Noise Analysis in Biochemical Complex Formation

Zikai Xu [1], Khem Raj Ghusinga [1], and Abhyudai Singh [1]

***Short Abstract* — Several biological functions are carried out via complexes that are formed via multimerization of either a single species (homomers) or multiple species (heteromers). Given functional relevance of these complexes, it is presumably desired to maintain their level at a set point and minimize fluctuations around it. Here we consider two simple models of complex formation -- one for homomer and another for heteromer of two species -- and analyze effect of important model parameters on the noise in complex level. In particular, we study the effect of (i) sensitivity of the complex formation rate with respect to constituting species' abundance, and (ii) relative stability of the complex as compared with that of the constituents. By employing an approximate moment analysis, we find that for a given steady state level, there is an optimal sensitivity that minimizes noise (quantified by fano-factor; variance/mean) in the complex level. Furthermore, the noise becomes smaller if the complex is less stable than its constituents. Finally, for the heteromer case, our findings show that noise is enhanced if the complex is comparatively more sensitive to one constituent. We briefly discuss implications of our result for general complex formation processes.**

***Keywords* — complex noise, stochastic process, linearization**

I. Introduction

Formation of biochemical complexes plays vital role for most cellular processes, including gene regulation, signal transduction [1]. Given their importance, it can be argued that their level must be closely regulated so as to achieve robust function. However, many species are present at low copy numbers in cells, and thereby stochasticity (or noise) in the reactions involving them is unavoidable. Previous work indeed has shown that complex formation might be an important mechanism in control of noise in gene regulation [2].

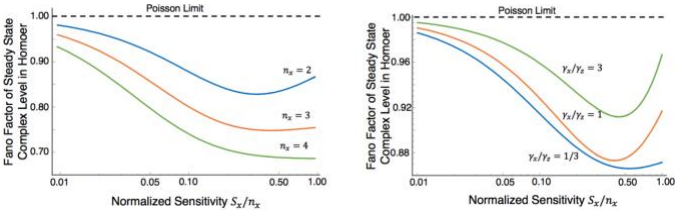
Here we investigate the effect of various attributes of the complex formation process on the noise in the complex level. We focus on the steady-state noise in two toy models of complex formation. In the first model, a single species forms a homomer whereas in the second model two species interact to form a heteromer. Not only these toy models themselves are appropriate for analysis of some real biological examples [3], but they also hint towards what behaviors might arise in more complicated scenarios.

Our strategy to analyze the noise behavior relies upon using moment dynamics of these toy models. Due to nonlinearities in these models, however, the moment dynamics is not closed and we use a linear approximation of the system at its steady-state to estimate the noise behavior.

Interestingly, our analysis reveals that noise in complex level has a U-shape profile with respect to sensitivity for both homomer and heteromers. Moreover, we find that for these toy models, if the complex is relatively unstable (i.e., it degrades faster) as compared with its constituents, the overall noise profile shifts downwards. We also analyze the heteromer with different sensitivities for each species. In this case, the overall noise profile shifts upwards.

II. Main Results

For a homomer, its steady state noise shows a non-monotonic behavior as the sensitivity of the complex formation rate to the species level is changed. Moreover, the noise in complex level reduces when the complex is relatively unstable as compared to the species.



For a heteromer, the noise exhibits similar behavior as in the homomer case if sensitivities and other parameters of both species are exactly same. However, when the complex formation rate is more sensitive to one species, then noise in the complex increases.

III. Summary, and Future Work

We analyzed two simple models of biochemical complex formation and explored the effect of different parameters in the models. In the future, it would be interesting to explore reversible kinetics for the complex formation (i.e., dissociates to its constituents), and also self-regulation in production of the species as found in production of a range of proteins.

References

[1] Blasi U, Young R (1996) Two beginnings for a single purpose: The dual-start holins in the regulation of phage lysis. Molecular Microbiolog 21: 675-682.

[2] Bundschuh R, Hayot F, Jayaprakash C (2003) The role of dimerization in noise reduction of simple genetic networks. Journal of Theoretical Biology 220: 261-269.

[3] BarzelB, BihamO (2009) Stochastic analysis of dimerization systems. Physical Review E80:031117.

[1]Department of Electrical and Computer Engineering, University of Delaware, Newark, DE, USA. E-mail: zikaixu@udel.edu, khem@udel.edu, absingh@udel.edu