Dominant Region Analysis: A Novel Framework for Quantifying Competitive Reactions Based on the Gillespie Algorithm

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Abstract

Understanding the quantitative relationships between competing reactions is crucial for analyzing chemical reaction systems. While conventional approaches often focus on static analysis, we propose a novel concept called "dominant region" to capture the dynamic nature of reaction competition. The dominant region concept can be viewed as an extension of the traditional rate-determining step in reaction kinetics. This enables quantitative prediction of how dominant reactions dynamically change with variations in reactant concentrations.

Keywords: Gillespie Algorithm, Stochastic process, Chemical reactions

1. Introduction

The behavior of chemical reaction systems has traditionally been understood within reaction kinetics and thermodynamics frameworks. However, while these frameworks are suitable for describing near-equilibrium systems and macroscopic-scale phenomena, they have limitations in capturing the stochastic behavior of small-scale systems in non-equilibrium states.

Stochastic fluctuations significantly influence the dynamics of small-scale systems, such as enzymatic reactions or genetic circuits, where molecular counts are low. For example, Gillespie (1977) demonstrated that stochasticity governs reaction pathways in these systems, providing a foundational framework for studying biochemical reactions [1].

In this study, we propose a new concept, the "dominance region," to understand the stochastic dynamics of reaction systems. The dominance region refers to the range of reactant concentrations and reaction rate constants in which a particular reaction proceeds more favorably than other reactions. This concept is defined based on the Gillespie algorithm and provides a framework for quantitatively evaluating reaction systems' robustness and switching phenomena.

In this study, we propose the "dominant region" concept to analyze stochastic dynamics of reaction systems. Based on the Gillespie algorithm, this concept provides a framework for understanding reaction switching and robustness.

Specifically, the favored region of a reaction is defined as the region of state space where the propensity function of the reaction is greater than the propensity functions of all other reactions, which represents a state in which the reaction is more favorable than other reactions and plays a vital role in understanding the dynamics of a reaction system.

2. Method

The Gillespie algorithm models a chemical reaction system as a set of stochastic reaction events. In this algorithm, the likelihood of each reaction R_i is expressed by the propensity function $h_i(x, k)$. If $x=(x_1, x_2, ..., x_N)$ is a vector of the number of molecules of each chemical species, and $k=(k_1, k_2, ..., k_m)$ is a vector of reaction rate constants, the propensity function h_i is defined as follows:

$$\hbar_i(x) = k_i \prod_{j=1}^{N} n_{ij}!\binom{x_j}{n_{ij}}, (x_j > n_{ij}).$$

However, if $x_j < n_{ij}$, $hi(x,k)=0$. This definition represents the expected number of times reaction R_i occurs per unit time. In other words, the propensity function is used as an index representing the probabilistic tendency for a reaction to occur.

The dominance region $D_i *$ of a reaction R_i is defined as the region of state space where the propensity function of reaction R_i is larger than the propensity functions of all other reactions by a certain threshold δ.

$D_i * =\{(x, k) \mid h_i(x, k) - h_j(x, k) \geq \delta, \forall j \neq i\}$, here, δ is a positive constant representing the difference required to be considered dominant. By setting the value of δ appropriately, the spread of the dominant region can be adjusted.

Boundary Conditions: The boundary of the dominance region ∂D_i is defined as the set of points (x, k) that satisfy the following condition: $\partial D_i = \{(x, k) \mid h_i(x, k) = h_j(x, k), \exists j \neq i\}$. Describes a state in which reaction R_i and at least one other reaction R_j occur with equal probability.

When multiple reactions are dominant simultaneously: When various reactions are simultaneously dominant, that is, when the propensity functions of multiple responses have the same value, the dominant regions of those reactions overlap. This overlapping region is defined as a shared dominant region. The shared dominance region D_{i1}, i_2 ,..., in is defined as the set of points (x,k) that satisfy the following conditions: $D_{i1}, i_2, \ldots, i_n = \{(x, k) \mid hi1(x, k) = h_{i2}(x, k) = \ldots = hin(x, k) > h_j(x, k), \forall j \in / \{i_1, i_2, \ldots, i_n\}\}$.

This definition describes a state in which reactions Ri1, Ri2, ..., and Rand occur with equal probability relative to all other reactions. From the definition of the dominant region, the following properties are self-evident.

Non-exclusivity: The regions of dominance for multiple responses can overlap, representing a state where more than one response is equally likely to occur.

Dynamic Change: The dominant region changes dynamically as the state of the reaction system changes. As the reaction progresses, the concentrations of the reactants change, and the dominant region changes accordingly.

Stability and correlation: The region of dominance is related to the stability of a reaction system. If the area of dominance of a particular reaction is significant, that reaction will tend to stabilize the system's state, making it easier to maintain equilibrium.

Relationship between dominant regions and potential functions: The favorable region is closely related to the potential function of the reaction system [2].

In a reversible reaction, the Gibbs free energy change ΔG of the response determines the direction of the reaction and the equilibrium constant. If ΔG is negative, the forward reaction prevails; if ΔG is positive, the reverse reaction prevails. This ΔG can be considered the reaction system's potential function U(x, k). $U_i(x, k) = -\Delta G_i(x, k)$. Within the dominance region of a reaction, the gradient of the potential function corresponding to that reaction is larger than the gradients of the other reactions. In other words, the dominance region can be interpreted as the region in which the gradient of the potential function shows the steepest direction.

Expressed mathematically, the favorable region D_i of reaction R_i is the region that satisfies the following conditions: $D_i = \{(x, k) \mid \|\nabla U_i(x, k)\| > \|\nabla U_j(x, k)\|, \forall j \neq i\}$ $\nabla U_i(x, k)$ denotes the gradient of the potential function $U_i(x, k)$[3].

Interpretation as Potential Topography: To visually understand this relationship, imagine the potential function as a "topography."

The potential function U(x, k) corresponds to the "elevation" of each point.

Potential gradient ∇ U(x, k): corresponds to the "slope" at each point.

Dominant Region: The dominant region of a reaction corresponds to the "slope" where the potential function for that reaction has the steepest slope.

The reaction system behaves like a ball rolling down this potential landscape: it rolls down the steepest slopes (the favored regions). Eventually, it settles in the lowest valleys (the equilibrium states).

In real reaction systems, the ball does not necessarily roll down the steepest slope because of thermal fluctuations. It may cross a small hill (potential barrier) and move to another valley (another stable state). The concept of dominant regions provides a new perspective for understanding and controlling the behavior of reaction systems in such potential landscapes. Near the boundaries of dominant regions, even a tiny perturbation can significantly change the state of the reaction system, which plays a vital role in understanding switching phenomena in reaction systems.

Consider the following three-reaction system:

$$A + B \rightarrow C \text{ (R1)}$$
$$C \rightarrow A + B \text{ (R2)}$$
$$A \rightarrow D \text{ (R3)}$$

Let k_1, k2, and k_3 be the reaction rate constants for each reaction, and assume that the reaction rate equation follows the law of mass action. In this case, the propensity function for each reaction is given by

$$h_1(x, k) = k_1 [A][B]$$
$$h_2(x, k) = k_2 [C]$$
$$h_3(x, k) = k_3 [A]$$

The dominant region of each reaction is determined by the magnitude relationship of the propensity functions as follows:

- The favored region of reaction R_1 is where $h_1>h_2$ and $h_1>h_3$ are satisfied.
- The favored region of reaction R_2 is where $h_2>h_1$ and $h_2>h_3$ are satisfied.
- The favored region of reaction R_3 is where $h_3>h_1$ and $h_3>h_2$ are satisfied.

By solving these inequalities, we can express the favoring region of each reaction as a region in the concentration space of A, B, and C. For example, the favoring region of reaction R1 is:$k_1 [A][B] > k_2 [C]$ and $k\_1 [A][B] > k_3 [A]$. If the reaction rate is constant and the concentrations of A, B, and C are more significant than 0 $[B] > \max((k2 [C])/(k\_1 [A]), k\_3/k\_1)$, Here, max is a function of n variables that returns the maximum value. The region represented by this inequality is the dominant region of reaction R_1. Similarly, the dominant region of reaction R_2 is $k_2[C] > k_1[A][B]$ and $k_2[C] > k_3[A]$, so $[C] > \max(k_1/k_2[A][B], k_3/k_2[A])$, the dominant region of R_3

is $k_3[A] > k_1[A][B]$ and $k_3[A] > k_2[C]$, $[B] < k_3/k_1$ and $[A] > k_2/k_3\ [C]$.

2.5 Evaluation of orbital fluctuations from the dominant region

The dominance region is beneficial for understanding the dynamics of a reaction system and evaluating the trajectory's fluctuation. In a Gillespie simulation, the reaction system evolves stochastically over time, and the trajectory fluctuates randomly. However, this fluctuation is not infinite. Using the concept of the dominance region, the range of the trajectory fluctuation can be quantitatively evaluated.

Specifically, when a specific reaction Ri is dominant, that reaction's driving force (potential gradient) is more significant than that of other reactions, so the reaction system is more likely to change in the direction of that reaction. However, due to stochastic fluctuations, the state of the reaction system may reach the boundary of the dominant region. At this time, to remain within the dominant region, the driving force of the reaction must be relatively more significant than that of the other reactions, which results in changes such as an increase in the concentration of the reactants involved.

It is likely to fluctuate significantly near the boundary of the dominant region. On the other hand, fluctuations are relatively suppressed inside the dominant region. Therefore, by evaluating the size of the dominant region, it is possible to estimate the magnitude of stochastic fluctuations indirectly.

2.6 Fluctuations and Compensation

When $h_i(x, k) > h_j(x, k)$, ∀ji, ≠R_i can be in the preferred region. In other words, although fluctuations occur in the orbit, A and B decrease and C increases. Even if x changes $h_i(x \pm \Delta x) > h_j(x \pm \Delta x), \forall i \neq j$ due to fluctuations,$\pm \Delta x$ If R_i is inside the dominant region, then the fluctuation that reaches the boundary of the dominant region isΔx_{ij}^B,$h_i(x \pm \Delta x_i^B) = h_k(x \pm \Delta x_i^B), \exists k \neq i$ Then, R_i the fluctuation that allows to be in the dominant region $\min(\pm \Delta x_{ik}^B, \forall k, k \neq i) = \delta_i$is at most. When the fluctuation δ_i exceeds, the dominant region becomes R_k $k \neq i$ will be moved to. In the model used in Section 2.2, the dominant region of R1is $[B] >$ 〚 max〛 ((k_2 [C])/(k_1 [A]), k_3/k_1) . $k_1 = k_2 = k_3 = 1.0, [A] = 1.0, [C] = 2.0$. When , the dominant region of $[B] = 3.0$R1 is maintained $[B]$. The fluctuation of $0 < \Delta B < 1.0$ If $[A], [B], [C]$ If all of the above fluctuates, $[B + \Delta B] > ([C + \Delta C])/([A + \Delta A])$ If the fluctuation satisfies the above, the dominant region of R1 is R_1 maintained $\Delta A,\ \Delta B, \Delta C$. $[1 + \Delta B] > ([1 + \Delta C])/([1 + \Delta A]) = 1 + 3\Delta A + \Delta B + \Delta A \Delta B > \Delta C$ This suggests that when a perturbation (change) is made to any of A, B, or C, the other elements compensate for it (Figure 1).

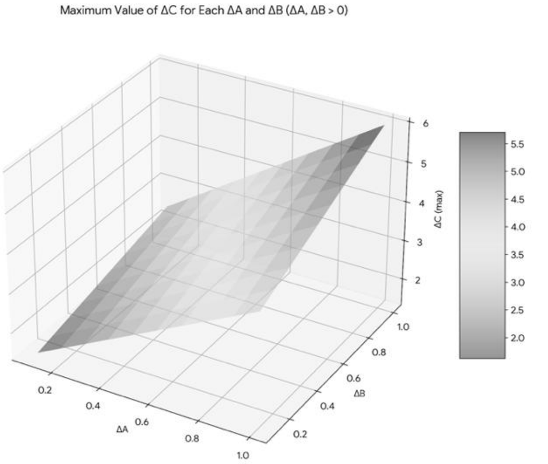

Figure 1 R_1shows the fluctuations of $\Delta A, \Delta B$[A], [B], and [C] that can remain within the dominant region: $= 1.0, [B] = 3.0, [C] = 2.0,\ k_1 = k_2 = k_3 = 1.0$, $\Delta C = 10$ for ΔC The vertical coordinate indicates the maximum value of the fluctuations dominant region does not change even when fluctuations occur , and the reactions$R_i$that$R_i$compose and have nonlinearity.

$h_{R_1}(x, y) = k_1[A][B] = H_{R_1}$ If $k_1[A]$ fluctuates to, for example $[B] = H_{R_1}/k_1[A + \Delta A]$, $k_1[A + \Delta A]$ if the dominant region does not change. In this way, when there is nonlinearity$R_i$in and, is in the dominant region, R_i Even if fluctuations occur in the elements that compose, changing other elements to stay in the dominant region is called the compensation action. If the fluctuations are large and it is impossible to stay in the dominant region, the dominant region will transition to the dominant region of another reaction.

3. Conclusion

In this study, we introduced the "dominant region" concept based on the Gillespie method to provide a novel framework for analyzing and controlling stochastic reaction dynamics [3]. By defining dominant regions as the range of reactant concentrations and rate constants where specific reactions are favored, we demonstrated its potential to capture dynamic changes and evaluate system robustness under stochastic fluctuations.

The results highlight the versatility of the dominant region framework in understanding switching phenomena and stability in chemical and biochemical networks. The compensation effect observed near dominant region boundaries offers a new perspective on how reaction systems maintain equilibrium under perturbations, paving the way for applications in synthetic biology and reaction engineering.

Future research will extend this framework to include more complex biochemical systems, such as genetic circuits and metabolic pathways. Additionally, integrating the dominant region concept with machine learning techniques could enhance its predictive power and enable real-time control of reaction systems. These advancements hold promise for improving the design of robust biochemical processes and therapeutic strategies.

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