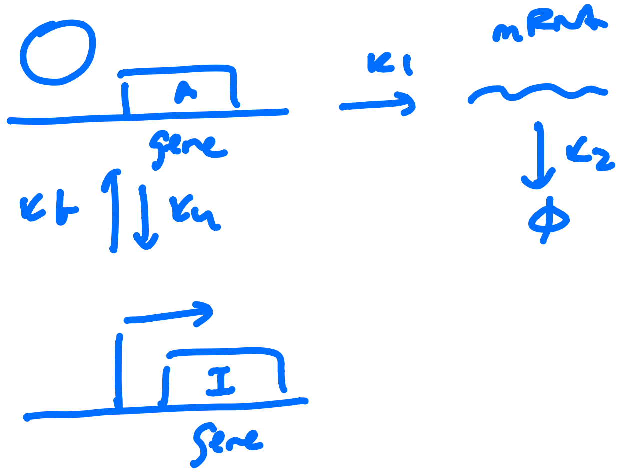
W10 - RNA regulation as a Markov process

$$G(I) \xrightarrow{k_b} G(A)$$
$$G(A) \xrightarrow{k_u} G(I)$$
$$G(A) \xrightarrow{k_1} RNA + G(A)$$
$$RNA \xrightarrow{k_2} \phi$$



r		W_r	$\eta_r(R)$
1	$G(I) \xrightarrow{k_b} G(A)$	k_b	0
2	$G(A) \xrightarrow{k_u} G(I)$	k_u	0
3	$G(A) \xrightarrow{k_1} G(A) + RNA$	k_1	+1
4	$RNA \xrightarrow{k_2} \phi$	$k_2 \cdot RNA$	-1

Master eq.

$$\begin{aligned}
P(A, R \mid t+\Delta t) = & + k_b \cdot \Delta t \; P(I, R \mid t) \\
& + k_1 \cdot \Delta t \; P(A, R-1 \mid t) \\
& + k_2 (R+1) \cdot \Delta t \; P(A, R+1 \mid t) \\
& + (1 - k_u \Delta t - k_1 \Delta t - k_2 R \Delta t) \; P(A, R \mid t)
\end{aligned}$$

$$P(I,R|t+\Delta t) = k_u \cdot \Delta t \; P(A,R|t)$$

no term on $P(I\,R-1|t)$

$$\left\{ \begin{array}{l} + k_2(R+1)\cdot\Delta t \; P(I,R+1|t) \\ + (1 - k_b\Delta t - k_2 R\Delta t)\, P(I,R|t) \end{array} \right.$$

$$\frac{dP(A,R|t)}{dt} = k_b P(I,R|t) + k_1 P(A,R-1|t) + k_2(R+1)\, P(A,R+1|t) - (k_u + k_1 + k_2 R)\, P(A,R|t)$$

$$\frac{dP(I,R|t)}{dt} = k_u P(A,R|t) + k_2(R+1)\, P(I,R+1|t) - (k_b + k_2 R)\, P(I,R|t)$$

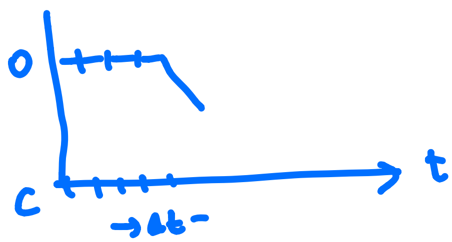
$\longrightarrow$ show code.

The Gillespie algorithm

For fast stochastic sampling.

instead of stopping at each Δt to make a decision, we model the "wait time" without change.

$$P(\tau) = P(\bar{x}, t+\tau \mid \bar{x}, t) \cdot p(\text{change at } \tau)$$



$$P(\bar{x}, t+\tau \mid \bar{x}, t) = P(\bar{x}, t+\tau \mid \bar{x}, t+\tau-\Delta t)$$
$$P(\bar{x}, t+\tau-\Delta t \mid \bar{x}, t+\tau-2\Delta t)$$
$$P(\bar{x}, t+\tau-3\Delta t \mid \bar{x}, t+\tau-4\Delta t)$$

$\tau = m\,\Delta t$

$$\vdots$$
$$P(\bar{x}, t+\Delta t \mid \bar{x}, t+2\Delta t)$$
$$P(\bar{x}, t)$$

$W_R = \sum_r W_r(\bar{x})$

$$= (1 - W_R \cdot \Delta t)^m$$
$$= \left(1 - W_R \frac{\tau}{m}\right)^m$$
$$\lim_{m \to \infty} = e^{-W_R \tau}$$

$$\boxed{P(\tau) = W_R\, e^{-W_R \tau}}$$

Stochastic process

start (A, R_0)

Δt draw r in $U[0:1]$

if $r \leq k_u \Delta t$ (I, R_0)

elif $r \leq k_u \Delta t + k_1 \Delta t$ (A, R_0+1)

elif $r \leq k_u \Delta t + k_1 \Delta t + k_2 R_0 \Delta t$ (A, R_0-1)

else (A, R_0)

Δt (A, R_0+1)

Stochastic process with Gillespie algo

Start t_0 (A, R_0)

$$w_R^0 = k_u + k_1 + k_2 R_0$$

Sample τ_0 from $P(\tau) = w_R^0 e^{-w_R^0 \tau}$

$t_1 = t_0 + \tau_0$

draw $r \in U[0;1]$ if $r < \frac{k_u}{w_R^0}$ $\rightarrow$ $I, R_1 = R_0$

elif $r < \frac{k_u + k_1}{w_R^0}$ $\rightarrow$ $A, R_1 = R_0 + 1$

elif $r < \frac{k_u + k_1 + k_2 R_0}{w_R^0}$ $\rightarrow$ $A, R_1 = R_0 - 1$

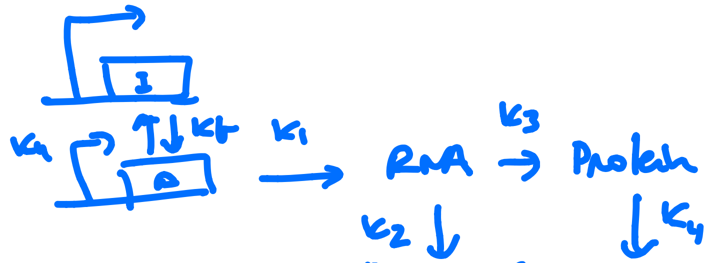
$t_1 = t_0 + \tau_0$ $\quad w_R^1 = k_u + k_1 + k_2 R_1$

draw τ_1 from $P(\tau) = w_R^1 e^{-w_R^1 \tau}$

$t_2 = t_1 + \tau_1$

draw r ....

Let's add proteins



$$G(I) \xrightarrow{k_b} G(A)$$

$$G(A) \xrightarrow{k_u} G(I)$$

$$G(A) \xrightarrow{k_1} G(A) + RNA$$

$$RNA \xrightarrow{k_3} RNA + P$$

$$RNA \xrightarrow{k_2} \phi$$

$$P \xrightarrow{k_4} \phi$$

w	n_R	n_P
k_b	0	0
k_u	0	0
k_1	+1	0
$k_3 R$	0	+1
$k_2 R$	−1	0
$k_4 P$	0	−1

$$
\begin{aligned}
P(A, R, P \mid t+\Delta t) = \quad & k_b \cdot \Delta t \quad P(I, R, P \mid t) \\
& k_1 \cdot \Delta t \quad P(A, R-1, P \mid t) \\
& k_2 \cdot (R+1) \cdot \Delta t \quad P(A, R+1, P \mid t) \\
& k_3 R \Delta t \quad P(A, R, P-1 \mid t) \\
& k_4 (P+1) \cdot \Delta t \quad P(A, R, P+1 \mid t) \\
& + (1 - k_b \Delta t - k_1 \Delta t - k_2 R \Delta t - k_3 R \Delta t - k_4 P \Delta t) \\
& \qquad P(A, R, P \mid t)
\end{aligned}
$$

$$
\begin{aligned}
P(I, R, P \mid t+\Delta t) = \quad & k_4 \cdot \Delta t \quad P(A, R, P \mid t) \\
& + k_2 (R+1) \cdot \Delta t \quad P(I, R+1, P \mid t) \\
& + k_3 R \Delta t \quad P(I, R, P-1 \mid t) \\
& + k_2 (P+1) \cdot \Delta t \quad P(I, R, P+1 \mid t) \\
& + (1 - k_b \cdot \Delta t - k_2 R \Delta t - k_3 R \Delta t \\
& \qquad - k_2 P \cdot \Delta t) \quad P(I, R, P \mid t)
\end{aligned}
$$