Modeling of Active Transport Systems

Yaşar Demirel
Department of Chemical and Biomolecular Engineering, University of Nebraska Lincoln,
ydemirel2@unl.edu

ABSTRACT

Nonisothermal reaction-diffusion systems control the behavior of many transport and rate processes in physical, chemical, and biological systems, such as pattern formation and molecular pumps. Considerable work has been published on mathematically coupled nonlinear differential equations by neglecting thermodynamic coupling between a chemical reaction and transport processes of mass and heat. The thermodynamic coupling refers that a flow occurs without or against its primary thermodynamic driving force, which may be a gradient of temperature, or chemical potential, or reaction affinity. Energy coupling in the membranes of living cells plays major role in the respiratory electron transport chain leading to synthesizing adenosine triphosphate (ATP). The ATP synthesis in turn, is matched and synchronized to cellular ATP utilization. Consequently, the hydrolysis of ATP is thermodynamically coupled to the transport of substrates. This study presents the modeling of thermodynamically coupled system of a simple elementary chemical reaction with molecular heat and mass transport. The modeling is based on the linear nonequilibrium thermodynamics (LNET) approach by assuming that the system is in the vicinity of global equilibrium. Experimental investigations revealed that LNET is capable of describing thermodynamically coupled processes of oxidative phosphorylation, mitochondrial H^+ pumps, and (Na^+ and K^+)-ATPase. Moreover, the LNET formulation does not require the detailed mechanism of the coupling. The modeling equations lead to unique definitions of cross coefficients between a chemical reaction and heat and mass flows in terms of kinetic parameters, transport coefficients, and degrees of coupling, which are measurable. These newly derived cross coefficients need to be determined to describe some coupled reaction-transport systems. Some methodologies are suggested for the determination of the cross coefficients and some representative numerical solutions for coupled reaction-transport systems are presented. Such modeling may improve our understanding of active transport by molecular pumps.

INTRODUCTION

Considerable work has been published on mathematically coupled differential equations on reaction-diffusion systems by neglecting the thermodynamic coupling. Here, the thermodynamic coupling refers that a flow (i.e. heat or mass flow or a reaction velocity) occurs without its primary thermodynamic driving force, or opposite to the direction imposed by its primary driving force. The principles of thermodynamics allow the progress of a process without or against its primary driving force only if it is coupled with another spontaneous process. This is consistent with the statement of second law, which states that a finite amount of organization may be obtained at the expense of a greater amount of disorganization in a series of coupled spontaneous processes.

Thermodynamically coupled chemical reaction-transport systems control the behavior of many transport and rate processes in biological systems, and require a through analysis accounting the induced flows by cross effects [1-10,11-13]. More than fifty years ago, Turing [1] demonstrated that a reaction-diffusion system with appropriate nonlinear kinetics can cause instability in a homogeneous steady state and generate stable concentration patterns. Also the energy coupling in the membranes of living cells plays major role in synthesizing adenosine triphosphate (ATP). The ATP synthesis in turn, is matched and synchronized to cellular ATP utilization $\mathrm{ADP} + \mathrm{P_i} + n\mathrm{H}^+_{\mathrm{in}} = \mathrm{ATP} + \mathrm{H_2O} + n\mathrm{H}^+_{\mathrm{out}}$. Here 'in' and 'out' denote two phases separated by a membrane, and n is the ratio H^+/ATP, showing the level of transmembrane proton transport for each ATP to be synthesized [7]. Consequently, the hydrolysis of ATP is coupled to transporting substrates and maintaining the essential thermodynamic forces of ion electrochemical gradients [2-6]. For example, Ca^{+2}-ATPase in the plasma membranes of most cells pump Ca^{+2} against a steep concentration gradient out of cytosol, while simultaneously counterport H^+ ions [5].

This study presents the modeling equations for thermodynamically and mathematically coupled system of a reversible elementary reaction with heat and mass flows. Such modeling may improve our understanding of some coupled processes, such as active transport by molecular pumps. The modeling is based on the linear nonequilibrium thermodynamics (LNET) formulations by assuming that the system is in the vicinity of global equilibrium (GE). Experimental investigations revealed that LNET is capable of describing thermodynamically coupled processes of oxidative phosphorylation, mitochondrial H^+ pumps, and (Na^+ and K^+)-ATPase, because mainly due to enzymatic feedback [2-5]. Moreover, the LNET formulation does not require the detailed mechanism of the coupling [4,5,15-18]. Kinetic description is based on specific model and lacks the generality characteristics of thermodynamic formulations [3].

BALANCE EQUATIONS

Consider a homogeneous elementary reaction between a substrate (S) and a product (P) $\mathrm{S}\underset{k_b}{\overset{k_f}{\rightleftarrows}}\mathrm{P}$ where k_f and k_b are the forward and backward reaction rate constants, respectively. This type of reaction system is common in chemical and biological systems [2,17,18]. The well-known balance equations are

$$\frac{\partial C_S}{\partial t} = -\nabla \cdot \mathbf{J}_S + \nu_S J_r \tag{1}$$

$$\frac{\partial C_P}{\partial t} = -\nabla \cdot \mathbf{J}_P + \nu_P J_r \tag{2}$$

$$\rho c_p \frac{\partial T}{\partial t} = -\nabla \cdot \mathbf{J}_q + (-\Delta H_r) J_r \tag{3}$$

where $\mathbf{J}_\mathrm{i}$ mass flow of component *i*, $\mathbf{J}_\mathrm{q}$ is the vector of reduced heat flow $\mathbf{J}_q = \mathbf{q} - \sum_{i=1}^{n} \mathbf{J}_i H_i$, $\mathbf{q}$ is the total heat flow, H_i is the partial molar enthalpy of species *i*, and ΔH_r is the heat of reaction. The reaction velocity is $\frac{dC_S}{\nu_S dt} = \frac{dC_P}{\nu_P dt} = J_r$, and the parameters ν_S and ν_P are the stoichiometric coefficients, ($\nu_S = -1$).

PHENOMENOLOGICAL EQUATIONS (PEs)

Reaction-diffusion systems with heat effects represent open and nonequilibrium systems with thermodynamic forces of temperature gradient, concentration gradient, and affinity. For the chemical reaction-transport system the local rate of entropy production is [8,21]

$$\Phi = \mathbf{J}_q \nabla\left(\frac{1}{T}\right) - \mathbf{J}_S \cdot \frac{(\nabla \mu_S)_{T,P}}{T} - \mathbf{J}_P \cdot \frac{(\nabla \mu_P)_{T,P}}{T} + J_{rS} \frac{A}{T} \geq 0 \tag{4}$$

For charged species, we would use electrochemical potential and electrochemical affinity. Using $(\nabla \mu_i)_{T,P} = \sum_{i=1}^{n-1} \frac{\partial \mu_i}{\partial C_i} \nabla C_i$, ($C_S \nabla \mu_S + C_P \nabla \mu_P = 0$), ($\mathbf{J}_S V_S + \mathbf{J}_P V_P = 0$), Eq. (4) becomes

$$\Phi = -\mathbf{J}_q \left(\frac{1}{T^2}\right) \nabla T - \mathbf{J}_S \frac{1}{T} \lambda_S \nabla C_S + J_{rS} \frac{A}{T} \geq 0 \tag{5}$$

where $\lambda_S = \left(1+\frac{C_S}{C_P}\right)\left(\frac{\partial \mu_S}{\partial C_S}\right)_{T,P}$ for ($V_S \approx V_P$), V_i is the partial molar volume of species i, μ_i the chemical potential of species i, and A is the affinity ($A = -\sum \nu_i \mu_i$). Equation (5) consists of scalar processes of chemical reactions and vectorial processes of heat and mass flows, while it excludes viscous, electrical, and magnetic effects. Equation (5) identifies the following independent conjugate flows J_i and forces X_k to be used in the linear phenomenological equations ($J_i = \sum L_{ik} X_k$) in the vicinity of GE [13,25,30,31]

$$\mathbf{J}_S = -L_{SS}\frac{1}{T}\lambda_S \nabla C_S - L_{Sq}\frac{1}{T^2}\nabla T + \mathbf{L}_{Sr}\frac{A}{T} \tag{6}$$

$$\mathbf{J}_q = -L_{qS}\frac{1}{T}\lambda_S \nabla C_S - L_{qq}\frac{1}{T^2}\nabla T + \mathbf{L}_{qr}\frac{A}{T} \tag{7}$$

$$J_r = -\mathbf{L}_{rS}\frac{1}{T}\lambda_S \nabla C_S - \mathbf{L}_{rq}\frac{1}{T^2}\nabla T + L_{rr}\frac{A}{T} \tag{8}$$

The phenomenological coefficients L_{ik} are related Onsager's reciprocity, Gibbs Duhem equation at equilibrium, and the choice of reference frame for diffusivities. Due to Onsager's reciprocal rules ($L_{ik} = L_{ki}$) the number coefficients to be determined would be six instead of nine. Onsager's reciprocal relations states that $L_{ik} = L_{ki}$ if J_i and J_k have the same parity under time reversal, and $L_{ik} = -L_{ki}$ if J_i and J_k have the opposite parity. In the absence of pertinent symmetries or invariances, all types of cross-couplings are possible and lead to nonvanishing cross coefficients L_{ik}. If these symmetries are not exact then the corresponding cross-couplings would be weak and negligible [22]. For the nonvanishing cross coefficients L_{ik}, all the forces contribute for each flow. Here, Eqs. (6) to (8) take into account the thermodynamic couplings between vectorial processes and between vectorial and scalar processes, which is possible in an anisotropic medium according to the Curie-Prigogine principle [15]. Therefore, the cross-coefficients $\mathbf{L}_{\mathrm{Sr}}$, $\mathbf{L}_{\mathrm{rS}}$, $\mathbf{L}_{\mathrm{qr}}$, and $\mathbf{L}_{\mathrm{rq}}$ would vanish in isotropic media, or would have vectorial character due to morphology of the interface, or due to compartmental structure with anisotropic character. In active transport in biological cells, the hydrolysis of ATP is coupled with the flow of sodium ions outside of the cell. The flow direction is controlled by the structure of the membrane and coupling mechanisms in mitochondria.

The cross coefficients determine the degrees of couplings between the pair of flows

$$r_{Sq} = \frac{L_{Sq}}{\left(L_{SS}L_{qq}\right)^{1/2}}, \quad \mathbf{r}_{Sr} = \frac{\mathbf{L}_{Sr}}{\left(L_{SS}L_{rr}\right)^{1/2}}, \quad \mathbf{r}_{rq} = \frac{\mathbf{L}_{rq}}{\left(L_{rr}L_{qq}\right)^{1/2}} \tag{9}$$

Here, r_{Sq} is the degree of coupling between heat and mass flows, $\mathbf{r}_{Sr}$ is between chemical reaction and mass flow, and $\mathbf{r}_{rq}$ between chemical reaction and heat flow. The vectorial character of the degrees of couplings $\mathbf{r}_{Sr}$ and $\mathbf{r}_{rq}$ may reflect the morphological and/or compartmental structure of medium where couplings occur as well as the properties of the cross-coefficients $\mathbf{L}_{Sr}$ and $\mathbf{L}_{rq}$ [2,5,8,15,16,18].

Identification of some of the phenomenological coefficients L_{ik} is discussed elsewhere [31]. We may define two new effective diffusion coefficients of ($D_{T,e}$ and $D_{D,e}$) that are related to the thermal diffusion and the Dufour effect, respectively

$$D_{T,e} = L_{Sq}\frac{1}{T^2} = s_T D_{S,e} C_S = D_T C_S \tag{10}$$

$$D_{D,e} = L_{qS}\frac{\lambda_S}{T} = D_D C_S \tag{11}$$

As the general transport equations are for an anisotropic medium to support the thermodynamic coupling between the scalar and the vectorial processes, the transport coefficients such as k and D may become tensors of the second rank $\boldsymbol{\kappa}$ and $\mathbf{D}$ [8,18,20]. Here the effective transport coefficients incorporating the effects of the medium are taken into account for the simplicity.

REACTION VELOCITY

The affinity for the reaction is $A = \mu_S - \mu_P$. The reaction velocity J_r in terms of affinity is [8,16,18]

$$J_r = J_{rf}\left(1 - \exp\left(-\frac{A}{RT}\right)\right) \tag{12}$$

where $J_{rf} = k_f C_S$. If we expand Eq. (12) at near GE state, which may be specified by the inequality $|A/RT| << 1$, then we have $J_r = \frac{J_{rf,eq}}{R}\frac{A}{T}$. Thus an elementary reaction rate is uniquely defined by the corresponding affinity since $J_{rf,eq}$ becomes constant due to uniform concentration at equilibrium when a system is in the vicinity of GE with fast diffusion and heat conduction processes. The coefficient L_{rr} is

$$L_{rr} = \frac{J_{rf,eq}}{R} = \frac{k_o \exp\left(-E_f / RT\right)\ C_{S,eq}}{R} \tag{13}$$

where k_o is the frequency and E_f is the activation energy for the forward reaction. The L_{rr} is dependent on the rate constant and consequently on the equilibrium concentration $C_{S,eq}$ and the amount of chemical catalyst.

Linear flow-force relations are valid when the Gibbs free energy ranges less than 1.5 kJ/mol for chemical reactions [15,18]. However, some selected biological pathways occur at near GE conditions [2,3], and for some chemical reactions, the formalism of LNET can be used in wider ranges than usually expected [14,25-28]. By conservation of mass, some flow-force relations of enzyme catalyzed and other chemical reactions can be described by a simple hyperbolic-tangent function. Therefore, a plot of reaction velocity versus affinity has three regions; the regions at very high positive and negative values of affinity, the reaction velocity is almost independent of affinity. In between, however, the reaction velocity varies smoothly leading to a quasi-linear region around the inflection point. This region extends the linear flow-force relations over a 7 kJ mol^{-1} with an error in the reaction velocity less than 15%. This behavior is independent of the reaction rate constants, and mainly occurs due to conservation conditions [27].

THE BALANCE EQUATIONS WITH THERMODYNAMIC COUPLINGS

With these newly defined primary and cross coefficients, Eqs. (6) to (8) become

$$\mathbf{J}_S = -D_{S,e}\nabla C_S - D_{T,e}\nabla T + \mathbf{L}_{Sr}\frac{A}{T} \tag{14}$$

$$\mathbf{J}_q = -D_{D,e}\nabla C_S - k_e\nabla T + \mathbf{L}_{qr}\frac{A}{T} \tag{15}$$

$$J_r = -\mathbf{L}_{rS}\frac{1}{T}\lambda_S\nabla C_S - \mathbf{L}_{rq}\frac{1}{T^2}\nabla T + \frac{k_f C_{S,eq}}{R}\frac{A}{T} \tag{16}$$

By inserting Eqs. (14) to (16) into Eq. (1) and Eq. (3), we may describe the thermodynamically and mathematically coupled system of chemical reaction and heat and mass flows

$$\frac{\partial C_S}{\partial t} = -\nabla\cdot\left(-D_{S,e}\nabla C_S - D_{T,e}\nabla T + \mathbf{L}_{Sr}\frac{A}{T}\right) - \left(-\mathbf{L}_{rS}\frac{\lambda_S}{T}\nabla C_S - \frac{\mathbf{L}_{rq}}{T^2}\nabla T + \frac{k_f C_{S,eq}}{R}\frac{A}{T}\right) \tag{17}$$

$$\rho c_p\frac{\partial T}{\partial t} = -\nabla\cdot\left(-D_{D,e}\nabla C_S - k_e\nabla T + \mathbf{L}_{qr}\frac{A}{T}\right) + (-\Delta H_r)\left(-\mathbf{L}_{rS}\frac{\lambda_S}{T}\nabla C_S - \frac{\mathbf{L}_{rq}}{T^2}\nabla T + \frac{k_f C_{S,eq}}{R}\frac{A}{T}\right) \tag{18}$$

Under mechanical equilibrium, we have

$$\nabla\left(\frac{\mu_i}{T}\right) = \left[\mu_i - T\left(\frac{\partial \mu_i}{\partial T}\right)\right]\nabla\left(\frac{1}{T}\right) + \frac{(\nabla \mu_i)_T}{T} = -H_i \frac{\nabla T}{T^2} + \frac{(\nabla \mu_i)_T}{T} \tag{19}$$

where H_i is the partial enthalpy of species i. By using the definition of affinity ($A = \mu_S - \mu_P$) and Eq. (19) for the two components S and P with the Gibbs-Duhem equation ($C_S \nabla \mu_S + C_P \nabla \mu_P = 0$) and the following relations $\lambda_S = \left(1 + \frac{C_S}{C_P}\right)\left(\frac{\partial \mu_S}{\partial C_S}\right)_{T,P}$ (for $V_S = V_P$), and $\Delta G_r^o + T\Delta S_r = \Delta H_r$, we obtain

$$\nabla\left(\frac{A}{T}\right) = \left(\nabla\left(\frac{\mu_S}{T}\right) - \nabla\left(\frac{\mu_P}{T}\right)\right) = \frac{\lambda_S}{T}\nabla C_S - \frac{(-\Delta H_r)}{T^2}\nabla T \tag{20}$$

Substituting Eq. (20) in Eqs. (17) and (18), we have

$$\frac{\partial C_S}{\partial t} = D_{S,e}\nabla^2 C_S + D_{T,e}\nabla^2 T + \frac{\mathbf{L}_{rq} + \mathbf{L}_{Sr}(-\Delta H_r)}{T^2}\nabla T - \frac{k_f C_{S,eq}}{R}\frac{A}{T} \tag{21}$$

$$\rho c_p \frac{\partial T}{\partial t} = D_{D,e}\nabla^2 C_S + k_e \nabla^2 T - \frac{\lambda_S[(-\Delta H_r)\mathbf{L}_{rS} + \mathbf{L}_{qr}]}{T}\nabla C_S + \frac{(-\Delta H_r)k_f C_{S,eq}}{R}\frac{A}{T} \tag{22}$$

where (A/RT) is the dimensionless affinity A^*. Arrhenius equation yields $\ln\left(k_f / k_b\right) = (E_b - E_f)/(RT)$, and Eqs. (21) and (22) become

$$\begin{aligned}\frac{\partial C_S}{\partial t} = {} & D_{S,e}\nabla^2 C_S + D_{T,e}\nabla^2 T + \frac{\mathbf{L}_{rq} + \mathbf{L}_{Sr}(-\Delta H_r)}{T^2}\nabla T \\ & - \left[C_{S,eq}k_o \exp\left(\frac{-E_f}{RT}\right)\right]\left(\frac{E_b - E_f}{RT} + \ln\left(\frac{C_S}{C_P}\right)\right)\end{aligned} \tag{23}$$

$$\begin{aligned}\rho c_p \frac{\partial T}{\partial t} = {} & D_{D,e}\nabla^2 C_S + k_e \nabla^2 T - \frac{\lambda_S[(-\Delta H_r)\mathbf{L}_{rS} + \mathbf{L}_{qr}]}{T}\nabla C_S \\ & + (-\Delta H_r)\left[C_{S,eq}k_o \exp\left(\frac{-E_f}{RT}\right)\right]\left(\frac{E_b - E_f}{RT} + \ln\left(\frac{C_S}{C_P}\right)\right)\end{aligned} \tag{24}$$

One-dimensional forms of Eqs. (23) and (24) in the y-direction are

$$\frac{\partial C_S}{\partial t} = D_{S,e}\frac{\partial^2 C_S}{\partial y^2} + D_{T,e}\frac{\partial^2 T}{\partial y^2} + \frac{b}{T^2}\frac{\partial T}{\partial y} - \left[C_{S,eq}k_o \exp\left(\frac{-E_f}{RT}\right)\right]\left(\frac{E_b - E_f}{RT} + \ln\left(\frac{C_S}{C_P}\right)\right) \tag{25}$$

$$\frac{\partial T}{\partial t} = \frac{D_{D,e}}{\rho c_p}\frac{\partial^2 C_S}{\partial y^2} + \alpha_e \frac{\partial^2 T}{\partial y^2} - \frac{\lambda_S b}{\rho c_p T}\frac{\partial C_S}{\partial y} + \frac{(-\Delta H_r)}{\rho c_p}\left[C_{S,eq}k_o \exp\left(\frac{-E_f}{RT}\right)\right]\left(\frac{E_b - E_f}{RT} + \ln\left(\frac{C_S}{C_P}\right)\right)$$

(26)

where $b = L_{rq} + L_{Sr}(-\Delta H_r) = \frac{k_f C_{S,eq} T}{R}\left(k_e T r_{rq}^2 + \left(\frac{D_{S,e}}{\lambda_S}\right) r_{Sr}^2 (-\Delta H_r)\right)$. For simple slab geometry the initial and boundary conditions are

$t = 0$ $\quad C_S = C_{So}$ $\quad C_P = C_{Po}$ $\quad T = T_o$

$y = \pm L$ $\quad C_S = C_{Ss}$ $\quad C_P = C_{Ps}$ $\quad T = T_s$ (surface conditions) (27)

$y = 0$ $\quad \frac{\partial C_S}{\partial y} = \frac{\partial C_P}{\partial y} = \frac{\partial T}{\partial y} = 0$ (symmetry conditions)

where L is the half thickness of the slab. Nondimensional forms of Eqs. (25) and (26) become

$$\frac{\partial \theta_S}{\partial \tau} = \frac{\partial^2 \theta_S}{\partial z^2} + \varepsilon \frac{\partial^2 \varphi}{\partial z^2} + \frac{\sigma}{\varphi^2}\frac{\partial \varphi}{\partial z} - A^{*}\mathrm{Da}_S \theta_{S,eq} \exp\left[\gamma_f \left(1 - \frac{1}{\varphi}\right)\right] \tag{28}$$

$$\frac{1}{\mathrm{Le}}\frac{\partial \varphi}{\partial \tau} = \frac{\partial^2 \varphi}{\partial z^2} + \omega \frac{\partial^2 \theta_S}{\partial z^2} - \frac{\kappa}{\varphi}\frac{\partial \theta_S}{\partial z} + A^{*}\mathrm{Da}_S \beta \theta_{S,eq} \exp\left[\gamma_f \left(1 - \frac{1}{\varphi}\right)\right] \tag{29}$$

where

$$z = \frac{y}{L},\ \tau = \frac{D_{S,e}t}{L^2},\ \mathrm{Da}_S = \frac{L^2 k_o \exp(E_f/RT_s)}{D_{S,e}},\ \gamma_f = \frac{E_f}{RT_s},\ \gamma_b = \frac{E_b}{RT_s},\ \mathrm{Le} = \frac{k_e/\rho C_p}{D_{S,e}} = \frac{\alpha_e}{D_{S,e}}$$

$$\varepsilon = \frac{D_{T,e}T_s}{D_{S,e}C_{Ss}},\quad \omega = \frac{D_{D,e}c_s}{k_e T_s},\quad \sigma = \frac{bL}{T_s D_{S,e} C_{Ss}} = \frac{[L_{rq} + L_{Sr}(-\Delta H_r)]L}{T_s D_{S,e} C_{Ss}},\quad \kappa = \frac{bC_{Ss}L\lambda_S}{k_e T_s^2}$$

$$A^{*} = \left(\frac{\gamma_b - \gamma_f}{\varphi}\right) + \ln\left(\frac{\theta_S}{K[a_1 + a_2(1-\theta_S)]}\right);$$

Da_S and Da_P are the Damköhler numbers and represent the ratios of the forward and backward reaction rates to the diffusion velocities ($D_{i,e}/L$). Therefore, they measure the intrinsic rates of the reactions relative to that of the diffusions, and represent an interaction between reaction and diffusion [20]. If the reaction is very fast, Damköhler number is large. The parameter b is defined in Eq. (26). These equations suggest that the degree of couplings beside the other parameters would control the evolution and stability of the system. Therefore, induced effects due to various coupling phenomena can increase the possibility that the system may evolve to multiple states and diversify its behavior [27, 30]. The parameters ε, σ, ω, and κ above are associated with the cross coefficients and hence control the coupled phenomena in the y-direction. Specifically, the ε and ω control the coupling between mass and heat flows, while the σ and κ control the coupling between the chemical reaction and mass flow, and chemical reaction and heat flow, respectively. The initial and boundary conditions become

$$\begin{array}{llll}
\tau = 0 & \theta_S = \theta_{So} & \theta_P = \theta_{Po} & \varphi = \varphi_o \\
z = \pm 1,\ \tau > 0 & \theta_S = 1 & \theta_P = 1 & \varphi = 1 \\
z = 0,\ \tau > 0 & \dfrac{\partial \theta_S}{\partial z} = \dfrac{\partial \theta_P}{\partial z} = \dfrac{\partial \varphi}{\partial z} = 0 & &
\end{array} \tag{30}$$

Accuracy of the solutions obtained from Eqs. (28) and (29) depends on the reliable data, such as the effective transport coefficients and cross coefficients. The parameter b in terms of the degrees of couplings r_{qr} and r_{Sr} may improve the accuracy since the degrees of couplings vary between –1 and +1. Some processes will not be dependent on some of the forces when some certain cross coefficients vanish naturally. For example, some degrees of imperfections due to parallel pathways of reaction or intrinsic uncoupling within the pathway itself may lead to leaks and slips in mitochondria [3,5].

Some special cases of coupled phenomena- Possible thermodynamically coupled systems: (a) Coupled phenomena at stationary state, (b) No coupling exists between the heat flow and chemical reaction: $L_{rq} = L_{qr} = 0$., (c) No coupling exists between the mass flow and chemical reaction: $L_{rS} = L_{Sr} = 0$. In all the systems above, heat and mass flows are still thermodynamically coupled [31].

Chemical reaction coupled to mass flow: $L_{rq} = L_{qr} = 0$- This specific coupling may approximately represent the active transport in biological cells in which hydrolysis of ATP is coupled with the uphill transport of ions. Experiments show that biological energy coupling systems shows that the LNET is capable of describing mitochondrial H^+ pumps [3] and helps understanding molecular slips and ion leaks of Ca^{+2} and H^+ [5,7].

A representative volumetric rate of entropy production equation for active transport is [2,31]

$$\Phi = -\mathbf{J}_S \frac{1}{T}\lambda_S \nabla C_S + J_{rS}\frac{A}{T} = \text{mass flow} + \text{chemical reaction} = \text{output} + \text{input} \geq 0 \tag{31}$$

For the active transport in a biological cell, the chemical reaction term $\left(J_{rS}A/T\right)$ represents the hydrolysis of ATP, which facilitates pumping the ions opposite to the direction imposed by their thermodynamic forces, and hence we have $\left(-\mathbf{J}_S \frac{1}{T}\lambda_S \nabla C_S\right) < 0$. The efficiency of energy conversion for active transport may be related to the degree of coupling by using Eq. (31)

$$\eta = \frac{\text{output}}{\text{input}} = \frac{-\mathbf{J}_S (1/T)\lambda_S \nabla C_S}{J_{rS}(A/T)} = \frac{x[(L_{SS}/L_{rr})^{1/2}x + r_{Sr}]}{[r_{Sr} + (L_{rr}/L_{SS})^{1/2}]} \tag{32}$$

where x is the ratio of thermodynamic forces $([(1/T)\lambda_S \nabla C_S/(A/T)]$. The optimal efficiency would be a function of the degree of coupling [2-4,13].

When the cross coefficients $\mathbf{L}_{rq}$ and $\mathbf{L}_{qr}$ vanish in Eqs. (14) to (16), the PEs become

$$\mathbf{J}_S = -D_{S,e}\nabla C_S - D_{T,e}\nabla T + \mathbf{L}_{Sr}\frac{A}{T}$$

$$\mathbf{J}_q = -D_{D,e}\nabla C_S - k_e \nabla T \tag{33}$$

$$J_r = -\mathbf{L}_{rS}\frac{1}{T}\lambda_S \nabla C_S + \frac{k_o \exp\left(-E_f/RT\right)C_{S,eq}}{R}\frac{A}{T} \tag{34}$$

so that the one-dimensional balance equations are

$$\frac{\partial \theta_S}{\partial \tau} = \frac{\partial^2 \theta_S}{\partial z^2} + \varepsilon \frac{\partial^2 \varphi}{\partial z^2} + \frac{\sigma'}{\varphi^2}\frac{\partial \varphi}{\partial z} - A^* \mathrm{Da}_S \theta_{S,eq} \exp\left[\gamma\left(1 - \frac{1}{\varphi}\right)\right] \tag{35}$$

$$\frac{1}{\mathrm{Le}}\frac{\partial \varphi}{\partial \tau} = \frac{\partial^2 \varphi}{\partial z^2} + \omega \frac{\partial^2 \theta_S}{\partial z^2} - \frac{\kappa'}{\varphi}\frac{\partial \theta_S}{\partial z} + A^* \mathrm{Da}_S \beta \theta_{S,eq} \exp\left[\gamma\left(1 - \frac{1}{\varphi}\right)\right] \tag{36}$$

where

$$\sigma' = \frac{[L_{Sr}(-\Delta H_r)]L}{T_s D_{S,e} C_{Ss}}; \quad \kappa' = \frac{[L_{Sr}(-\Delta H_r)]C_{Ss}L\lambda_S}{k_e T_s^2}$$

By relating the cross coefficient to the degree of coupling r_{Sr}, the cross coefficient L_{Sr} may be eliminated

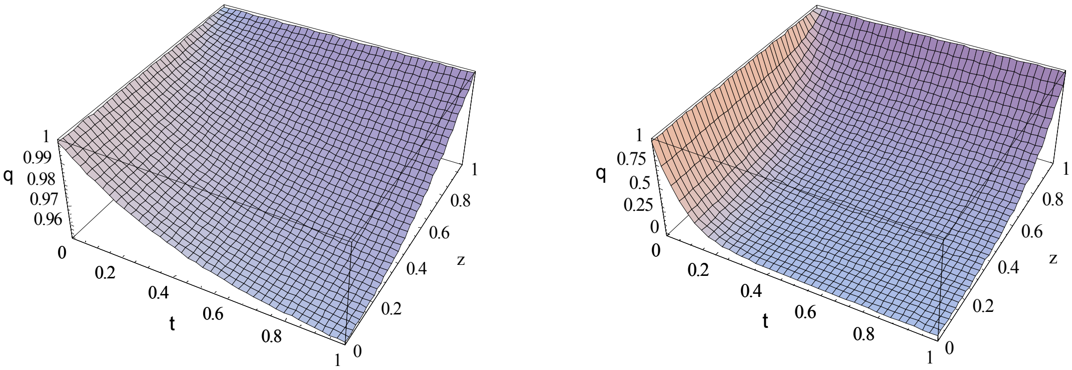
$$L_{Sr} = r_{Sr}\left(L_{SS}L_{rr}\right)^{1/2} = r_{Sr}\left(\frac{D_{S,e}T}{\lambda_s}\frac{k_f C_{S,eq}}{R}\right)^{1/2} \tag{37}$$

and the parameters σ' and κ' are defined in terms of the degree of coupling r_{Sr}

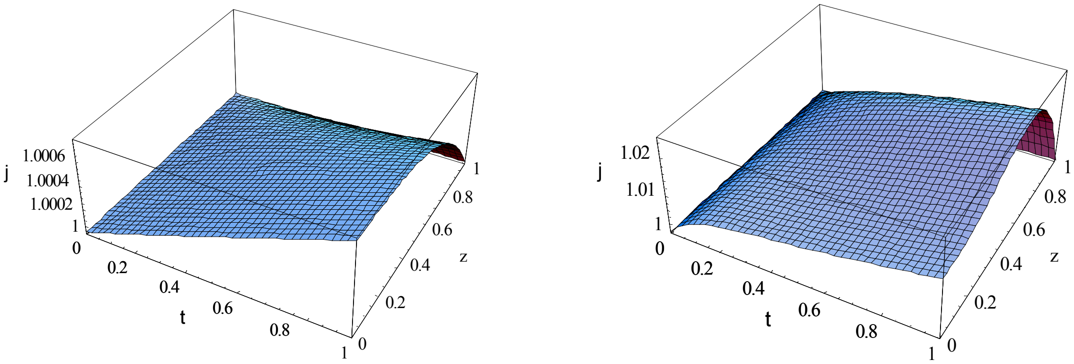
$$\sigma' = r_{Sr}\left(\frac{D_{S,e}T}{\lambda_s}\frac{k_f C_{S,eq}}{R}\right)^{1/2}\frac{(-\Delta H_r)]L}{T_s D_{S,e} C_{Ss}}, \qquad \kappa' = r_{Sr}\left(\frac{D_{S,e}T}{\lambda_s}\frac{k_f C_{S,eq}}{R}\right)^{1/2}\frac{(-\Delta H_r)C_{Ss}L\lambda_S}{k_e T_s^2} \tag{38}$$

The parameter κ' combines the forward reaction rate constant, diffusivity coefficient, and thermal conductivity, and hence may reflect an 'indirect interaction' between chemical reaction and heat flow with vanishing cross coefficients of L_{rq} and L_{qr}. During a diffusion-controlled reaction, the progress of the reaction may be affected by the morphology of the interface, which controls the boundary conditions for the transport problem [27-29]. Morphological stability of interfaces in nonequilibrium systems may lead to self-organization and/or pattern-formation in biological, physical, chemical, and geological systems [26,29].

Concentration and temperature profiles - The Mathematica is used to solve Eqs. (35) and (36). Figure 1 displays the dynamic behavior of the concentrations and temperatures at two different Damköhler numbers. For the fast reaction case with $\mathrm{Da}_S = 100.0$, nonequilibrium region is considerably smaller and attained at a shorter time. For the slow reaction case with $\mathrm{Da}_S = 1.0$, the system remains in nonequilibrium for most of the time and throughout the thickness of the film. The surfaces of temperature closely follow the change in concentrations, and reflect the effect of Damköhler numbers. As expectedly, the rise of temperature is small as the value of β is relatively small [31].



(a) $Da_S = 1.0$ (a) $Da_S = 100.0$



(b) $Da_S = 1.0$ (b) $Da_S = 100.0$

Figure 1. Dimensionless temperature and concentration profiles obtained from Eqs. (35) and (36) with $\gamma = 27$, $\beta = 0.066$, Le= 0.11, $\varepsilon = 1.0$, $\omega = 0.01$, $A^* = 0.1$, $\sigma' = 0.1$, $\kappa' = 0.001$.

SUMMARY and CONCLUSIONS

The balance equations are derived for thermodynamically and mathematically coupled system of chemical reaction and heat and mass flows. This effort may be a starting point to understand the molecular coupled phenomena between vectorial and scalar processes, such as active transport in biological cells. These modeling equations are based on the linear nonequilibrium thermodynamics approach assuming that the system is in the vicinity of global equilibrium and has anisotropic character. The equations have revealed definitions of some unique parameters related to the cross coefficients between the scalar process of chemical reaction and the vectorial processes of heat and mass flows. These parameters combine kinetic parameters, transport coefficients, and degrees of thermodynamic couplings, which are measurable quantities. The representative solutions of the modeling equations for the coupled chemical reaction-mass flow system are in line with the behavior of fast and slow chemical reactions in a film.

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