Sample exam, *Modelling the Dynamics of Living Systems*
October 15, 2022

Allowed aids: Physics handbook, Beta mathematics handbook, calculator and dictionaries.
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Grades: 3 (9p), 4 (14p), 5 (19p), Max: 24p

NOTE: Write your solutions in a clear and understandable way. That means you must declare all definitions and approximations that you use, as well as all necessary steps in your calculations. If I have to guess what you did you will get zero points.

Results: I will let you know by email when I corrected your exams. Save the exam code!

Q1: Short questions and simple back of the envelope calculations (6p)

(a) Roughly how long are mRNA half lives? As a guide, *E.coli*'s life time is about 30 min. (1p)

(b) Calculated diffusion time scales. 10 seconds: this is the equilibration time $\tau_{\text{eq.}}$ for a single protein that diffuses in a cell with volume V. Given this, how long does it take the protein to find a target in V, if its radius a is 10 times smaller than the volume's radius R, that is $R/a = 10$? Use that the diffusion-limited search time is given by $\tau_{\text{target}} = V/(4\pi a D)$. (1p)

(c) Pseudo code for a Gillespie simulation. Consider a protein C that is repressing its own production and decays with $1/\tau$. If N_C is the number of C proteins, then

$$\frac{dN_C}{dt} = \frac{k_p}{1+N_C} - \frac{N_C}{\tau}$$

Using the Gillespie algorithm, write a pseudo code for the stochastic evolution of N_C. You may assume that N_C increases or decreases in units of one (i.e. $N_C \to N_C \pm 1$). Pay special attention to how you calculate the transition probabilities and the time step. (2p)

(d) Estimate bacterial translation rates. Assume that there are 40,000 ribosomes and 10^9 amino acids in *E. coli*. If all these are used during the 30 min the cell cycle, what is the average translation rate measured in codons/(ribosome $\times$ second). (1p)

(e) *Note: this question is not relevant 2022.* Volume of DNA in *E. coli*. Let's treat DNA as a simple polymer (ideal and no correlations) with n segments that are ℓ long, so that the total length of DNA is $L = n\ell$. If we let the polymer equilibrate, say from a linear chain, what will be the average distance between the first and last segment R_n (the so-called end-to-end distance)? You may use that $n = 4.6 \cdot 10^6$ bp and $\ell = 0.3$ nm. Taking R_n as a proxy for the polymer's radius, what is the ratio of the polymer's volume to the cell volume? *E. coli*'s volume is roughly 0.5 μm^3. (1p)

Q2: Simple model for transcription regulation in *E. coli* (7p)

Consider a simple one-state model for transcription where (1) the RNAp binds to the promoter with rate k_b [1/s] and (2) starts elongating with elongation rate constant k_e [1/s].

(a) Forbidding double RNAp occupancy at the promoter, what is the firing rate $\Omega = k_e\bar{\theta}$? Here, $\bar{\theta}$ is the average occupation probability for the operator site. (1p)

(b) Now we introduce a regulator R that binds to a regulatory site next to the gene (with equilibrium constant K), where R must be present to help RNAp to start transcription. Under steady-state conditions show that Ω depends on the [R] as follows? (3p)

$$\Omega = \frac{k_e k_b}{k_b + k_e(1 + [R]/K)}$$

(c) Generalise this expression for Ω to *two* regulators (R_1, R_2 and K_1, K_2), that must be bound simultaneously to allow transcription (2p)

(d) What about n regulators ($R_1, \ldots, R_n$ and $K_1, \ldots, K_n$)? (1p)

Q3: Simple model for epigenetics (6p)

Consider a piece of chromatin with L nucleosomes (=histones+DNA), where each nucleosomes can be either methylated (M) or acetylated (A).

(a) Consider simple linear transitions $A \to M$ with rate k_M and $M \to A$ with rate k_A. Formulate differential equations for the density da/dt and dm/dt, where $a = A/L$ and $m = M/L$, and show that the steady-state densities are $\bar{a} = k_A/(k_A + k_M)$, and $\bar{m} = k_M/(k_M + k_A)$. (1p)

(b) Now we introduce feedback and let A amplify its own transition from M, i.e $k_A \to k_A \times a$ (leave the transition $A \to M$ unchanged). With this addition, derive a new set of equations and find *all* new steady states for $\bar{a}$ and $\bar{m}$. (2p)

(b) As final (and more realistic) step, we need *two* of A to for the $M \to A$ transition. We also require two of M to go from $A \to M$. In this setting, find *all* steady states for $\bar{a}$ and $\bar{m}$ and argue which ones that are stable (use equations if you want, but it's just as fine to motivate it in words) (3p)

Q4: Networks (5p)

(a) Apart from that the degree distributions have different functional form, what stands out as the main difference between random (Poisson) and scale-free networks? (1p)

(b) For scale-free networks, the degree distribution is $p(k) = Ck^{-\gamma}$, where $C = \int_1^N k^{-\gamma} dk$ is a normalisation factor so that $\int_1^N p(k)dk = 1$. Show that the amplification factor $\mathcal{A} = \langle k^2 \rangle / \langle k \rangle - 1$ is

$$\mathcal{A} = \frac{2-\gamma}{3-\gamma} \frac{N^\gamma - N^3}{N^\gamma - N^2} - 1, \quad \text{where } \langle k^q \rangle = \int_1^N k^q k^{-\gamma} dk, \quad \text{(2p)}$$

(c) Furthermore, assuming that $2 < \gamma$ and $N \gg 1$, show that

$$\mathcal{A} \simeq \frac{2-\gamma}{3-\gamma} \times (1 - N^{3-\gamma}) - 1$$

Also, use the large-N behaviour of $\mathcal{A}$ to discuss the implications for signalling across the network when γ becomes > 3. (2p)