siRNA MODEL

S_0 : AMOUNT / CONCENTRATION OF siRNA DELIVERED AT $T=0$.

REACTION MODEL

$$S + m \underset{k_-}{\overset{k_+}{\rightleftharpoons}} C \xrightarrow{k_2} S$$

(1) $\dot{C} = k_+ m \cdot s - (k_- + k_2) C \overset{!}{\doteq} 0$ ← VALID IF $k_- \ll k_2$ AND IF REACTIONS ARE FAST COMPARED W/ SPONTANEOUS mRNA AND sRNA DECAY/DILUTION.

$\Rightarrow C$

(2) $\dot{s} = -\gamma_s s - k_+ m s + (k_- + k_2) C \underset{(1)}{\overset{\downarrow}{=}} -\gamma_s s \quad \Rightarrow \quad s(t) = s_0 e^{-\gamma_s t}$

(3) $\dot{m} = \alpha_m - \gamma_m m - k_+ m s + k_- C \underset{(1)}{\overset{\downarrow}{=}} \alpha_m - \gamma_m m - k_2 C$

From (1) : $C = \dfrac{k_+}{k_- + k_2} m \cdot s = m s / K_m, \quad K_m := (k_- + k_2)/k_+$

Into (3) : $\dot{m} = \alpha_m - \gamma_m m - \dfrac{k_2}{K_m} m s \overset{!}{\doteq} 0$ ↓

SHOULD HOLD AFTER mRNA HAS EQUILIBRATED WITH siRNA

$$\Rightarrow m = \frac{\alpha_m}{\gamma_m + \frac{k_2}{K_m} s(t)} = \frac{\alpha_m / \gamma_m}{1 + \frac{k_2}{\gamma_m} \frac{s_0 e^{-\gamma_s t}}{K_m}}$$