How phenotypes shape cell-to-cell variations of protein abundances?

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***Short Abstract* — To what extent phenotypes influence single cell variation of relevant proteins? In the context of *E. coli* chemotaxis, we find that the observed near perfect adaptation in chemotaxis imposes correlations among protein abundances in individual cells, however, chemotaxis alone does not determine the entire distribution of the proteins. We also show that normal distributions of protein abundances constructed using observed average and co-variances are able to reproduce the cell-to-cell variation of the chemotactic response. Therefore, the long tails of the protein distributions, observed experimentally, could arise from additional constraints other than the ability of *E. coli* cells to execute chemotaxis.**

***Keywords* — Maximum Entropy, Data driven modeling, Robustness, Bacterial chemotaxis.**

I. Phenotype Vs. Protein Abundance

Protein abundances critically influence cell responses in individual cells. Cell-to-cell variations in the protein abundances even in a genetically identical cell population, are a very common phenomenon. Recent experiments relate variations in protein concentrations in individual cells to specific cell phenotypes. For example, differences in protein abundances can produce distinct lineage commitments in hematopoietic stem cells [1], or, co-variation of protein abundances increases efficiency of chemotactic responses in *E. coli*. [2,3]. However, it is not clear from these studies to what extent the observed structure in the protein distributions are absolutely essential to produce a particular phenotype or cell response. How does the ability of individual cells to respond to changes in the local environmental shape the nature of variations of protein abundances in a cell population? This still remains an open question.

II. MaxEnt: Prediction Of Single Cell Protein Abundance

Using a Maximum Entropy based method [4] we quantify to what extent variations of protein abundances in single cells are shaped by a specific phenotype that affect growth or fitness of a cell population in the context of *Escherichia coli* (*E. coli*) chemotaxis. We show the nearly perfect nature of adaptation of *E. coli* cells to a change in nutrient concentration in the medium and the experimentally observed distribution of adaptation time in individual *E. coli* cells enforce co-variations between protein abundances involved in the chemotaxis signaling network. However, our calculations also show that the observed chemotactic response can accommodate a much wider variation in protein abundances in single cells compared to the distributions observed in experiments. This suggests that additional constraints imposed by gene regulatory processes controlling protein synthesis and coupling of chemotactic proteins to other cell functions further restrict variation of protein abundances. We found that Gaussian distributions of protein abundances consistent with average values and pairwise correlations in protein abundances measured in an *E. coli* cell population can remarkably generate the chemotactic response observed in single cells. Thus, the observed long tails or deviations from the Gaussian distribution in the distributions of protein abundances could arise to satisfy constraints imposed by non-chemotactic processes.

Furthermore, single cell measurements for activation of proteins can be challenging due to low abundances of those proteins in single cells, or, lack of good antibodies. In such situation, immunoblots measuring protein concentration in a cell population are used. Our approach provides a way to generate predictions at the single cell level based on population averaged experimental data.

III. Conclusion

Our analysis shows that even though the phenotypes observed in bacterial chemotaxis induce correlations among different chemotactic proteins, the cells can accommodate a much wider distribution of chemotactic proteins to what has been measured in experiments. Thus, the narrow variations in the protein abundance have to come from some additional constraints not just the phenotype of chemotactic performance alone.

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