David Van Valen
APh 161 PS3

Biological Search

Over the term, it has become increasing evident that for many biological systems the concept of concentration has become obsolete. Concentration is in essence a bulk quantity whose purpose is to allow us to think about how chemical systems evolve without considering the vast number of microstates available to each molecule. As one travels to smaller and smaller length scales, the total number of molecules in our system becomes miniscule, to the point that concentration is no longer useful in helping predict the behavior of our system. At the scale of the cell, it is necessary to abandon concentrations and reconsider the microstates available to individual molecules.

As we begin to adapt to this new framework, we will need new insight into how fundamental processes function inside the cell. One such process is search. Out of millions of base pairs to choose from, how does RNA polymerase find the right promoter to bind to? Given the crowded nature of the cytoplasm, how are two proteins that need to interact to initiate a signaling cascade able to find each other? How do the subunits of G-coupled protein receptors find each other in the membrane if they are able to move around freely? How does search function in the cell, and what physical tricks can the cell use to speed up the process? I propose to address this question by performing some order of magnitude estimates for a number of case studies and following them up with more detailed calculations. The biological systems I would like to examine are the search mechanisms of RNA Polymerase and the search mechanisms of cytoplasmic kinases. My order of estimate calculations would include an estimated time for RNAP and a protein kinase to find their respective targets. More detailed calculations would include following Grosberg's analysis for RNAP and Monte Carlo simulations to find a scaling relationship between the number of kinases and the time required to complete the search. My calculations will be compared with literature data and should provide insight into how search mechanisms operate.

References

[1] http://lanl.arxiv.org/pdf/q-bio.BM/0510043