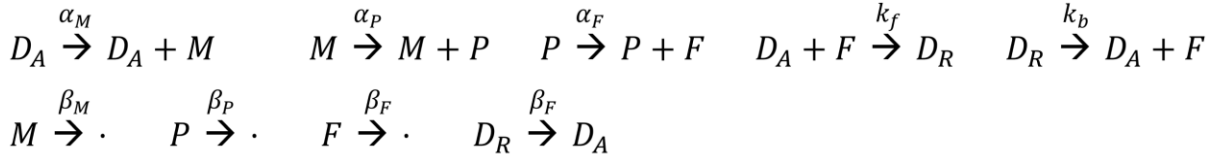


## BCS410. Practical Class 6 & Homework 5 [Due: May 23]

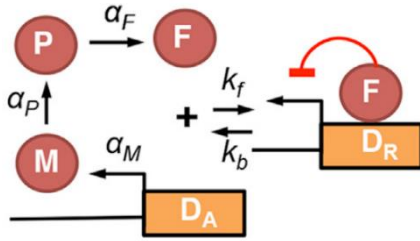
### Background:

Consider the following genetic negative feedback loop model:

#### Chemical reaction network



#### Model diagram



**Table 1.** Parameters of the genetic negative feedback loop model

Name	Description	Value
$\alpha_M$	Transcription rate constant for $M$	15.1745/hr
$\alpha_P$	Translational rate constant for $P$	1/hr
$\alpha_F$	Production rate constant for $F$	1/hr
$\beta_M$	Degradation rate constant for $M$	1/hr
$\beta_P$	Degradation rate constant for $P$	1/hr
$\beta_F$	Degradation rate constant for $F$	1/hr
$k_f$	Binding rate constant for $F$ and $D_A$	200Ω/hr
$k_b$	Unbinding rate constant for $D_R$	50/hr
$D_T$	The concentration of total DNA	165/Ω

**Problem 1:** Write down propensity functions of all reactions.

**Problem 2:** Let  $n_M$  denote the number of mRNA molecules, i.e.,  $M = n_M/\Omega$  where  $\Omega$  represents the volume of the system. Let  $n_{D_A}/n_{D_T}$  denote the fraction of active DNA. Plot a single sample time trace of  $n_M$  and  $n_{D_A}/n_{D_T}$  until  $t=40$  with the initial condition:  $D_A = 165$ ,  $D_R = 0$ ,  $M = 0$ ,  $P = 0$ , and  $F = 0$ , and the system volume  $\Omega = 1$ .

**Problem 3:** Plot a single sample time trace of  $n_M$  and  $n_{D_A}/n_{D_T}$  until  $t=40$  under the same condition as in Problem 2 except with varying  $\Omega = 0.01, 0.1, 10, 100, 1000$ . How does the result differ from that obtained in Problem 2? Which system exhibits more noise, and why?

**Problem 4:** Let  $K_d = (k_b + \beta_F)/k_f$  and consider the propensity function in Table 2, which are derived using the standard quasi-steady state approximation (sQSSA). Using these propensity functions, simulate a single sample trace of  $n_M$  and  $n_{D_A}/n_{D_T}$  under the same condition as in Problem 2, and compare the results to those obtained from the full stochastic model in Problem 2 and the full deterministic model in homework 2.

**Problem 5:** Let  $K_d = (k_b + \beta_F)/k_f$  and consider the propensity function in Table 3, which are derived using the total quasi-steady state approximation (tQSSA). Using these propensity functions, simulate a single sample trace of  $n_M$  and  $n_{D_A}/n_{D_T}$  under the same condition as in Problem 2, and compare the results to those obtained from the full stochastic model in Problem 2 and the full deterministic model in homework 2.

**Table 2.** Propensity functions obtained using the stochastic sQSSA

Reaction	Propensity function
$\phi \rightarrow M$	$\frac{\alpha_M n_{D_T} K_d \Omega}{n_F + K_d \Omega}$
$M \rightarrow M + P$	$\alpha_M n_M$
$P \rightarrow P + F$	$\alpha_P n_P$
$M \rightarrow \phi$	$\beta_M n_M$
$P \rightarrow \phi$	$\beta_P n_P$
$F \rightarrow \phi$	$\beta_F (n_F + \frac{n_{D_T} n_F}{n_F + K_d \Omega})$

**Table 3.** Propensity functions obtained using the stochastic tQSSA

Reaction	Propensity function
$\phi \rightarrow M$	$\frac{\alpha_M}{2} (n_{D_T} - n_R - K_d \Omega - \sqrt{(n_{D_T} - n_R - K_d \Omega)^2 + 4 n_{D_T} K_d \Omega})$
$M \rightarrow M + P$	$\alpha_M n_M$
$P \rightarrow P + R$	$\alpha_P n_P$
$M \rightarrow \phi$	$\beta_M n_M$
$P \rightarrow \phi$	$\beta_P n_P$
$R \rightarrow \phi$	$\beta_F n_R$

**Bonus problem 1 (5 bonus points):** Please compare the computation time required to simulate 1000 time traces using the full model and the stochastic tQSSA model, under the same condition as in Problem 2, except with  $k_f = 10000\Omega/\text{hr}$  and  $k_b = 100/\text{hr}$ .