Biomolecular Feedback Systems

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Preface

This text serves as a supplement to *Feedback Systems* by Åström and Murray [1] (refered to throughout the text as AM08) and is intended for researchers interested in the application of feedback and control to biomolecular systems. The text has been designed so that it can be used in parallel with *Feedback Systems* as part of a course on biomolecular feedback and control systems, or as a standalone reference for readers who have had a basic course in feedback and control theory. The full text for AM08, along with additional supplemental material and a copy of these notes, is available on a companion web site:

`http://www.cds.caltech.edu/~murray/AMwiki/BFS`

The text is intended to be useful to three overlapping audiences: graduate students in biology and bioengineering interested in understanding the role of feedback in natural and engineered biomolecular systems; advanced undergraduates and graduate students in engineering disciplines who are interested the use of feedback in biological circuit design; and established researchers in the the biological sciences who want to explore the potential application of principles and tools from control theory to biomolecular systems. We have written the text assuming familiarity with the material in AM08, but have tried to provide insights and motivation so that the material can be learned in parallel. We also assume some familiarity with cell biology, at the level of a freshman course for non-majors. The individual chapters in the text indicate the pre-requisites in more detail, most of which are covered either in AM08 or in the supplemental information available from the companion web site.

Notation

This is an internal chapter that is intended for use by the authors in fixing the notation that is used throughout the text. In the first pass of the book we are anticipating several conflicts in notation and the notes here may be useful to early users of the text.

Protein dynamics

We use P to refer to a protein, mP to refer to the mRNA associated with that protein and p to refer to the gene that encodes P. The concentration of P can be written either as P or [P], with a preference for the former. The concentration of mP can be written either as m_p (preferred) or [mP]. Parameters that are specific to gene p are written with a subscripted p: α_p, δ_p, etc.

The dynamics of protein production are given by

$$\frac{dm_p}{dt} = \alpha_{p,0} - \gamma_p m_p, \qquad \frac{dP}{dt} = \beta_p m_p - \delta_p P,$$

where $\alpha_{p,0}$ is the (constitutive) rate of production, γ_p parameterizes the rate of dilution and degradation of the mRNA mP, β_p is the kinetic rate of protein production and δ_p parameterizes the rate of dilution and degradation of the protein P.

When we ignore the mRNA concentration, we write the simplified protein dynamics as

$$\frac{dP}{dt} = \beta_{p,0} - \delta_p P.$$

Assuming that the mRNA dynamics are fast compared to protein production, then the constant $\beta_{p,0}$ is given by

$$\beta_{p,0} = \beta_p \frac{\gamma_p}{\alpha_{p,0}}.$$

For regulated production of proteins using Hill functions, we modify the constitutive rate of production to be $f_p(Q)$ instead of $\alpha_{p,0}$ or $\beta_{p,0}$ as appropriate. The Hill function is written in the form

$$f_p(Q) = \frac{\alpha_{pq}}{k_{pq} + Q^{n_{pq}}}.$$

The subscripts can be dropped if there is only one Hill function in use.

Chemical reactions

We write the symbol for a chemical species A using roman type. The number of molecules of a species A is written as n_a. The concentration of the species is occasionally written as [A], but we more often use the notation A, as in the case of proteins, or x_a. For a reaction $\mathrm{A} + \mathrm{B} \longleftrightarrow \mathrm{C}$, we use the notation

$$\mathrm{R}_1 : \mathrm{A} + \mathrm{B} \underset{k^r_{r1}}{\overset{k^f_{r1}}{\rightleftharpoons}} \mathrm{C} \qquad \frac{dC}{dt} = k^f_{r1} AB - k^r_{r1} C$$

It will often be the case that two species A and B will form a covalent bond, in which case we write the resulting species as AB. We will distinguish covalent bonds from much weaker hydrogen bonding by writing the latter as A:B. Finally, in some situations we will have labeled section of DNA that are connected together, which we write as A−B, where here A represents the first portion of the DNA strand and B represents the second portion. When describing (single) strands of DNA, we write A′ to represent the Watson-Crick complement of the strand A. Thus A−B:B′−A′ would represent a double stranded length of DNA with domains A and B.

The choice of representing covalent molecules using the convential chemical notation AB can lead to some confusion when writing the reaction dynamics using A and B to represent the concentrations of those species. Namely, the symbol AB could represent either the concentration of A times the concentration of B or the concentration of AB. To remove this ambiguity, when using this notation we will write [A][B] as $A \cdot B$.

When working with a system of chemical reactions, we write S_i, $i = 1, \ldots, n$ for the species and R_j, $j = 1, \ldots, m$ for the reactions. We write n_i to refer to the molecular count for species i and $x_i = [\mathrm{S}_i]$ to refer to the concentration of the species. The individual equations for a given species are written

Missing. Figure out notation here. BST?

The collection of reactions are written as

$$\dot{x} = N v(x, \mu), \qquad \dot{x}_i = N_{ij} v_j(x, \mu)$$

where x_i is the concentration of species S_i, $N \in \mathbb{R}^{n \times m}$ is the stochiometry matrix, v_j is the reaction flux vector for reaction j, and μ is the collection of parameters that the define the reaction rates.