Field Theory of Reaction-Diffusion: Mass Action with an Energetic Variational Approach

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Abstract

In this paper, we present a systematic variational description of general mass action kinetics of chemical reactions with detailed balance by an energetic variational approach. Our approach starts with an energy-dissipation law of a chemical reaction system. We show the dynamic of the system is determined by the choice of the dissipation. This approach enables us to couple chemical reactions with other effects, such as diffusion and drift in an electric field. As an illustration, we apply our approach to a non-equilibrium reaction-diffusion system in a specific but canonical set-up. We show the input-output relation of such a system depends on the choice of dissipation via numerical simulation.

1. Introduction

Chemistry describes reactions that convert one compound into another. In biological systems, chemical reactions are catalyzed by enzymes and combined to perform many of the functions of life. The reactions are combined in networks analogous to networks of electrical circuits: enzymes localize individual reactions (as well as catalyze them). The products of one reaction move by diffusion (and perhaps migration and convection) to become the reactants of another reaction catalyzed by another enzyme in a different location. Reactions in biology occur in different physical locations, so the products move as they become reactants in a subsequent reaction.

Here we try to link chemical reactions using the approach of electrical engineering. We describe each reaction as a separately defined device (loosely speaking) with an input and output and its own input output relations. We think of enzymes as two terminal devices, as diodes, that move reactants into products, from one chemical state to another, much as channels are diodes that move ions from one physical location to another through a reaction path [10]. We do not try to construct a single reaction diffusion system of (for example) partial differential equations, just as engineers do not describe an amplifier (for example) by a single grand partial differential equation.

In our approach, the output of one reaction is one of the inputs of another reaction, after the chemical species involved diffuse from one location to another. The output of one device can be connected to the input of another device using the theory of networks particularly the beautifully neat matrix form that describes two port networks and their connections, some much more complicated than simply connecting outputs to inputs. The two port formulation avoids the need to solve different coupled differential equations for each network configuration.

Many types of forces and flows can move the chemical species and the partial differential equations of one type of field interact with those of another. We turn to the theory of complex fluids, and its variational formulation, energetic variational approaches (EnVarA), to describe these interactions because of its success in dealing with otherwise intractable problems. In this paper, we aim to embed the classical

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description of simple chemical reactions into the theory of complex fluids, hoping this interdisciplinary interchange will bring new insight, questions, and techniques to both fields.

Since the 1950's, a huge amount of work has sought to understand the mathematical structure of chemical reaction systems [41, 38, 18, 22, 36, 27, 42, 28, 2, 1, 35, 13, 14, 29, 17, 11]. As pointed out in [2]: "a biochemical reaction system consists of two parts: (i) a reaction network, and (ii) a choice of dynamics." Depending on the scale of the system, either deterministic or stochastic model are used to describe the dynamics of chemical reactions.

The simplest deterministic description of chemical reactions is *the law of mass action*, which states that the rate of a reaction is proportional to the concentrations of the reactants and the proportionality constant k is called the *rate constant* [5, 20]. This approach originally arises from the treatment of ideal gases [40], where molecules/atoms only interact when they collide. For example, for a single reversible reaction, which occurs in both forward and reverse directions,

$$\alpha \mathrm{A} + \beta \mathrm{B} \underset{\mathrm{k}_r}{\overset{\mathrm{k}_f}{\rightleftharpoons}} \gamma \mathrm{C}, \tag{1.1}$$

where k_f and k_r are rate constants for forward and reverse directions, the reaction rate is defined by

$$r = r_f - r_r = k_f[A]^\alpha[B]^\gamma - k_r[C]^\gamma, \tag{1.2}$$

according to the law of mass action [20]. Hence, the rate of changes of $[A]$, $[B]$ and $[C]$ satisfy a system of ordinary differential equation

$$\begin{aligned} \frac{\mathrm{d}[A]}{\mathrm{d}t} &= -\alpha(k_f[A]^\alpha[B]^\beta - k_r[C]^\gamma) \\ \frac{\mathrm{d}[B]}{\mathrm{d}t} &= -\beta(k_f[A]^\alpha[B]^\beta - k_r[C]^\gamma) \\ \frac{\mathrm{d}[C]}{\mathrm{d}t} &= \ \gamma(k_f[A]^\alpha[B]^\beta - k_r[C]^\gamma) \end{aligned} \tag{1.3}$$

At an equilibrium, in which concentrations are not changing, we have

$$\frac{[A]_{eq}[B]_{eq}}{[C]_{eq}} = \frac{k_r}{k_f} \triangleq K_{eq}, \tag{1.4}$$

where $K_{eq} = \frac{k_r}{k_f}$ is called the equilibrium constant.

Although the law of mass action has been widely used, as aptly pointed out in Ref. [20], *"the law of mass action is not a law in the sense that it is inviolable, but rather is a useful model, much like Ohms law or Newtons law of cooling."* Moreover, the law of mass action is mostly used in equilibrium treatments of chemical reactions and so does not immediately apply to the biological and electrochemical systems in which physical chemistry finds some of its most important applications. Equilibrium treatments assume that the system will reach a chemical equilibrium, in which each reversible reaction in the system is in *detailed balance*, that is each species has zero flow and zero velocity.

Nonequilibrium treatments require significant extension to deal with flow, involving new variables and the field equations that describe the new variables, along with boundary conditions, some within and others on the edge of the system. Most of biology and nearly all of electrochemistry occurs in systems with large flows and significant dependence on friction. Friction is always present in condensed phases like biological solutions, because there is so little empty space between molecules. Innumerable collisions of molecules occur in any chemical reaction on the biological time scale. The macroscopic effect of these collisions is friction. It has been a challenge to couple the law of mass action with these effects.

One of the goals of this paper is to provide a seamless and expository extension of the equilibrium treatment of chemical reactions to nonequilibrium systems with diffusion and boundary effects. We adapt and exploit the theory of complex fluids [24, 9, 15] that has dealt with flows in systems with many components successfully for many years. These components often each have internal structure and dynamics and the theory of complex fluids deals with these as well.

In our model, the species of ions (and solvent) in electrolyte solutions are the components of the

complex fluid. We treat all chemically reactive species as ideal gases, so the entropy of the components is that of an ideal gas. The nonequilibrium free energy $\mathcal{F}$ of the ideal gas also includes an internal energy used to describe their ability to enter into chemical reactions. [For us, a chemical reaction is one in which covalent bonds change and the spatial distribution of electrons in the products is not a small perturbation of that in the reactants.] Our treatment is always nonequilibrium so $\mathcal{F}$ includes the effects of friction, coupling of flows of different species, as well as the effects of multiple fields, e.g., concentration fields (diffusion) and electrical fields (migration). The extension to systems with variable temperature is well underway by adopting the methods in [26]. We provide a variational version of the theory of complex fluids because it guarantees a consistent mathematical formulation, in which all variables satisfy all equations, of all fields, and their boundary conditions. Unlike most previous work, which aims to establish the underlying energy-dissipation structure for given chemical kinetic equations, our variational approach starts with the energy-dissipation law of a chemical reaction system. We show that the chemical reaction are driven by the difference of internal energy between "reactants" and "products", and the dynamic of the system is determined by the choice of dissipation, which can be obtained from experimental measurements.

2. Chemical Reactions in Ideal Gases

As an illustration, we focus on a single reversible chemical reaction,

$$\alpha \mathrm{A} + \beta \mathrm{B} \rightleftharpoons \gamma \mathrm{C}. \tag{2.1}$$

Our framework can be extended to more complicated reaction networks with detailed balance. We assume that the entropy of each component in 2.1 can be well described by the ideal gas model without chemical reaction [23], so that other types of interactions can be ignored. We are surely aware of the significance of those interactions [9] but have to start somewhere. In particular, we follow the usual practice [9] of ignoring effects of the shape of the molecule.

2.1. Free energy and equilibrium constant

The key idea is to treat each species in chemical reactions as "ideal gases" with internal energy. The internal energy is determined by the atomic structure of the molecule [34]. Then we can adopt energetic variational approaches (EnVarA) [24, 9, 15], which are widely used in modeling complex fluids, to show that the chemical fluxes, and changes of concentration of each component, are functions of the difference of internal energy. The internal energy is treated as the internal structure of each chemical species. It is the internal energy that might be calculated by quantum chemistry, in the case of no interactions with other atoms or molecules.

The mechanisms of chemical reaction can be very complicated, as the chemical bonds break and form. In our approach, we ignore these mechanisms by treating the molecules (which are sometimes bare atoms, of course) as objects in a complex fluid that have an internal energy given by their internal structure and its internal dynamics.

These energies can either be measured experimentally, or computed by electronic structure calculations. The energy of one species of molecules or atoms can be determined by experiments, or in favorable cases by calculations of electronic structure, using the techniques of quantum chemical computations. Since in a certain sense the internal energy of the electrons of a molecule or atom is electrostatic (once the spatial distribution and correlations of the electron orbitals are determined from quantum calculations), it is natural to include this term as an energy of a species. Our system then falls naturally in the class of complex fluids, studied by the theory of complex fluids [24].

What is important here is that we assign an internal energy to each molecule–really to each molecular or atomic species–that acts as an input to our further calculations. In our model, chemical reactions are driven by the change in the internal energies between reactants and products, along with any forces provided by external sources, e.g., boundary conditions.

In order to simplify the algebra, in the following, we take $\alpha = \beta = \gamma = 1$. Then the reaction becomes

$$\mathrm{A} + \mathrm{B} \rightleftharpoons \mathrm{C}, \tag{2.2}$$

We denote the internal energy of A, B and C by U_A, U_B and U_C respectively. So the nonequilibrium free energy $\mathcal{F}$ of this system used in the variational theory of complex fluids can be written as

$$\begin{aligned}\mathcal{F}([A],[B],[C];U_A,U_B,U_C) = \int_\Omega \mathsf{RT}\Big([A](\ln[A]-1)+[B](\ln[B]-1)+[C](\ln[C]-1)\Big) \\ + [A]U_A + [B]U_B + [C]U_C \mathrm{d}\boldsymbol{x},\end{aligned} \tag{2.3}$$

where U_A, U_B and U_C are inputs (parameters). Note that our free energy $\mathcal{F}$ is a nonequilibrium quantity that depends on friction, coupling between flows, and several kinds of forces. It cannot be derived by mathematics alone because it involves a physical model of the effects of friction, of coupling between flows, and of the various force fields. We adopt very simple models here to illustrate our approach. Confrontation with real experimental data will undoubtedly motivate more complex models.

The first three terms in (2.3) are the free energy of a mixture of ideal gases without chemical reaction, which corresponds to the entropy. Indeed, for a mixture of ideal gases with N species, the chemical potential of a substance j is expressed by [23]

$$\mu_j = \mu^0 + \mathsf{RT}\ln x_j, \tag{2.4}$$

where μ^0 is the reference chemical potential, and x_j is the mole fraction of the substance j. Since the chemical potential is defined relative to its value at the arbitrary reference state, we can take $\mu^0 = 0$. The free energy of the mixture of ideal gases, corresponding to the chemical potential (2.4) with $\mu_0 = 0$, is given by

$$\mathcal{F}[x_i] = \int_\Omega \mathsf{RT}\sum_{i=1}^{N} x_i(\ln x_i - 1)\mathrm{d}x. \tag{2.5}$$

The last three terms in (2.3) are the internal energies stored inside the molecular A, B and C. In the case without chemical reaction, since $[A]$, $[B]$ and $[C]$ do not change with respect to time, these terms are constants that can be ignored.

For given free energy $\mathcal{F}([A],[B],[C];U_A,U_B,U_C)$ defined in (2.3), the corresponding chemical potential of A, B and C are

$$\begin{aligned}\mu_A &= \frac{\delta\mathcal{F}}{\delta[A]} = \mathsf{RT}\ln[A] + U_A, \\ \mu_B &= \frac{\delta\mathcal{F}}{\delta[B]} = \mathsf{RT}\ln[B] + U_B, \\ \mu_C &= \frac{\delta\mathcal{F}}{\delta[C]} = \mathsf{RT}\ln[C] + U_C.\end{aligned} \tag{2.6}$$

At an equilibrium, the chemical potential of both sides of reaction (2.2) are equal, that is

$$\mu_A + \mu_B = \mu_C, \tag{2.7}$$

so we have

$$\ln\left(\frac{[A]_{eq}[B]_{eq}}{[C]_{eq}}\right) = \frac{1}{\mathsf{RT}}(U_C - U_A - U_B) := \frac{\Delta U}{\mathsf{RT}}, \tag{2.8}$$

where $\Delta U = U_C - U_A - U_B$ is the difference of internal energy between state $\{A,B\}$ and state $\{C\}$. So

$$\frac{[A]_{eq}[B]_{eq}}{[C]_{eq}} = e^{\frac{\Delta U}{\mathsf{RT}}} \triangleq K_{eq}, \tag{2.9}$$

where K_{eq} is called the *equilibrium constant* of the reaction (2.2) [20]. It can be noticed that K_{eq} is an exponential representation of the difference in internal (chemical) energy that drives the chemical reaction.

Remark 2.1. *$\mu_A + \mu_B - \mu_c$ is known as* affinity *of a chemical reaction, introduced by De Donder as a new state variable of the system. This affinity is the driving force of chemical reaction [41, 21].*

In the literature, the free energy of a chemical reaction system with detailed balance has been written down in various equivalent forms [38, 7, 27, 1, 33, 13]. For the reversible chemical reaction

$$\mathrm{A} + \mathrm{B} \underset{\mathrm{k}_r}{\overset{\mathrm{k}_f}{\rightleftharpoons}} \mathrm{C}, \tag{2.10}$$

a conventional form of the free energy (Lapin functional) of the system is given by [38, 7, 27, 1, 13]

$$\mathcal{F}([A],[B],[C]) = \int [A](\ln\left(\frac{[A]}{a}\right) - 1) + [B](\ln\left(\frac{[B]}{b}\right) - 1) + [C]\ln\left(\frac{[C]}{c}\right) - 1)\mathrm{d}\boldsymbol{x}, \tag{2.11}$$

where (a, b, c) is the concentrations of A, B and C in a steady-state of system. Another form of free energy is given in [33] as

$$\mathcal{F}([A],[B],[C]) = \int [A]\ln\left(k_f[A]\right) - 1) + [B]\ln\left(k_f[B]\right) - 1) + [C]\ln\left(k_r[C]\right) - 1)\mathrm{d}\boldsymbol{x}, \tag{2.12}$$

Although the forms of these free energy seem different, they produce the same equilibrium satisfying

$$\frac{[A]_{eq}[B]_{eq}}{[C]_{eq}} = K_{eq}, \tag{2.13}$$

where $K_{eq} = \frac{k_r}{k_f} = \frac{ab}{c}$. The choice of 'best' form of the free energy depends on experimental measurements and other consideration.

2.2. EnVarA description for chemical reactions

We are now ready to give an EnVarA description [24, 9, 15] for the kinetics of chemical reactions, and to reach towards our goal of showing how the (chemical) internal energy changes the experimentally measured variables, namely the number density of products as a function of the concentration of reactants and other parameters.

We start with a brief introduction to an energetic variational approach, which is an extension of a variational principle proposed by Rayleigh [39] for purely frictional systems that Onsager tried to extend to physical systems in general [30, 31]. During the last decades, EnVarA and its equivalent forms have been successfully used to model many complicated systems [24, 9, 8, 32, 15, 16].

The starting point of an EnVarA description is a prescribed energy-dissipation law, which is a consequence of the first and second laws of thermodynamics. For a closed isothermal system, the energy-dissipation law is given by

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathcal{F}[\boldsymbol{z}] = -\mathcal{D}[\boldsymbol{z}, \boldsymbol{z}_t], \tag{2.14}$$

where $\boldsymbol{z}$ is the state variable, $\boldsymbol{z}_t$ is the rate of the state variable, $\mathcal{F}$ is the free energy for the nonequilibrium system, and $\mathcal{D}[\boldsymbol{z}, \boldsymbol{z}_t]$ is the rate of energy-dissipation. Here we assume the kinetic energy of the system can be ignored due to the time scale being considered.

For a given energy-dissipation law (2.14), EnVarA provides a general framework to determine the dynamics of a complex system through two distinct variational processes: Least Action Principle (LAP), taking variation of action functional $\mathcal{A} = \int_0^T -\mathcal{F}\mathrm{d}\boldsymbol{x}$ with respect to $\boldsymbol{z}$, and Maximum Dissipation Principle (MDP), taking variation of $\frac{1}{2}\mathcal{D}$ with respect to $\boldsymbol{z}_t$.

The dissipation $\mathcal{D}[\boldsymbol{z}, \boldsymbol{z}_t]$ is often assumed to take a simple form [8, 27],

$$\mathcal{D}[\boldsymbol{z}, \boldsymbol{z}_t] = \left(\mathcal{G}(\boldsymbol{z})\boldsymbol{z}_t, \boldsymbol{z}_{\boldsymbol{t}}\right), \tag{2.15}$$

where $(.,.)$ is an inner product, $\mathcal{G}\boldsymbol{z}$ is a positive-definite matrix for given $\boldsymbol{z}$. The assumption (2.15) corresponds to linear response theory in nonequilibrium thermodynamics [30, 31, 6]. Then by a standard

energetic variational procedure, the dynamics of the system are given by

$$\frac{\delta \frac{1}{2}\mathcal{D}}{\delta \boldsymbol{z}_t} = -\frac{\delta \mathcal{F}}{\delta \boldsymbol{z}}, \tag{2.16}$$

that is

$$\mathcal{G}(\boldsymbol{z})\boldsymbol{z}_t = -\frac{\delta \mathcal{F}[\boldsymbol{z}]}{\delta \boldsymbol{z}}. \tag{2.17}$$

We can extend the standard energetic variational approach to a system, in which the dissipation rate $\mathcal{D}$ is not a quadratic function of $\boldsymbol{z_t}$. Indeed, the dissipation $\mathcal{D}$ can be written as

$$\mathcal{D}[\boldsymbol{z}, \boldsymbol{z}_t] = (\Gamma(\boldsymbol{z}, \boldsymbol{z}_t), \boldsymbol{z_t}) \geq 0. \tag{2.18}$$

then

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathcal{F}[\boldsymbol{z}] = \left(\frac{\delta \mathcal{F}[\boldsymbol{z}]}{\delta \boldsymbol{z}}, \boldsymbol{z}_t\right), \tag{2.19}$$

implying

$$\Gamma(\boldsymbol{z}, \boldsymbol{z}_t) = -\frac{\delta \mathcal{F}[\boldsymbol{z}]}{\delta \boldsymbol{z}}, \tag{2.20}$$

as a consequence of the chain rule. It can be noticed that if $\mathcal{D}$ satisfies (2.15), then

$$\frac{\delta \frac{1}{2}\mathcal{D}}{\delta \boldsymbol{z}_t} = \Gamma(\boldsymbol{z}, \boldsymbol{z}_t), \tag{2.21}$$

which is consistent with the maximum dissipation principle.

The main difficulty in applying the above EnVarA to a chemical reaction system is to deal with constraints that come from the conservation of chemical elements. For the reversible reaction 2.1, the reaction rate r for this reaction is defined by (see p. 569 in [5])

$$r = -\frac{1}{\alpha}\frac{\mathrm{d}[A]}{\mathrm{d}t} = -\frac{1}{\beta}\frac{\mathrm{d}[B]}{\mathrm{d}t} = \frac{1}{\gamma}\frac{\mathrm{d}[C]}{\mathrm{d}t}. \tag{2.22}$$

A direct consequence of such definition is that

$$\frac{\mathrm{d}}{\mathrm{d}t}\left(\gamma[A] + \alpha[C]\right) = 0, \quad \frac{\mathrm{d}}{\mathrm{d}t}\left(\gamma[B] + \beta[C]\right) = 0, \tag{2.23}$$

if there is no other reaction involving A, B and C. Then

$$\gamma[A] + \alpha[C] = Z_0, \quad \gamma[B] + \alpha[C] = Z_1, \tag{2.24}$$

where Z_0 and Z_1 are constants determined by the initial amount of A, B and C. Experiments often report the concentration (i.e., number density) of A, B and C as a function of time.

Remark 2.2. *For a system that has* 3 *species, and* 1 *reaction, we have two conserved quantities. The choice of conserved quantity may not be unique in general. For example, for a simple chemical reaction*

$$\mathrm{H^+ + OH^- \rightleftharpoons H_2\,O}, \tag{2.25}$$

the conservation of the numbers of H-atoms and O-atoms give us

$$\begin{aligned} &[\mathrm{H^+}] + [\mathrm{OH^-}] + 2\,[\mathrm{H_2\,O}] = C_H \\ &[\mathrm{OH^-}] + [\mathrm{H_2\,O}] = C_O \end{aligned} \tag{2.26}$$

where C_H and C_O are numbers of H atoms and O-atoms. The conservation of (chemical) elements (2.26)

is equivalent to the conservation property

$$[\mathrm{H}^+] + [\mathrm{H_2\,O}] = Z_0, \quad [\mathrm{OH}^-] + [\mathrm{H_2\,O}] = Z_1 \tag{2.27}$$

as in (2.24).

In order of overcome this difficulty, we introduce a reaction coordinate $\boldsymbol{R}(t)$ to describe a chemical reaction system and use the reaction coordinate $\boldsymbol{R}(t)$ as the state variable. The idea of using chemical reaction coordinates to describe chemical reactions appeared in [36, 1] for both deterministic and stochastic descriptions of chemical reactions, but apparently has not yet been used to describe chemical reactions in a variational treatment.

Roughly speaking, the reaction coordinate accounts for the "number" of each chemical reaction that has occurred by time t. We take the system with single chemical reaction (2.2) as an example. By introducing the reaction coordinate $R(t)$, the concentrations of A, B and C are given by

$$\begin{aligned} [A(t)] &= [A(0)] - R(t), \\ [B(t)] &= [B(0)] - R(t), \\ [C(t)] &= [C(0)] + R(t), \end{aligned} \tag{2.28}$$

which is a kinematic description of the system that embodies the constraint (2.24).

By using (2.28), the energy $\mathcal{F}([A],[B],[C];U_A,U_B,U_C)$ defined in (2.3) can be written in terms of $R(t)$, so the energy-dissipation law can be reformulated as

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathcal{F}[R;U_A,U_B,U_C] = -\mathcal{D}[R,R_t], \tag{2.29}$$

with a proper (but not unique) choice for the dissipation $\mathcal{D}[R,R_t]$. Here, the energy $\mathcal{F}[R;U_A,U_B,U_C]$ is a functional of $R(t)$ with U_A, U_B and U_C as inputs (parameters). The energy dissipation law (2.29) embodies the constraints 2.24.

We can derive the equation of $R(t)$ by the generalized energetic variational approach 2.20. Note by the kinematic equation (2.28), we have

$$\frac{\mathrm{d}[A]}{\mathrm{d}t} = -R_t, \quad \frac{\mathrm{d}[B]}{\mathrm{d}t} = -R_t, \quad \frac{\mathrm{d}[C]}{\mathrm{d}t} = R_t \tag{2.30}$$

so the reaction rate law r is uniquely determined by the choice of the dissipation $\mathcal{D}[R,R_t]$.

2.2.1. Law of mass action

In the law of mass action, the reaction rate is given by

$$r = k_f[A][B] - k_r[C] \tag{2.31}$$

where k_f and k_r are **rate constants** for the forward and reverse directions, the corresponding equilibrium constant is

$$K_{eq} = \frac{[A]_{eq}[B]_{eq}}{[C]_{eq}} = \frac{k_r}{k_f}. \tag{2.32}$$

The law of mass action can be derived from the energy-dissipation law (2.29) by taking the dissipation as

$$\mathcal{D}[R,R_t] = \mathsf{RT}\ R_t \ln\left(\frac{R_t}{k_r[C]} + 1\right), \tag{2.33}$$

where k_r is the reverse rate constant of this reaction. Indeed, the energetic variational procedure gives

$$\mathsf{RT}\ln\left(\frac{R_t}{k_r[B]} + 1\right) = -\frac{\delta}{\delta R}\mathcal{F}[R;U_A,U_B,U_C]. \tag{2.34}$$

Note

$$\begin{aligned}\frac{\delta}{\delta R}\mathcal{F}[R;U_A,U_B,U_C] &= (-\mu_A-\mu_B+\mu_C)\\ &= \mathsf{RT}\ln\left(\frac{[C]}{[A][B]}\right)-U_A-U_B+U_C\end{aligned} \tag{2.35}$$

by using (2.6). So we have

$$\ln\left(\frac{R_t}{k_r[B]}+1\right)=\ln\left(\frac{[A][B]}{[C]}\right)-\frac{\Delta U}{\mathsf{RT}} \tag{2.36}$$

where the right-hand side is determined by the difference of internal energy ΔU between state $\{A,B\}$ and state $\{C\}$.

Although (2.36) looks complicated, direct computation gives

$$r=R_t=k_r[C]\left(\frac{1}{K_{eq}}\frac{[A][B]}{[C]}-1\right)=k_f[A][B]-k_r[C], \tag{2.37}$$

where

$$K_{eq}=e^{\frac{\Delta U}{\mathsf{RT}}}=\frac{k_r}{k_f} \tag{2.38}$$

is used.

Other forms of the dissipation functional are possible. As a generalization of (2.33), we can consider a more general form of the dissipation

$$\mathcal{D}[R,R_t]=\eta_1(R)\partial_t R\ln(\eta_2(R)R_t+1), \tag{2.39}$$

where $\eta_1(R)>0$ and $\eta_2(R)>0$, then $\mathcal{D}(\partial_t R)\geq 0$ for the admissible R_t. In this case, by (2.20), we have

$$\begin{aligned}\eta_1(R)\ln(\eta_2(R)R_t+1) &= -\frac{\partial}{\partial R}\mathcal{F}[R;U_A,U_B,U_C]\\ &= \mathsf{RT}\ln\left(\frac{[C]}{[A][B]}\right)-\Delta U\end{aligned} \tag{2.40}$$

In this case, the forward and reverse rate k_f and k_r can depend on the concentrations of $[A]$, $[B]$ and $[C]$. For instance, if $\eta_1(R)=\mathsf{RT}$ and $\eta_2(R)=1$, then

$$r=R_t=\frac{1}{K_{eq}}\frac{[A][B]}{[C]}-1=k_f([C])[A][B]-k_r([C])[C], \tag{2.41}$$

where

$$k_f([C])=\frac{1}{[C]K_{eq}},\quad k_r([C])=\frac{1}{[C]}. \tag{2.42}$$

2.2.2. Linear Response Theory

In nonequilibrium thermodynamics [30, 31, 6], it is often assumed that the dissipation of total energy is a quadratic function of the "rate" of state variables and that is known as linear response theory.

It is important to note the distinction between the linear response used so widely in chemical kinetics and the linear response used in engineering. In engineering, an operating point in a complex multidimensional space describes the nonlinear properties of a system. This point is usually remote from, and has little to do with the properties of the system with no flows, i.e., no sources of energy, mass, charge or current, that is called equilibrium in chemistry. Linearization around that operating point is an essential tool in understanding most engineering systems, even those as nonlinear as digital modules (say a shift register, to be specific) in a digital computer. But systems without flows are rarely considered in engineering since they have so little to do with the systems that actually perform engineering function. Think of an amplifier without a power supply, or an automobile engine with water in the gas tank.

In our case, the linear response theory of chemistry gives us a form of the dissipation term

$$\mathcal{D}[R, R_t] = \eta(R)|R_t|^2. \tag{2.43}$$

Then a standard variational procedure gives us

$$\begin{aligned} \eta(R)R_t &= -\frac{\partial}{\partial R}\mathcal{F}[R; U_A, U_B, U_C] \\ &= \mathsf{RT}\ln\left(\frac{[C]}{[A][B]}\right) - \Delta U. \end{aligned} \tag{2.44}$$

By choosing $\eta(R) = \mathsf{RT}$, the reaction rate is given by

$$\begin{aligned} r = R_t &= \ln\left(\frac{[C]}{[A][B]}\right) - \frac{\Delta U}{\mathsf{RT}} \\ &= \ln\left(\frac{1}{K_{eq}}\frac{[A][B]}{[C]}\right), \end{aligned} \tag{2.45}$$

which is much more complicated than the classical reaction rate (2.31). The different reaction rates obviously will predict different dependence of rate on concentration and different time courses of the chemical reaction. We reiterate that the choice of dissipation function is a scientific not mathematical decision. The dissipation function must be chosen to fit data and/or to describe a model or simulation, as well as the mathematical requirements of EnVarA. The linear response theory arose from the near equilibrium assumption. For the chemical reaction, we have $R_t \approx 0$ near equilibrium, and the Taylor expansion gives us

$$\eta_1(R)\ln(\eta_2(R)R_t + 1) \approx \frac{\eta_1(R)}{\eta_2(R)}|R_t|^2. \tag{2.46}$$

So one can view the dissipation (2.43) as a linear approximation near equilibrium to (2.39).

Remark 2.3. *The law of mass action gives a simple form of the reaction rate r in terms of $[A]$ and $[B]$, however, the dissipation in terms of R and R_t would become complicated (See equation 2.33). On the other hand, if the dissipation is taken to be simply that described by linear response theory, the the reaction rate r becomes complicated [See eq. (3.12)].*

Remark 2.4. *Note K_{eq} is defined as an exponential representation of the difference in internal ('chemical') energy. Measurements of just K_{eq} cannot distinguish these dissipation mechanism. Measurements of the concentration dependencies of the forward and backwards rates can distinguish them. However, it is difficult to measure the forward and backwards rate individually.*

3. Diffusion and boundary effects

In our EnVarA description, the dynamic of a chemical reaction is determined by the choice of dissipation. The dissipation is best specified in the context a specific experimental set up. Such setups are chosen to give reproducible input-output functions that are useful in applications. Ideally, the setup also defines a device as in electrical systems that can be connected simply to make a network.

Our analysis will show how the setup determines a dissipation function in a particular case, as an example of how that might be done more generally. The setup of the system is shown in Fig. 3.1.

In this system. a narrow channel connects two baths. In the left bath, the average concentration of A, B and C are maintained by the boundary condition. We only consider the chemical reaction

$$\mathrm{A} + \mathrm{B} \rightleftharpoons \mathrm{C} \tag{3.1}$$

that happens inside the channel. The species in the left bath are sources. We are concerned with the change of the amount of C in the right bath, and assume both A and B cannot diffuse into the right bath.

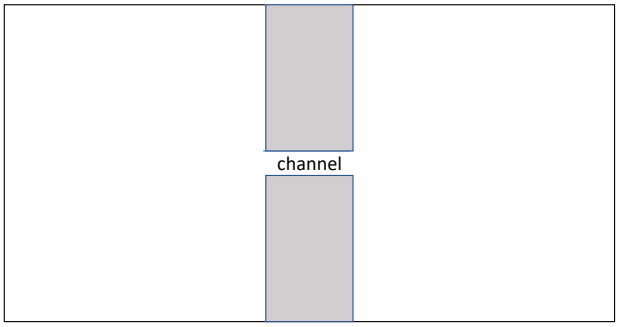

Figure 3.1: Setup of system

The flux of C or the rate of change of amount of C in the right bath is our output. The concentration in the left bath are our inputs. The chemical reaction is the "transfer function".

Mathematically, this system can be modeled by coupling the reaction with diffusion in the framework of the energetic variational approach. Since the channel is very narrow, we can treat this problem as one dimensional. Let c_A, c_B and c_C be concentrations in the channel $[-\epsilon, \epsilon]$. Due to the above setup, we have boundary conditions for

$$\begin{aligned} &c_A(-\epsilon, t) = c_A^b, \quad \partial_x c_A(\epsilon, t) = 0, \\ &c_B(-\epsilon, t) = c_B^b, \quad \partial_x c_B(\epsilon, t) = 0, \\ &\partial_x c_C(-\epsilon, t) = 0, \quad c_C(\epsilon, t) = c_C^b. \end{aligned} \tag{3.2}$$

Here we impose the non-flux boundary condition for c_C on the left-end of the channel, and Dirichlet boundary condition on the right-end of the channel. The boundary conditions of c_A and c_B are Dirichlet boundary conditions, which are inputs of our system. Since c_C satisfies the Dirichlet boundary condition on the right-end of the channel, the amount of C that diffuses into the right bath by time T can be approximately computed by

$$C_{out}(T) = \int_{-\epsilon}^{\epsilon} R(x, T)\mathrm{d}x - \int_{-\epsilon}^{\epsilon} (c(x, T) - c_0(x))\mathrm{d}x, \tag{3.3}$$

which is the output of our system. The flux of C or the rate of change of amount of C in the right bath can be computed as $\dfrac{\mathrm{d}}{\mathrm{d}t} C_{out}$.

We choose reaction coordinate R and fluxes J_A, J_B and J_C as state variables of this system. The kinematic equations for c_A, c_B and c_C are given by

$$\begin{cases} c_A(x, t) + \nabla \cdot J_A(x, t) = c_A^0(x) - R(x, t), \\ c_B(x, t) + \nabla \cdot J_B(x, t) = c_B^0(x) - R(x, t), \\ c_C(x, t) + \nabla \cdot J_C(x, t) = c_C^0(x) + R(x, t), \end{cases} \tag{3.4}$$

where the initial conditions $c_A^0(x)$, $c_B^0(x)$, and $c_C^0(x)$ satisfy the boundary conditions. The energy-dissipation law of the system can be formulated as

$$\begin{aligned} &\frac{\mathrm{d}}{\mathrm{d}t} \int_{-\epsilon}^{\epsilon} c_A(\ln c_A - 1) + c_B(\ln c_B - 1) + c_C(\ln c_C - 1) + c_A U_A + c_B U_B + c_C U_C \mathrm{d}x \\ &= -\int_{-\epsilon}^{\epsilon} D(R(x, t), \partial_t R(x, t)) + \eta_A |\partial_t J_A|^2 + \eta_B |\partial_t J_B|^2 + \eta_B |\partial_t J_C|^2 \mathrm{d}x, \end{aligned} \tag{3.5}$$

where the energy part is exactly the same as the energy in the previous section with U_A, U_B and U_C as inputs, the dissipation part includes dissipation with respect to $\partial_t R$ and $\partial_t \boldsymbol{J}$.

By using the generalized energetic variational approach 2.20, we have

$$\begin{cases} \dfrac{1}{\partial_t R} D(R, \partial_t R) = \mu_A + \mu_B - \mu_C \\ \\ \eta_i(\boldsymbol{J}) \partial_t J_i = -\nabla \mu_i(R, \boldsymbol{J}), \quad i = A, B, C, \end{cases} \tag{3.6}$$

where μ_i $(i = A, B, C)$ is the chemical potential for each species, as given in (2.6). By choosing $\eta_i = \frac{1}{c_i} (i = A, B, C)$ and combining with (3.4), we can obtain a standard reaction-diffusion equation

$$\begin{cases} \partial_t c_A = \nabla \cdot (\nabla c_A) - r(\boldsymbol{x}, t) \\ \partial_t c_B = \nabla \cdot (\nabla c_B) - r(\boldsymbol{x}, t) \\ \partial_t c_C = \nabla \cdot (\nabla c_C) - r(\boldsymbol{x}, t), \end{cases} \tag{3.7}$$

where $r(\boldsymbol{x}, t)$ is determined by the choice of $D(R, \partial_t R)$ as discussed in subsection 2.2.1 and 2.2.2.

3.1. Simulations and discussion

In this subsection, we show some simulation results for the above system with different choices of dissipation. We fix $\epsilon = 0.1$ throughout this subsection. As mentioned previously, the inputs of the system are concentrations of A, B and C in the left bath, which gives us the Dirichlet boundary conditions of A, B and C in the left-end of the channel. We assume that

$$c_A^b = c_B^b = c_0 \tag{3.8}$$

such that c_0 is the single input of our system. The initial concentrations of A, B and C in the channel are constants $c_A^0(\boldsymbol{x}) = c_B^0(\boldsymbol{x}) = c_0$ and $c_C^0(\boldsymbol{x}) = 0.1$. The output of system is C_{out} defined in 3.3, which corresponds to the amount of C that diffuses into the right bath, or $\frac{\mathrm{d}C_{out}}{\mathrm{d}t}$, the flux to the right bath.

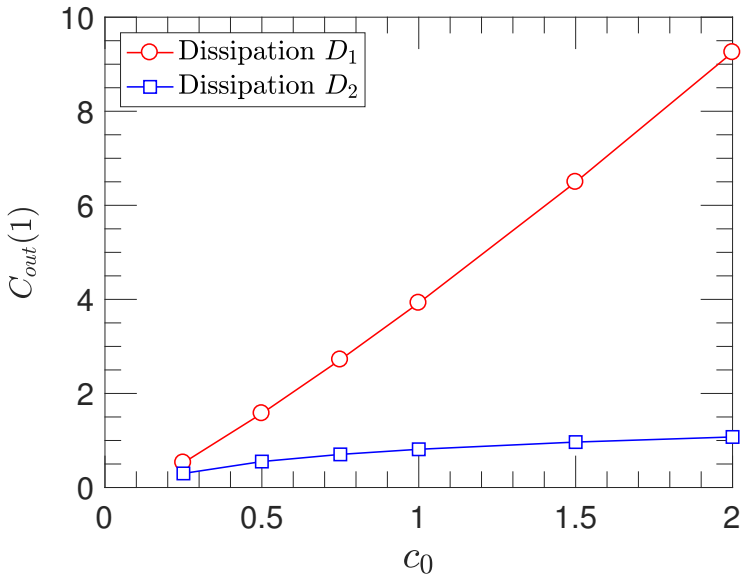

Figure 3.2: The output $C_{out}(t)$ as a function of input c_0 when $t = 1$ for dissipation (3.9) [circle] and dissipation (3.10) [square].

We fix $K_{eq} = 0.1$ through this section and show that the input-output relation depends on the choice of dissipation. We focus on two types of dissipation, as discussed in subsection 2.2.1 and 2.2.2. The first form of dissipation is taken as

$$D_1(R, \partial_t R) = \eta_1(R) R_t \ln(\eta_2(R) R_t + 1), \tag{3.9}$$

which corresponds to generalized law of mass action. The second form of dissipation is taken as

$$D_2(R, \partial_t R) = \eta_0(R)|R_t|^2, \tag{3.10}$$

which corresponds to linear response theory. We take $\eta_0(R) = \eta_1(R) = \eta_2(R) = 1$ in our simulations. In general, $\eta_i(R)$ is also a changeable variable that depends on R.

Fig. 3.2 shows the output $C_{out}(t)$ as a function of input c_0 when $t = 1$ for the two choices of dissipation. It can be noticed that for small c_0, the output are close between two choices for dissipations. However, the output for dissipation (3.9) is much larger than that for the dissipation (3.10) when c_0 is large.

Formally, from the computations in subsection 2.2.1 and 2.2.2, we know

$$r = R_t = \ln\left(\frac{1}{K_{eq}}\frac{[A][B]}{[C]}\right) \tag{3.11}$$

for the dissipation (3.9), while

$$r = R_t = \frac{1}{K_{eq}}\frac{[A][B]}{[C]} - 1 \tag{3.12}$$

for the dissipation (3.10). For $c_0 = 0.1$, the system is at the equilibrium, so $C_{out} = 0$. When c_0 is large, the dissipation (3.10) determines large reaction rate.

We also consider the $\frac{\mathrm{d}}{\mathrm{d}t}C_{out}$ as a function of t for two choices of dissipation for various values of c_0. The results are shown in Fig. 3.3. The time courses in Fig. 3.3 show that for both dissipations and

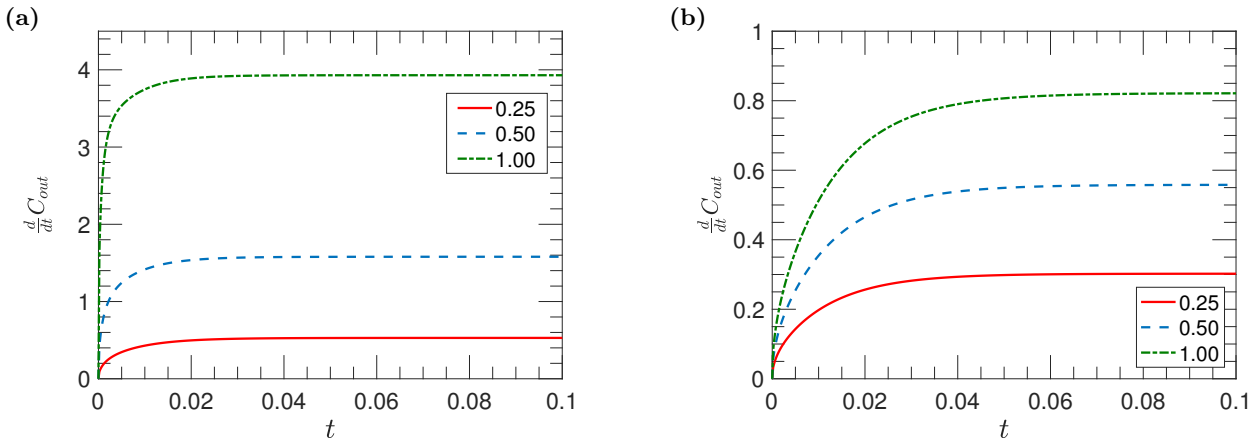

Figure 3.3: $\frac{\mathrm{d}}{\mathrm{d}t}C_{out}$ as a function of t for two choices of dissipation for various of c_0 ($c_0 = 1, 0.5$ and 0.25 from top to bottom in each figure). (a) Dissipation (3.9), (b) Dissipation (3.10).

different inputs, $\frac{\mathrm{d}}{\mathrm{d}t}C_{out}$ tends to a constant, which is a function of input for a given dissipation.

The above simulation results suggest that the dissipation can be determined through experimental measurements and solving the inverse problem.

4. Summary

In this paper, we establish a variational structure to a chemical reaction system with detailed balance, which enable us to couple chemical reactions with diffusion, boundary effects and other effects of systems. In our approach, the dynamics of a chemical reaction is determined by the choice of the dissipation. The classical law of mass action can be derived via a particular form of dissipation.

As an illustration, we apply our approach to a nonequilibrium system with boundary effects and show that the input-output of such a system depends on the choice of the dissipation via numerical simulation. Since such a system is experimentally reproducible, it indicates that the dissipation functional can be obtained by experimental measurements and studying an inverse problem.

There are potential applications in our energetic variational description to a system involving chemical reaction. For instance, new numerical schemes can be designed based on our energetic variational formulation. It is often a challenge to preserve non-negative and conservation properties [37, 12]. Since we have embodied the conservation properties by choosing the proper state variable, such conservation properties can be naturally preserved for the numerical methods based on our energetic variational form. Moreover, such energetic variational formulas also enable us to design Lagrangian-Eulerian schemes for reaction-diffusion systems by applying some recently developed methods for general diffusions [19, 4, 25, 3].

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