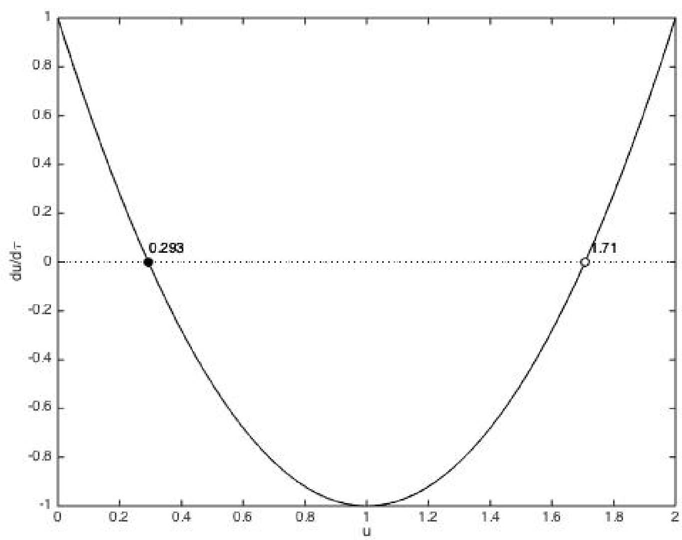
Solutions to PS1
February 23, 2015

Problem 1

(a) For $\eta = 2$ and $\frac{L_o}{K_d} = 1$,

$$\frac{du}{d\tau} = f(u) = (1 - 2u)(1 - u) - u \tag{1}$$

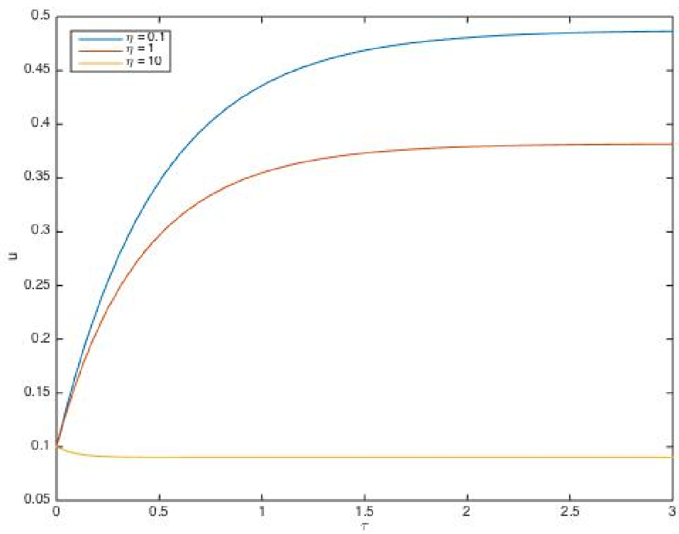
Using Matlab (see code), we plot $f(u)$ vs u and identify the fixed points where the plot intersects the x-axis. We determine whether these fixed points are stable (small shifts return the system to the fixed point) or unstable (small shifts propel the system away from the fixed point). Note that stable fixed points have $\frac{df}{du} < 0$.



Alternatively, we could plot the two terms of $f(u)$ separately and examine the intersection of these two curves (not shown here). This is analogous to the above approach except that it is more intuitive to plot the two terms separately.

Note that the goal is to find all the fixed points for the system. Since $0 \leq u \leq 1$, we consider only the fixed points within this domain. There is only one fixed point (stable) in this domain.

The convention is that this fixed point should be denoted with a solid circle. If there were an unstable fixed point, it would be denoted with an empty circle. There is an unstable fixed point outside the domain of interest for this system (see figure above).



(b) The plot below was generated in Matlab (see attached code). Note that for the case of $\eta = 10$, the steady-state value is less than the initial condition.

(c) The approach is to determine the steady-state value of u_{ss} as $\tau \to \infty$. We see that at $\tau = 3$, the response has reached steady-state in all cases; therefore, for computational purposes, we set $u_{ss} = u(\tau = 3)$. Next, we determine u_{90}, which is 90% of u_{ss}. Note that for $\eta = 10$, $u_{90} = 1.1u_{ss}$. In the next step, we determine τ_{90} when u reaches the value of u_{90}. This involves using the `Events` option in the Matlab ODE solver (see attached code). Finally, we convert τ_{90} into dimensional time (t_{90}) for the EGF-EGFR system using an estimated value for k_r using the following relationship:

$$\tau = k_r t \tag{2}$$

A reasonable estimate for k_r for the EGF-EGFR system is 0.12 min^{-1} (see Table 2–1 in Lauffenburger & Linderman, *Receptors*).

The solutions are provided in the table below.

η	u_{ss}	u_{90}	τ_{90}	t_{90} (min)
0.1	0.4866	0.4379	1.0184	8.5
1	0.3817	0.3435	0.8454	7.0
10	0.0901	0.0991	0.0093	0.078

Problem 2

(a) See attached figure for a sketch of the elementary reactions.The elementary reactions are:

$$R + L \rightleftharpoons C_1$$

$$C_1 + L \rightleftharpoons C_2$$

The rate equations given by mass-action kinetics are:

$$\frac{dC_1}{dt} = 2k_{f1}RL - k_{r1}C_1$$

$$\frac{dC_2}{dt} = k_{f2}C_1L - k_{r2}C_2$$

Note the statistical factor of 2 in the first term of the first equation. It accounts for the fact that the ligand can bind an empty receptor in two ways. Also note that mass-action rate equations are not written for R and L as they are not independent of the mass balances given below:

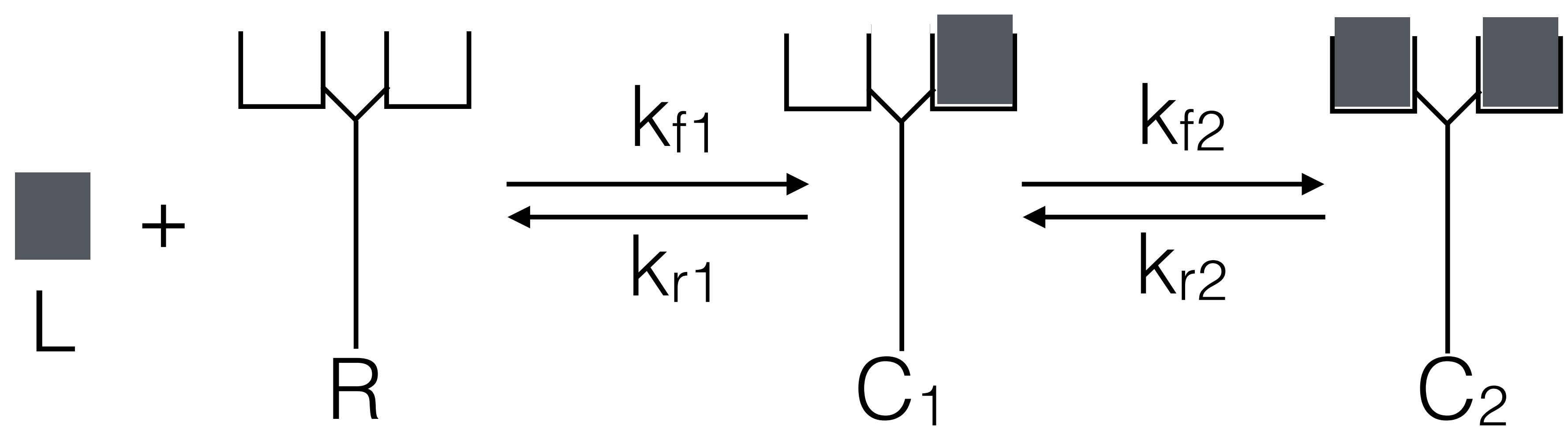
$$R + C_1 + 2C_2 = R_T$$

$$L + \eta C_1 + 2\eta C_2 = L_o$$

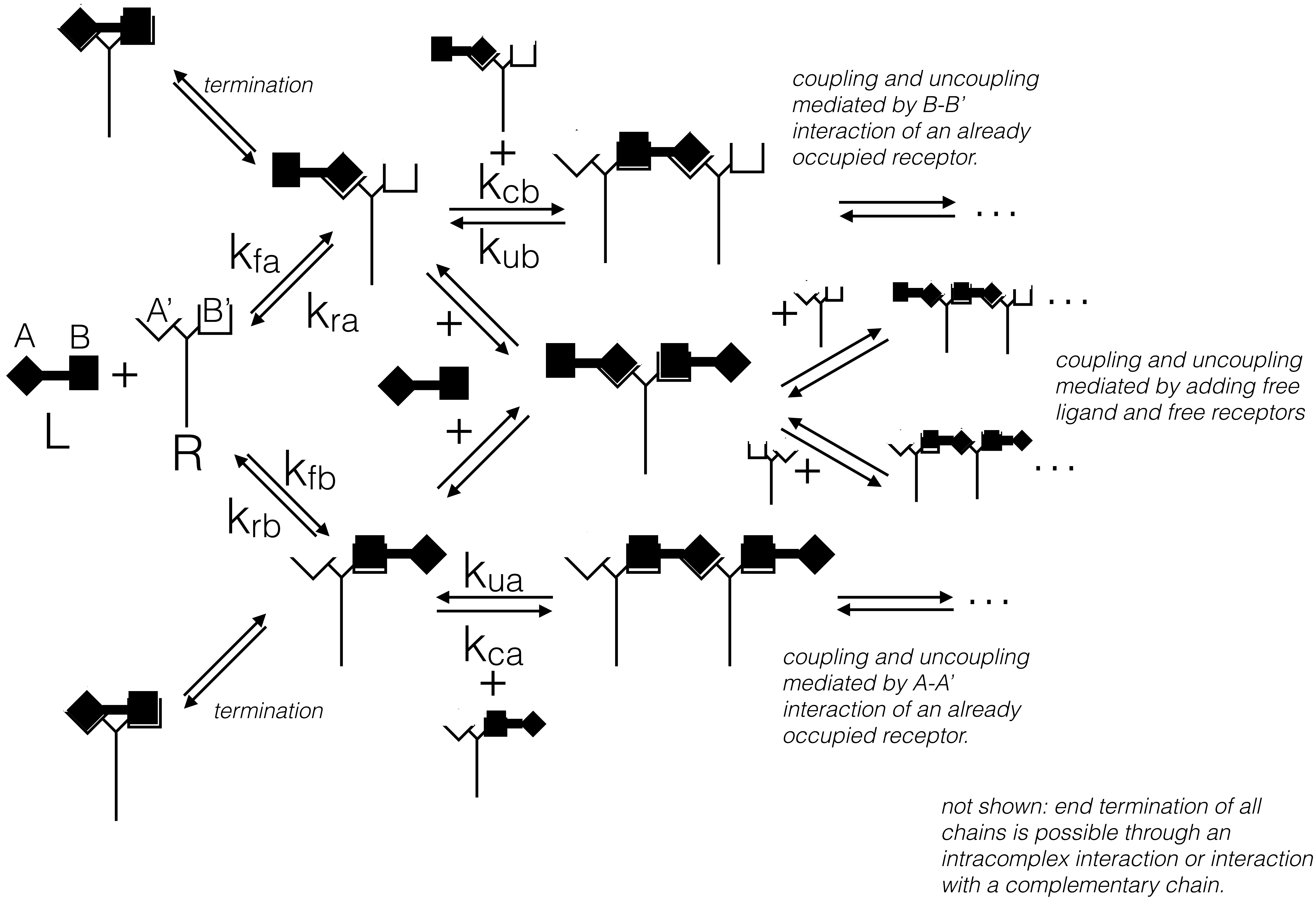
where R_T is the total number of receptors, L_o is the total amount of ligand and η is a conversion factor to account for the fact that complexes are given in terms of #/cell while ligand concentration is provided in molar quantity. For a cell density of n (# cells/L), the correction factor η is n/N_{Av} where N_{Av} is Avogadro's number.

(b) see attached figure.

Problem 2a



Problem 2b


termination
k_{cb}
k_{ub}
coupling and uncoupling mediated by B-B' interaction of an already occupied receptor.
k_{fa}
k_{ra}
A'
B'
A
B
L
R
coupling and uncoupling mediated by adding free ligand and free receptors
k_{fb}
k_{rb}
k_{ua}
k_{ca}
coupling and uncoupling mediated by A-A' interaction of an already occupied receptor.
termination
not shown: end termination of all chains is possible through an intracomplex interaction or interaction with a complementary chain.