} m + P \ , \ P \xrightarrow{\gamma_P} \emptyset$

(i) $\dot{m} = \alpha_m - \gamma_m m - kms \overset{!}{=} 0$

(ii) $\dot{s} = \alpha_s - \gamma_s s - kms \overset{!}{=} 0$

(iii) $\dot{P} = \alpha_p m - \gamma_P P \overset{!}{=} 0$

Solving (i) for s in steady state yields

$$s = \frac{\alpha_m - \gamma_m m}{km}$$

Substituting onto (ii) gives

$$\gamma_m m^2 + \left(\alpha_s - \alpha_m + \frac{\gamma_m \gamma_s}{k}\right) m - \alpha_m \frac{\gamma_s}{k} = 0$$

Solving the quadratic equation gives

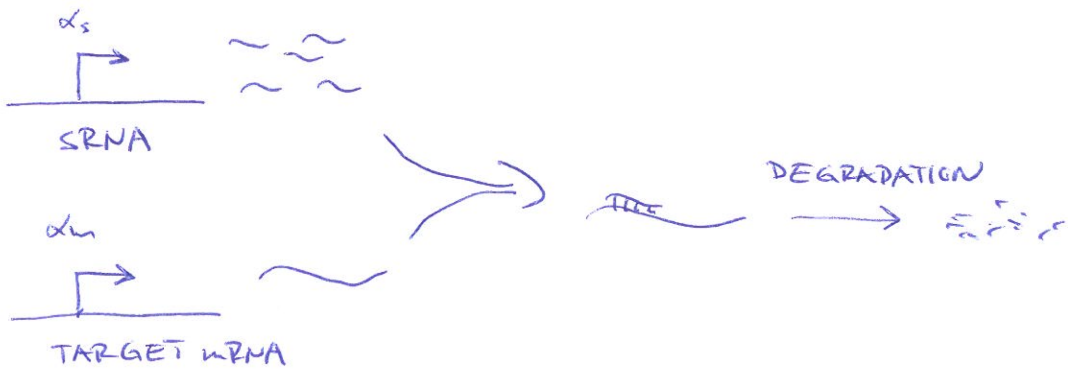
$$m_\pm = \frac{1}{2\gamma_m}\left(\alpha_m - \alpha_s - \mu \pm \sqrt{(\alpha_m - \alpha_s - \mu)^2 + 4\alpha_m \mu}\right)$$

only the positive sign is biologically relevant

$$\mu := \frac{\gamma_m \gamma_s}{k}$$

Parameter for interaction strength.

CASE II $\alpha_s >> \alpha_m$



Assume strong interactions: $\mu = \gamma_m \gamma_s / k \to 0$

$$m = \frac{\alpha_s - \alpha_m}{2\gamma_m}\left(-1 - \frac{\mu}{\alpha_s - \alpha_m} + \sqrt{1 + 2\mu\frac{\alpha_s + \alpha_m}{(\alpha_s - \alpha_m)^2} + \frac{\mu^2}{(\alpha_s - \alpha_m)^2}}\right)$$

Expand to linear order in the small parameter $\mu/(\alpha_s - \alpha_m)$, use $\sqrt{1+x} \cong 1 + x/2$:

$$\underline{m} = \frac{\alpha_s - \alpha_m}{2\gamma_m}\left(-1 - \frac{\mu}{\alpha_s - \alpha_m} + 1 + \mu\frac{\alpha_s + \alpha_m}{(\alpha_s - \alpha_m)^2}\right)$$

$$= \underline{\frac{\alpha_m}{\gamma_m}\,\frac{\mu}{\alpha_s - \alpha_m}} \qquad \alpha_s >> \alpha_m$$

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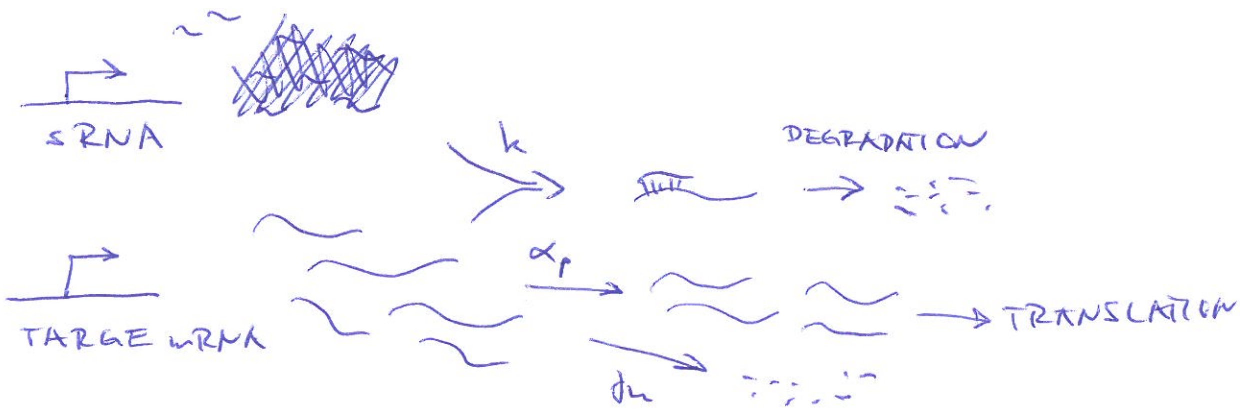
CASE 1: $\alpha_m >> \alpha_s$



Assume strong interactions: $\mu = \gamma_m \gamma_s / k \to 0$

$$m = \frac{\alpha_m - \alpha_s}{2\gamma_m}\left(1 - \frac{\mu}{\alpha_m - \alpha_s} + \sqrt{\left(1 + 2\frac{\mu(\alpha_m + \alpha_s)}{(\alpha_m - \alpha_s)^2} + \frac{\mu^2}{(\alpha_m - \alpha_s)^2}\right)}\right)$$

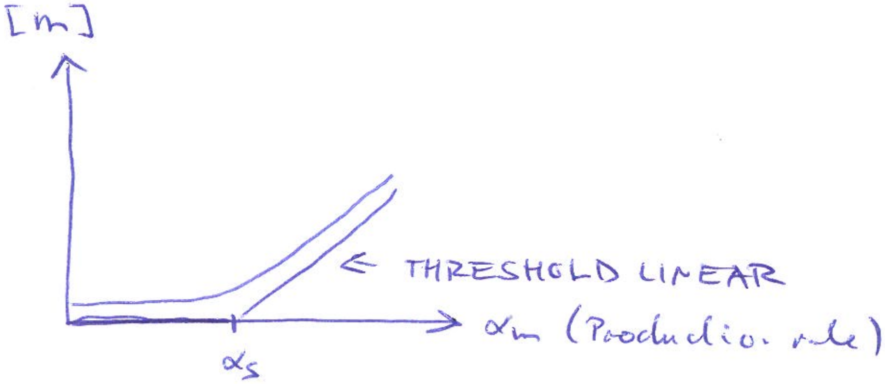
Expand this expression to linear order in the small parameter $\mu/(\alpha_m - \alpha_s)$ using $\sqrt{1 \pm x} \cong 1 \pm x/2$:

$$\underline{m} \cong \frac{\alpha_m - \alpha_s}{2\gamma_m}\left(1 - \frac{\mu}{\alpha_m - \alpha_s} + 1 + \frac{\mu(\alpha_m + \alpha_s)}{(\alpha_m - \alpha_s)^2}\right)$$

$$= \underline{\frac{\alpha_m - \alpha_s}{\cancel{2}\gamma_m} + \mu \frac{\alpha_s / \gamma_m}{\alpha_m - \alpha_s}} \qquad \alpha_m >> \alpha_s$$

NO LEAKAGE: $\mu = 0$

$$m \cong \begin{cases} (\alpha_m - \alpha_s)/\gamma_m & \alpha_m \gg \alpha_s \\ \approx 0 & \alpha_s \gg \alpha_m \end{cases}$$



5.2 RIBOSWITCHES, CRISPR AND OTHER BACTERIAL SRNA

SEE REVIEW BY WATERS + STORZ, CELL 136, 615 (2009)