

Effects of Tsr–CheBp and CheA–CheYp affinity in bacterial chemotaxis

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Abstract

Escherichia coli chemotaxis provides a well-characterized model system for the bacterial signaling. Two features of this system include signal amplification and robustly accurate adaptation. Recent simulation studies considering the effects of multiple receptors have suggested possible mechanisms for signal amplification. Although precise adaptation to aspartate has been explained by conventional kinetic models, the adaptation behavior of models incorporating the effects of multiple receptors remain unclear. We analyzed these models by perturbation of kinetic parameters. The results suggest that accurate adaptation can be maintained through control of both the interaction of cytoplasmic proteins and the activity of the receptor complex.

Introduction

The bacterial chemotaxis signal transduction pathway is recognized as a model two-component regulatory system. The structure of the chemotaxis signal transduction system is well-characterized, including the kinetic rate constants for the interactions of Che proteins (recent review: [1]).

Recent simulation studies using models that incorporate the coupling effects of receptor activity among different receptors have suggested mechanisms for signal amplification [4]. The model reproduces signal amplification consistent with the experimental data [6]. Although precise adaptation to aspartate has been explained by conventional kinetic models, further investigation is needed to elucidate the adaptation behavior of these models. The main goal of this study was to elucidate how these proposed mechanisms of receptor crosstalk affect the error minimization in the model system.

Methods

We analyzed a dynamic model that represented each methylation of the receptor complex and phosphorylation of proteins [4, 7] to assess the individual effects of various states of methylation and phosphorylation of the chemotaxis proteins.

Results

To address signal response magnitude and adaptation error, we added 10 μ M aspartate to medium devoid of any attractant (Figure 1). We performed simulations in which we individually varied each kinetic rate constant from 0.1- to 10-fold for all the chemical reactions in the

model. The adaptation error simulated with the original rate constant was 8%. The decreasing the dissociation rate constant of Tsr to CheBp and increasing Tsr–CheA to CheYp has the effect of decreasing the adaptation error to 2%, while maintaining sufficient magnitude of the response.

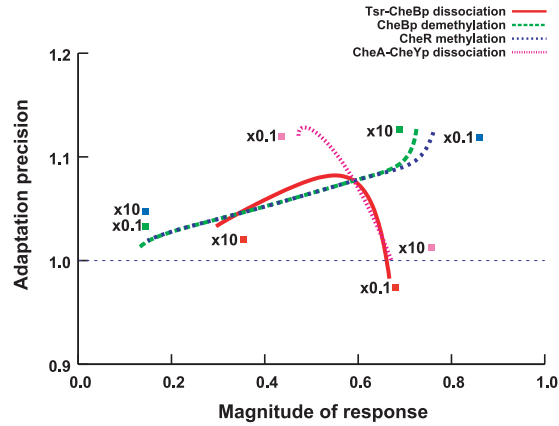


Figure 1: Phase-space plot of adaptation precision and response magnitude. To medium lacking attractant, $10\mu\text{M}$ aspartate was added. The x-axis indicates the magnitude of the response, that is, the ratio of the amount of CheYp reduced after stimulation to the CheYp level before stimulation. Precision of adaptation (the ratio between the CheYp levels before stimulation and after adaptation) is plotted on the y-axis. An adaptation precision of 1.0 (thin line) indicates perfect adaptation. The simulated values of adaptation precision and response magnitude are shown for the various rate constants (from 0.1- to 10-fold) for the chemical reactions. The reactions associated with an error in adaptation of less than a 2% throughout are shown.

Figure 2 shows the response rate and adaptation precision in response to $10\mu\text{M}$ aspartate added to an environment lacking aspartate, with the model repeatedly simulated as rate constants of CheA–CheYp and Tsr–CheBp dissociation were modulated 0.01- to 100-fold. Enhancing the dissociation rate constant of CheA–CheYp increases the response rate and precision of adaptation. Although Figure 1 indicates a decreased Tsr–CheBp dissociation rate constant produces both a larger signal response and more precise adaptation, precise adaptation is not maintained as the rate of Tsr–CheBp dissociation decreases further.

We added $0.1\mu\text{M}$ to 10mM attractant to medium containing 0, 0.1, 0.5, and 5mM aspartate to see the effects of alterations in the CheA–CheYp and Tsr–CheBp affinities. The dissociation rate constants are 0.25-, 1.0-, and 4.0-fold. Both way of alterations in kinetic constants minimize adaptation error over the applied range of stimulation.

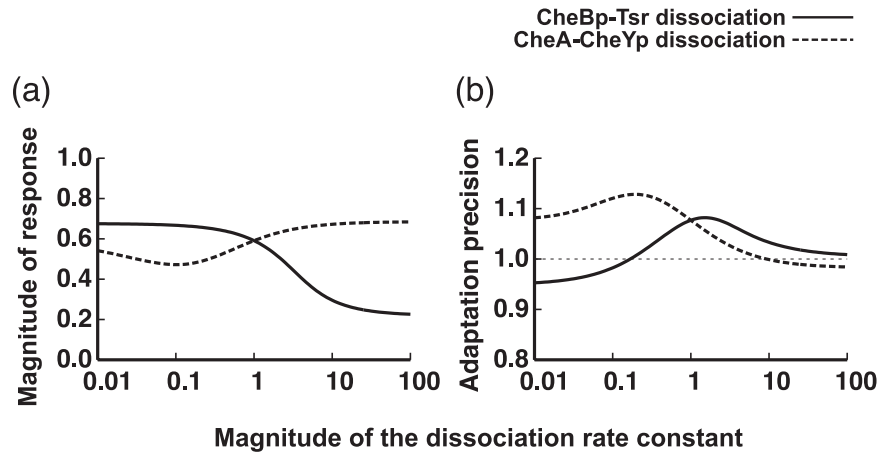


Figure 2: The response rate and adaptation precision in response to $10\mu\text{M}$ attractant aspartate added to an environment lacking aspartate. (a) Simulated response rate for various CheA–CheYp and Tsr–CheBp dissociation rate constants. (b) Simulated adaptation precision for different CheA–CheYp and Tsr–CheBp dissociation rate constants. The x-axis is the magnitude of each rate constant, and the y-axis is the response rate (a) and adaptation precision (b). An adaptation precision of 1.0 means perfect adaptation.

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