BE 25 Winter 2026
Homework #2
Due at 9 AM PST, January 20, 2026

Problem 2.1 (Dependence on extramolecular species, 30 pts)**.**
Consider the Lindemann mechanism from Problem 1.1. As a reminder, here is the reaction scheme.

$$\mathrm{A} + \mathrm{M} \underset{\mathrm{k}_{-1}}{\overset{\mathrm{k}_1}{\rightleftharpoons}} \mathrm{A}^* + \mathrm{M} \tag{2.1}$$

$$\mathrm{A}^* \xrightarrow{\mathrm{k}_2} \mathrm{P}\,. \tag{2.2}$$

Phenomenologically, we might consider a chemical reaction for unimolecular conversion to products as

$$\mathrm{A} \xrightarrow{k_{\mathrm{uni}}} \mathrm{P}. \tag{2.3}$$

Assuming that a Lindemann mechanism is behind this unimolecular conversion, write an expression for k_{uni} in terms of the rate constants k_1, k_{-1} and k_2 and the concentration of the activating species c_{M}. You should use a quasi-steady state approximation to do so. Then, sketch a plot of k_{uni} as a function of c_{M}.

Problem 2.2 (Protein misfolding, 35 pts)**.**
This problem is based on Problem 15.17 of KKW. Imagine a test tube with buffer conditions such that it is full of denatured protein (D). The buffer conditions are suddenly changed such that the denatured protein can fold into one of two configurations, a natively folded configuration (N) or a misfolded configuration (M). That is, the following two reactions may happen.

$$\mathrm{D} \xrightarrow{k_1} \mathrm{N}, \tag{2.4}$$

$$\mathrm{D} \xrightarrow{k_2} \mathrm{M}. \tag{2.5}$$

In the experimental setup, we can only measure the concentration of folded (natively or otherwise) protein over time. That is, we can only monitor the reaction

$$\mathrm{D} \xrightarrow{k_{\mathrm{eff}}} \text{folded}. \tag{2.6}$$

It is determined that $k_{\mathrm{eff}} = 15\ \mathrm{s}^{-1}$. Though it is not fast enough to measure kinetics, another experimental technique can measure the ratio of natively folded to misfolded proteins. After a long time (presumably at steady state), it is determined that the ratio of the concentration of natively folded proteins to the concentration of misfolded proteins is 9. From these measurements, deduce the values of k_1 and k_2.

Problem 2.3 (Switching time of bacteria, 35 pts)**.**
This problem is based on a thought experiment proposed by Robijn Bruinsma in Bruinsma, Physica A, ***313, 211–237, 2002.***

Say we are interested in assessing how fast a bacterial cell can respond to a change in environment. Specifically, imagine a cell is in a sea of delicious lactose and suddenly the lactose is washed away. The cell should then repress expression of β-galactosidase by having a repressor bind to the appropriate operator. Of course, many other mechanisms will be at play in the cellular response, but the fastest the response could possibly be is given by how fast the repressor could bind to its operator.

To establish this speed limit, imagine the following experiment. Many short oligonucleotides are in a buffered solution with concentration c_{D}^0 (where the subscript D means "DNA"). Suddenly, at $t = 0$, repressors are added to give a concentration c_{R}^0 with $c_{\mathrm{R}}^0 \ll c_{\mathrm{D}}^0$. The repressors are added in such a way that the volume of the reaction mixture does not change appreciably. The repressors bind reversibly according to

$$\mathrm{D} + \mathrm{R} \underset{k_{\mathrm{d}}}{\overset{k_{\mathrm{a}}}{\rightleftharpoons}} \mathrm{DR}. \tag{2.7}$$

In this experiment, the concentration of repressor, c_{R}, is monitored over time.

a) Show that at short times, $c_{\mathrm{R}}(t) \propto \mathrm{e}^{-t/\tau}$. Write an expression for τ.

b) In similar in vitro experiments, it was determined that $k_{\mathrm{a}} \approx 10^{10}\ \mathrm{M}^{-1}\mathrm{s}^{-1}$ and $k_{\mathrm{d}} \approx 10^{-2}\ \mathrm{s}^{-1}$. Given than an *E. coli* cell has a volume of about one femtoliter, estimate the characteristic time it takes for the repressor to bind the operator. That is, plug numbers into your expression for τ. (Note that in a cell, the condition that $c_{\mathrm{R}}^0 \ll c_{\mathrm{D}}^0$ does not hold, but we can still take the response time to be approximately τ.)

c) We already reasoned that τ is a lower bound on the switching time of a bacterium. We can say further that this is a lower bound on the time it takes repressor to bind. Why?