

Cross-diffusion and pattern formation in reaction–diffusion systems

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Cross-diffusion, the phenomenon in which a gradient in the concentration of one species induces a flux of another chemical species, has generally been neglected in the study of reaction–diffusion systems. We summarize experiments that demonstrate that cross-diffusion coefficients can be quite significant, even exceeding “normal,” diagonal diffusion coefficients in magnitude in systems that involve ions, micelles, complex formation, excluded volume effects (*e.g.*, surface or polymer reactions) and other phenomena commonly encountered in situations of interest to chemists. We then demonstrate with a series of model calculations that cross-diffusion can lead to spatial and spatiotemporal pattern formation, even in relatively simple systems. We also show that, in the absence of cross-diffusion among the reacting species, introduction of a nonreactive species that induces appropriate cross-diffusive fluxes with reactive species can lead to pattern formation.

1. Introduction

Reaction–diffusion (RD) systems have attracted increasing attention from the scientific community in recent years as investigators have begun to seek insights into the fascinating patterns that occur in living organisms, in ecological systems, in geochemistry and in physicochemical systems. The rapid growth of the field of systems biology has further contributed to interest in RD systems. Thermodynamically stable spatial structures,¹ like crystals (for example, snowflakes²), micelles, membranes and other aggregates are said to arise *via self-assembly*. Another class of structures, of which Turing patterns³ are perhaps the best known example, occur only far from equilibrium. They are said to involve *self-organization* and

result from mechanisms that may be called kinetic or dissipative. Introduced theoretically by Turing,³ extensively studied by Prigogine and collaborators,⁴ and then realized experimentally in Bordeaux,⁵ Austin,⁶ and Brandeis⁷ among other places, these routes to pattern formation couple nonlinear chemical kinetics and diffusion. These dissipative or nonequilibrium patterns include spiral waves,⁸ Turing patterns,^{5,7} standing waves^{7,9} and other spatiotemporal phenomena that require an input of energy and/or matter.

Diffusion processes play a role in both self-assembly and self-organization, while chemical kinetics is important only in the latter case. Detailed understanding of self-assembly requires knowledge of the explicit form of the interaction potential between particles or molecules, which allows us to calculate such thermodynamic functions as energy and entropy. In chemical kinetics, the mechanisms of chemical and physical interaction between species are hidden in the reaction rate constants, which significantly simplifies the description of chemical processes. When analyzing RD mechanisms, one

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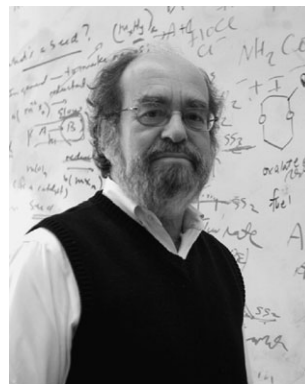
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usually assumes that chemical and diffusion processes can be separated without any harm, at least for relatively slow reactions. Note, however, that there is a well known and venerable example in which a diffusion process directly determines the rate of a chemical process, namely a diffusion-controlled bimolecular reaction, whose rate, $k_d[A][B]$, is characterized by^{10–13}

$$k_d = 4\pi f\rho DN_A \quad (1)$$

where k_d is the diffusion-controlled reaction rate constant, ρ is the encounter diameter of the molecules A and B, $D = D_A + D_B$ is the diffusion coefficient of their relative motion and N_A is Avogadro's number. The factor f takes into account the charges on species A and B. If their charges have the same (opposite) signs, then $f < (>) 1$, and $f \cong 1$ for neutral A or B.

Nearly all efforts to explain the patterns found experimentally in RD systems, such as the CIMA (chlorite–iodide–malonic acid) reaction,^{5,6} the BZ-AOT (Belousov–Zhabotinsky in aerosol OT microemulsion) system^{7,14} or the FIS (ferrocyanide–iodide–sulfite) reaction,^{15–17} employ only the diagonal elements of the diffusion matrix. That is, they assume that the diffusion of species A depends only upon gradients in the concentration of A, and not on the spatial distribution of any other species. In this case, an RD system can be written in the following general form

$$\partial u_i / \partial t = R_i(\mathbf{u}) + D_{ii} \nabla^2 u_i, \quad i = 1, 2, \dots, N \quad (2)$$

where the vector \mathbf{u} consists of the concentrations u_j ($j = 1, 2, \dots, N$) of the N species, the $R_i(\mathbf{u})$ give the reaction kinetics, and D_{ii} is the diffusion coefficient of the i th species. Patterns found in such RD systems generally arise *via* either Turing instability or wave instability.³ These instabilities can lead to patterns in spatially extended systems if the homogeneous steady state is subjected to an infinitesimal perturbation.^{5,7} In some cases, patterns can emerge only if a sufficiently large perturbation with a suitable spatial structure is applied.^{18–20} This latter (subcritical) group of mechanisms can also produce localized patterns.²¹

The Turing instability, which leads to patterns that are stationary in time and periodic in space, can be characterized as arising from “long range inhibition and short range activation”, at least for two-variable models. Translating these biologically-oriented terms into physicochemical ones, we may say that the autocatalytic species (activator) must have a diffusion coefficient smaller (often much smaller) than that of the other (inhibitor) species. The conditions for wave instability, which can occur only in systems with three or more variables, and which leads to patterns periodic in both time and space, are more complex. Typically, a third species coupled to the activator must have a diffusion coefficient that differs significantly from the diffusion coefficients of both the activator and the inhibitor.

Chemical and physical interaction between species can be concealed not only in the reaction rate constants, as mentioned above, but also in the parameters used to describe the diffusion process, especially when cross-diffusion is present. Cross-diffusion refers to the phenomenon in which a flux of species A is induced by a gradient of species B. Such processes can be characterized by the Fickian diffusivity matrix \mathbf{D} or by the Maxwell–Stefan diffusion matrix \mathcal{D} , where the diffusion coefficient \mathcal{D}_{ij} has the

physical meaning of an inverse drag coefficient in the Maxwell–Stefan equations,²² rather than by a vector of coefficients D_{ij} . Examples of systems that exhibit cross-diffusion include strong electrolytes,^{23–25} micelles,^{26,27} or microemulsions,²⁸ and systems containing molecules of significantly different sizes, for example protein–salt.^{29–31} Similar phenomena also occur in biological systems, but since the transport process is driven by an input of energy, as, for example, in bacterial chemotaxis^{32–34} or in predator–prey systems,^{35–38} these are not true diffusion processes. Nonetheless, the mathematical description of biological or ecological cross-diffusion is the same as in physicochemical systems, as we discuss below.

Following the Fickian interpretation of the diffusion process, the general RD equations with cross-diffusion terms take the form:

$$\partial u_i / \partial t = R_i(\mathbf{u}) + D_{ii} \nabla^2 u_i + \sum_{j \neq i} \text{div}(D_{ij} \nabla u_j), \quad i, j = 1, 2, \dots, N \quad (3)$$

where the new term, $\sum \text{div}(D_{ij} \nabla u_j)$, takes into account the flux of u_i , $D_{ij} \nabla u_j$, induced by the gradient of species u_j . Note that eqn (3) can include nonreactive species for which the reactive term $R_i(\mathbf{u})$ equals zero. These species may be crucial for pattern formation, since cross-diffusion between reactive and non-reactive species can induce significant fluxes of reactive species.

In this Perspective, we first describe several processes that can give rise to cross-diffusion, like chemotaxis,³⁹ weak nonbonding solute–solute interactions,^{40,41} electrostatic^{42,43} or excluded volume effects.^{30,42,44–49} Methods of measurement of cross-diffusion constants are briefly described. We present our own theoretical results that predict patterns in very simple chemical systems (described by eqn (3)), patterns that do not require the usual condition of activator–inhibitor species having significantly different diffusion coefficients.

2. Cross-diffusion without reaction

At first glance, diffusion might seem to be a simple process, but in multi-component systems this is rarely the case. The complex range of possibilities becomes apparent if we simply consider the various terms used to characterize diffusive processes. Indeed, such expressions as self-diffusion, tracer diffusion, intradiffusion and interdiffusion, mutual diffusion, cross-diffusion, uphill diffusion^{50,51} and incongruent or negative diffusion^{52,53} require careful definition. If we look back at the history of diffusion, we find that its experimental investigation in binary liquid mixtures began in 1850,⁵⁴ and its theoretical description started in 1855 with Fick.⁵⁵ The possibility of cross-terms in multi-component systems was suggested only in 1932.⁵⁶ In 1955, Gosting and collaborators undertook the experimental verification of the existence of cross-diffusion.^{57,58} They used optical interferometry, Gouy and Rayleigh methods.^{59,60} Other approaches, like the diaphragm-cell technique^{61–63} and the Taylor method^{64–67} have also been adapted to measure cross-diffusion coefficients. The Taylor method, which we discuss below, is probably the most widely employed technique at present.

The term “mutual diffusion coefficients” is used as a synonym for interdiffusion coefficients. These are the coefficients used in eqn (3), both the diagonal and off-diagonal elements of

matrix \mathbf{D} . For a binary solution, only a single coefficient is necessary to describe diffusion, while for a ternary solution, we already need four diffusion coefficients, and nine are required for quaternary systems. These diffusion coefficients, including the diagonal elements of the matrix \mathbf{D} , are dependent on both concentration and temperature. Negative diffusion provides a striking example of the dependence of D_{ii} on concentration.^{52,53}

The term intradiffusion was probably first introduced by Albright and Mills.^{68,69} Following these authors, in the book by Tyrrell and Harris,⁷⁰ self-diffusion is considered as a special case of intradiffusion in a system which contains only two distinguishable (by isotopic labeling, for example) forms of the same chemical species. Self-diffusion can be measured at low concentrations when the interaction between particles is negligible. As concentrations approach zero, the diagonal elements of \mathbf{D} tend to the self-diffusion coefficients.

The self-diffusion coefficient of any component α in a system can be defined as⁷¹

$$D_\alpha = \frac{1}{3N_\alpha} \sum_{i=1}^{N_\alpha} \int_0^\infty \langle \bar{u}_i(t) \bar{u}_i \rangle dt \quad (4)$$

where $\langle \bar{u}_i(t) \bar{u}_i \rangle$ is the velocity autocorrelation function of an individual particle and N_α is the number of these particles.⁷² From this definition, it was noted⁷³ that, unlike mutual diffusion coefficients, self-diffusion coefficients are independent of reference frame and of the chemical potential derivatives. Relations between self-diffusion and mutual (interdiffusion) diffusion coefficients can be established,^{73,74} for example, as Darken's equation^{75,76} or the Hartley–Crank relation.^{77,78}

Since diffusion coefficients characterize the motion of particles, and the velocity of any motion is measured in some reference frame, the choice of reference frame is very important for determining diffusion coefficients.⁵³ The diffusion flows (or fluxes) in some arbitrary reference frame \mathbf{R} can be written as

$$J_j^{\mathbf{R}} = c_j(u_j - u_{\mathbf{R}}) \quad (5)$$

where c_j is the concentration of component j , and u_j and $u_{\mathbf{R}}$ are the local velocities of j and the reference frame \mathbf{R} , respectively. Any one component flow (for n components) can be eliminated by the definition of the reference frame *via* the relation

$$\sum_{j=1}^n a_j^{\mathbf{R}} J_j^{\mathbf{R}} = 0 \quad (6)$$

where $a_j^{\mathbf{R}}$ is an appropriate weighting factor. Usually, it is the solvent that is eliminated. The final form of Fick's equations (analogous to eqn (3) without reaction terms) contains diffusion coefficients D_{ij} that depend on the reference frame.

There are three important reference frames, the *solvent-fixed* reference frame, the *mass-fixed* (or barycentric) reference frame, and the *volume-fixed* reference frame. For these frames, the coefficients $a_j^{\mathbf{R}}$ are as follows: all $a_j^0 = 0$ except $a_n^0 = 1$ for the solvent-fixed frame, where n corresponds to solvent molecules and the superscript 0 denotes the solvent-fixed frame; $a_j^{\mathbf{M}} = M_j$ for the mass-fixed frame, where M_j is the molecular mass; and $a_i^{\mathbf{V}} = \bar{V}_i$ for the volume fixed frame, where \bar{V}_i is the partial molar volume of component i . For most laboratory diffusion experiments, the volume-fixed reference frame is most appropriate.

There are well-established rules for transformations of diffusion coefficients from one reference frame to another.^{53,79}

Independent of the reference frame, the matrix of diffusion coefficients must obey constraints that follow from the second law of thermodynamics.^{53,80–85} The most important of these is that all eigenvalues of the matrix \mathbf{D} must be real and positive. As a consequence, $\det(\mathbf{D}) > 0$ and $\text{tr}(\mathbf{D}) > 0$. One mathematical proof of this statement is based on the fact that the matrix \mathbf{D} can be related to the symmetric matrix \mathbf{L} consisting of the well-known Onsager coefficients,⁵⁶ for which $L_{ij} = L_{ji}$. The phenomenological coefficients L_{kj} link the generalized forces F_j , for example, the gradient of chemical potential μ_j , to the generalized fluxes J_k , for example, the diffusion flux.^{86,87} \mathbf{D} can be decomposed into the product of two positive definite matrixes, one of which is \mathbf{L} .⁵³ Since all the eigenvalues of a positive definite matrix, by definition, are real and positive, the matrix \mathbf{D} , which is the product of two positive definite matrixes, must also have only real, positive eigenvalues.⁸¹ Physically, a complex eigenvalue of \mathbf{D} would result in oscillatory relaxation of any small perturbation to the equilibrium state, even in the absence of reaction.

In some works, in which the effect of cross-diffusion on pattern formation or wave propagation was investigated with the aid of eqn (3), this fundamental restriction on the diffusion matrix \mathbf{D} has been ignored.^{35,36,88,89} As a result, surprising and probably physically unrealistic dynamic behaviors of the model RD systems were obtained. However, in biological, ecological and even social systems that can be described by eqn (3), the matrix \mathbf{D} need not follow this thermodynamic restriction, since the diffusion processes, chemical or not, in these systems are driven by a source of external energy. The fundamental theoretical question that we pose, and address further below, is whether, in chemical systems far from equilibrium, the thermodynamic restriction on mutual diffusion coefficients, which derives from the linear phenomenological laws that hold close to equilibrium, can be violated due to interaction between chemical reactions and diffusion processes. This issue does not appear to have been considered in the theoretical literature, and measurements of diffusion coefficients in chemical systems far from equilibrium are lacking.

There are many methods for measuring diffusion coefficients in physicochemical systems.⁷⁰ Three approaches, the optical interferometry technique,⁵⁹ the diaphragm-cell technique,⁶¹ and the Taylor dispersion technique^{64–66} have been adapted for measuring cross-diffusion coefficients. Such powerful methods as dynamic light scattering (DLS) and pulsed NMR have not thus far been utilized to determine cross-diffusion coefficients. Pulsed NMR is used to measure self-diffusion coefficients, while DLS probably measures the smallest eigenvalue of the matrix \mathbf{D} .⁹⁰ In ternary systems [particular in glycerol(0)–acetone(1)–water(2)] it is found that the diffusion coefficient D_m obtained from DLS experiments is not related to any of the diffusion coefficients D_{ij} in the Fick's diffusion coefficient matrix \mathbf{D} ,⁹⁰ but it does coincide with the lowest eigenvalue of \mathbf{D} . This result may be general, at least for molecules of similar size.

One of the most widely employed techniques for measuring diffusion coefficients is the Taylor dispersion method. Although it dates back over half a century, it is only in the past two decades

that this technique has been adapted for measuring cross-diffusion in three- and even four-component systems.^{65,91–93} The Taylor method is based on the diffusive spreading of a drop of solution injected into a laminarily flowing stream of a mixture of the same components but with slightly different concentrations (see Fig. 1). A small volume of the perturbing solution is injected into the flowing eluent at the entrance of a long capillary tube. As it moves along the tube, the injected sample is deformed by the flow, the rate of which has a parabolic shape across the capillary, and by radial diffusion. The drop spreads out into a shape that can be fitted by a combination of n Gaussian functions for an $(n + 1)$ -component system. The eluted peak, sometimes called the Taylor peak, is monitored by a suitable detector such as a flow-through spectrophotometer, refractive index detector (RID) or Raman spectrometer.^{93,94} The diffusion coefficients are calculated from the parameters of the Gaussian functions that fit the eluted peak. A typical peak is shown in Fig. 2.

In general, the cross-diffusion coefficients or off-diagonal elements of matrix \mathbf{D} can be either positive or negative and can be quite large in certain cases. Three important mechanisms responsible for cross-diffusion are electrostatic interactions, excluded volume effects, and “complexation”.

Cross diffusion for charged particles at very low concentrations (infinitely dilute solutions) can be described with the Nernst–Hartley equations,^{70,95–97} valid when the off-diagonal Onsager coefficients are zero. These equations are often used, even at large concentrations of charged species, to provide at least a qualitative description of diffusion processes.^{27,29,98,99} The Nernst–Hartley equations are based on the hypothesis of electroneutrality: charged particles cannot move independently, since each volume element in the solution must be neutral. For a binary mixture with a univalent single electrolyte, for example, the Nernst–Hartley equation takes the form

$$D_{\pm}^{\infty} = 2D_{+}^{\infty}D_{-}^{\infty}/(D_{+}^{\infty} + D_{-}^{\infty}) \quad (7)$$

where the superscript ∞ denotes the limit of infinite dilution, and D_{\pm}^{∞} is the diffusion coefficient of an entire electrolyte molecule.

For ternary mixtures in which one component is a large molecule (*e.g.*, a protein) and the other is salt, the Nernst–Hartley equations are⁹⁶

$$D_{11} = D_p[1 + z_p^2 C_1(D_c - D_p)/Q] \quad (8)$$

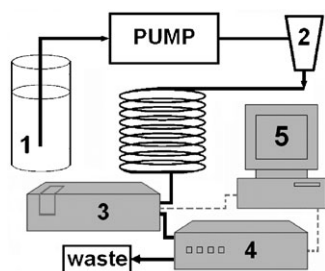


Fig. 1 Schematic drawing of an experimental setup for Taylor dispersion measurements: 1, reservoir containing the eluent; “pump”, isocratic pump; 2, injector; the long (30 m) coiled Teflon tubing is connected to the outlet of the injector; 3, spectrophotometer; 4, refractive index detector (RID); 5, personal computer.

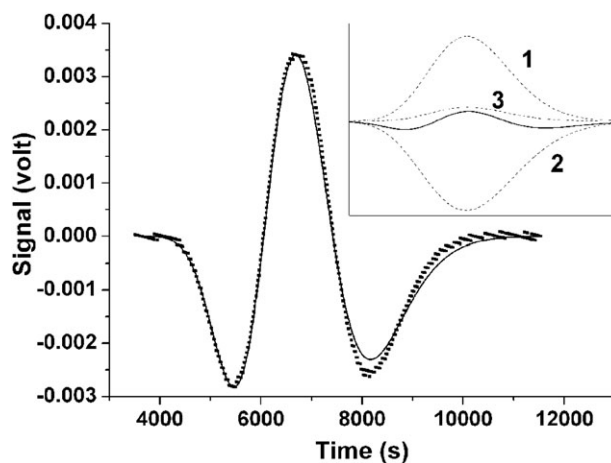


Fig. 2 Taylor dispersion peak for 4-component system water/AOT/MA/octane. Injected samples contain an excess of MA (malonic acid). Dotted line is the experimental Taylor peak (signal) and solid line is the fitted curve. Inset shows the contribution of each component to the fitted (analytical) curve (solid line): curves 1, 2, and 3 correspond to the signals of H₂O, AOT (Aerosol OT, surfactant), and MA, respectively. From ref. 93.

$$D_{12} = D_p z_p z_M C_1 (D_c - D_M) / Q \quad (9)$$

$$D_{21} = D_M z_p z_M C_2 (D_c - D_p) / Q \quad (10)$$

$$D_{22} = D_M [1 + z_M^2 C_2 (D_c - D_M) / Q] \quad (11)$$

where D_p , D_M , and D_c are the (tracer) diffusion coefficients of the macromolecule (cation or anion), the co-ion (*e.g.*, Na⁺, $z_M = 1$; Cl⁻, $z_M = -1$; Mg²⁺, $z_M = 2$, where z_M is the charge of the ion), and the common ion (*e.g.* chloride), respectively; and z_p is the charge, which depends on pH and on the macromolecule (z_p and z_M have the same sign); C_1 is the concentration of macromolecule, C_2 is the concentration of co-ion, and $Q = z_p C_1 (D_p z_p + D_c) + z_M C_2 (D_M z_M + D_c)$. Eqn (8)–(11) are valid only for $z_p C_1 \ll z_M C_2$.

The excluded volume effect can be explained in terms of the effective concentration of component i , c_i^* , given by

$$c_i^* = c_i / (1 - \phi_k), \quad i \neq k \quad (12)$$

Here ϕ_k is the volume fraction of component k , $\phi_k = V_k c_k$, where V_k is the partial molar volume of k . Using mostly intuitive relations and assuming that, in the absence of interactions, the flux of component i generated by the gradient ∇c_k should be the same of the flux of i produced by its own concentration gradient ∇c_i^* :

$$D_{ik} \nabla c_k = D_{ii} \nabla c_i^* \quad (13)$$

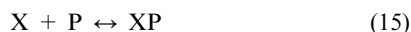
the following relation between D_{ik} and D_{ii} was obtained:^{43,45}

$$D_{ik} = D_{ii} V_k c_i / (1 - V_k c_k)^2 \quad (i \neq k) \quad (14)$$

from which we see that D_{ik} should be positive (assuming that D_{ii} is positive).

Cross-diffusion can arise *via* complexation through a variety of physical interactions between species, like the entropic interaction in micelles or the weak interaction between enzyme and substrate or host–guest complexes. Suppose that two species X and P interact rapidly and reversibly so as to

maintain local reaction equilibrium due to formation of the transient complex XP:



Then the mutual diffusion coefficients for species 1 = X + XP (total X) and species 2 = P + XP (total P) are given by^{100–104}

$$D_{11} = D_X + \phi_2(D_{XP} - D_X) \quad (16)$$

$$D_{12} = \phi_1(D_{XP} - D_X) \quad (17)$$

$$D_{21} = \phi_2(D_{XP} - D_P) \quad (18)$$

$$D_{22} = D_P + \phi_1(D_{XP} - D_P) \quad (19)$$

where D_A is the diffusion coefficient of species A (= X, P, or XP) without any interaction and

$$\phi_1 = c_X c_{XP} / (c_X c_{XP} + c_{XP} c_X + c_P c_X) \quad (20)$$

$$\phi_2 = c_P c_{XP} / (c_X c_{XP} + c_{XP} c_X + c_P c_X) \quad (21)$$

If for example P is a very large molecule (*e.g.*, a polymer or starch bound to a gel), we can assume that $D_P = D_{XP} = 0$ and eqn (16)–(19) give

$$D_{11} = (1 - \phi_2)D_X \quad (22)$$

$$D_{12} = -\phi_1 D_X \quad (23)$$

$$D_{21} = D_{22} = 0 \quad (24)$$

The cross-diffusion coefficients D_{12} and D_{21} are always negative or zero, since $D_{XP} < D_X$ and $D_{XP} < D_P$, for example, D_{12} takes values between 0 and $-D_X$. The negative sign of D_{12} indicates that X is attracted toward higher concentrations of P as a result of the complexation reaction (15).

In an actual experimental system, any of these mechanisms is likely to interact with one or more other processes. In the following we summarize several results that illustrate different cases of cross-diffusion in physical–chemical systems without reaction. These experiments were performed either with the highly accurate Gouy or Rayleigh optical interferometry technique using a unique Gosting diffusimeter¹⁰⁵ or by the Taylor method. We will see that cross-diffusion coefficients can be quite significant, even in apparently simple systems.

Salt–salt. Very careful investigation of cross-diffusion coefficients has been carried out in aqueous solutions of NaCl (c_1) and MgCl₂ (c_2), as well as in solutions of NaCl (c_1) and Na₂SO₄ (c_2).^{40,106–109} For the NaCl–MgCl₂ system, at molar ratios $c_1/c_2 > 1$ (*e.g.*, $c_1/c_2 = 3$),^{40,107} the positive cross-term D_{12} becomes quite large at moderate and high concentrations, and it can even exceed the diagonal coefficients D_{11} and D_{22} .

$$\mathbf{D} = \begin{pmatrix} 1.156 & 1.284 \\ 0.131 & 0.751 \end{pmatrix} \times 10^{-5} \text{ cm}^2 \text{ s}^{-1}$$

$$\text{at } c_1 = 2.845 \text{ M}, c_2 = 0.948 \text{ M}$$

However, when $c_1/c_2 \leq 1$,^{108,109} both of the cross-diffusion coefficients D_{12} and D_{21} remain small. For the NaCl–Na₂SO₄ system at a constant total molarity of 0.5 M,¹⁰⁶ D_{21} , the cross diffusion coefficient of Na₂SO₄ due to a concentration gradient of NaCl, was found to be negative, while D_{12} is positive, in

agreement with the ternary Nernst–Hartley eqn (8)–(11) for electrolytes.

Polymer–salt. A very large positive cross-diffusion coefficient D_{21} was obtained for the aqueous ternary system lysozyme (c_1)–MgCl₂ (c_2) at $c_1 = 0.5987$ mM, and $c_2 = 0.9304$ M (pH = 4.5, 25 °C) with an almost linear dependence of D_{21} on c_2 .²⁹ In units of $10^{-5} \text{ cm}^2 \text{ s}^{-1}$, the authors found

$$\mathbf{D} = \begin{pmatrix} 0.0833 & 0.000145 \\ 12.3 & 1.080 \end{pmatrix}$$

In that work, the diffusion of charged macromolecules in the presence of an electrolyte solution was discussed in terms of two models: (a) the Nernst–Hartley equations,⁹⁶ applicable to an ideal dilute ternary solution with two ionic components, and; (b) the Stokes–Einstein equation,¹¹⁰ which describes the tracer diffusion coefficient (or mobility) of macromolecules in the limit of $c_1 \rightarrow 0$. For both models, the diffusion coefficients are independent of the reference frame, because they apply at infinite dilution. The Nernst–Hartley equations are able to qualitatively describe the observed concentration dependences of the coefficients D_{ij} . A partial explanation of these D_{ij} can be obtained with an excluded volume model, which we discuss in the next paragraph. Analogous results were obtained for a lysozyme chloride–NaCl system.⁸⁷

Investigation of transport of electrolytes in poly(ethylene glycol) (PEG) revealed strong cross-diffusion due to excluded volume effects.⁴² For a PEG2000 (c_1)–NaCl (c_2)–H₂O ternary system, at $c_1 = 0.1250$ M and $c_2 = 1.2485$ M, it was found that (in units $10^{-5} \text{ cm}^2 \text{ s}^{-1}$)

$$\mathbf{D} = \begin{pmatrix} 0.23 & 0.0132 \\ 3.49 & 0.654 \end{pmatrix}$$

with an almost linear dependence of D_{21} on c_2 . This behaviour is consistent with that observed in other PEG–NaCl–H₂O systems.^{47,48} The excluded-volume mechanism applied to the PEG–NaCl system assumes that the volume occupied by the large PEG molecules is unavailable to the salt ions, thus increasing the effective concentration of NaCl: $c_2^* = c_2/(1 - \phi_1) \equiv c_2/(1 - V_1 c_1)$, where V_1 is the effective hydrodynamic volume of a PEG molecule.^{45,47}

Polymer–salt_1–salt_2. A more complex variant of the lysozyme–NaCl system consists of H₃PO₄ ($c_1 = 0.1$ M)–KH₂PO₄ ($c_2 = 0.1$ M)–BSA ($c_3 = 0.1$ mM)–water(0), where BSA = bovine serum albumin. At 25 °C and pH 2.2, where the average charge on the BSA species is +92, the matrix of diffusion coefficients is found to be¹¹¹

$$\mathbf{D} = \begin{pmatrix} 1.26 & -0.55 & -104 \\ -0.42 & 1.32 & 60 \\ -0.00013 & 0.00004 & 0.07 \end{pmatrix} \times 10^{-5} \text{ cm}^2 \text{ s}^{-1}$$

A related system,¹¹¹ which illustrates the strong dependence of the cross-diffusion coefficients on the polymer charge, consists of KH₂citrate($c_1 = 0.1$ M)–K₂Hcitrate($c_2 = 0.1$ M)–BSA($c_3 = 0.1$ mM). The isoelectric point for BSA is \sim pH 5.4.¹¹² At 25 °C and pH 4.5, where BSA has an average charge of +40

$$\mathbf{D} = \begin{pmatrix} 0.66 & 0.08 & -12 \\ 0.07 & 0.81 & 11 \\ -0.00002 & 0 & 0.061 \end{pmatrix} \times 10^{-5} \text{ cm}^2 \text{ s}^{-1}$$

while at pH 5.9, where the BSA charge is negative,

$$\mathbf{D} = \begin{pmatrix} 0.67 & 0.06 & 36 \\ 0.14 & 0.87 & -23 \\ 0.00006 & 0.0001 & 0.064 \end{pmatrix} \times 10^{-5} \text{ cm}^2 \text{ s}^{-1}$$

Note the change in sign of the elements D_{i3} .

Leaist and Hao¹¹¹ develop a simple procedure to estimate the multicomponent Fick diffusion coefficients (D_{ik}) from the diffusion coefficients D_s of the species that appear in the Nernst-Planck equation¹¹³

$$j_s = -D_s \partial c_s / \partial x + (F/RT) D_s c_s z_s E \quad (25)$$

where j_s is the molar flux of species s in the x -direction, and D_s , c_s , and z_s are the diffusion coefficient, concentration and charge of that species; F is the Faraday constant, R the gas constant and T the temperature. The diffusion of the ionic species is coupled to the electric field E , which slows down the more mobile ions and speeds up the slower ones, so that all parts of the solution remain electrically neutral. Linking the two sets of equations, Fick and Nernst-Planck, allows the better features of both treatments to be exploited.

Micelle-salt. A large negative cross diffusion coefficient was found in a micelle system with salt: DSDMAOH (distearyldimethylammonium hydroxide) (c_1)-NaCl (c_2) at pH 7.5 with $c_1 = 40$ mM, and $c_2 = 5$ mM or 15 mM.²⁷

$$\mathbf{D} = \begin{pmatrix} 0.349 & 0.006 \\ -7.2 & 1.5 \end{pmatrix} \quad (c_2 = 5 \text{ mM}),$$

$$\mathbf{D} = \begin{pmatrix} 0.349 & 0.014 \\ -2.5 & 1.54 \end{pmatrix} \quad (c_2 = 15 \text{ mM})$$

in units of $10^{-5} \text{ cm}^2 \text{ s}^{-1}$

Another experiment with a micelle-salt system, SDS (sodium dodecyl sulfate) ($c_1 = 0.1$ M)-NaCl ($c_2 = 0.1$ M)¹¹⁴ gives negative D_{12} .

Polymer-micelle. Large positive cross-diffusion coefficients were observed in a mixture of aqueous solutions of the polymer PEG3400 [poly(ethyleneglycol) with average molecular weight 3400 g mol^{-1}] (c_1) with micelles of SDS (c_2).⁴³ For example, at $c_1 = 0.00296$ M and $c_2 = 0.2501$ M, the following coefficients (in units of $10^{-5} \text{ cm}^2 \text{ s}^{-1}$) were obtained

$$\mathbf{D} = \begin{pmatrix} 0.17 & 0.01 \\ 5.87 & 0.74 \end{pmatrix}$$

The large coefficient D_{21} is almost linearly proportional to c_2 . Analogous results (large positive D_{21}) were obtained with aqueous solutions of poly(vinylpyrrolidone) (PVP, 24000 g mol^{-1}) and sodium octyl sulfonate.¹¹⁵ The large cross-diffusion ($D_{21} \gg D_{22}, D_{11}$) was interpreted as a result of electrostatic coupling, which prevents ionic species from moving independently due to electroneutrality.

Reverse micelles. Very large positive and negative cross-diffusion coefficients have been found in three-component water-in-oil AOT microemulsions consisting of water(1)-AOT(2)-heptane^{28,116,117} and water(1)-AOT(2)-octane, and in the analogous four-component systems water(1)-AOT(2)-ferroin(3)-octane and water(1)-AOT(2)-malonic acid(3)-octane.⁹³ The large positive D_{12} grows almost linearly with the radius of the

water nanodroplets, which is proportional to the ratio $\omega = c_1/c_2$, and can be approximately expressed as^{28,116}

$$D_{kl} = c_k (\partial D_k^* / \partial c_l), \quad (l \neq k) \quad (26)$$

where D_k^* is the intradiffusion coefficient, approximately equal in this case to the diffusion coefficient D_d of an entire droplet, and consequently all D_k^* are equal.

The quaternary diffusion coefficients (in $10^{-6} \text{ cm}^2 \text{ s}^{-1}$) for the water(1)/AOT(2)/MA(3)/octane system at $\omega = 11.84$, $\varphi_d = 0.18$, $[\text{MA}] = 0.032$ M, and $T = 23$ °C are⁹³

$$\mathbf{D} = \begin{pmatrix} 0.57 & 6 & 8 \\ -0.012 & 1.6 & 1.8 \\ -0.0006 & -0.08 & 0.56 \end{pmatrix}$$

In the water(1)-AOT(2)-ferroin(3)-octane system at $\omega = 11.84$, $\varphi_d = 0.18$, $[\text{ferroin}] = 1.61 \times 10^{-5}$ M, and $T = 23$ °C⁹³

$$\mathbf{D} = \begin{pmatrix} 0.5 & 5.2 & -45 \\ -0.012 & 1.2 & -12 \\ 0.00022 & 0.0032 & 0.4 \end{pmatrix} \times 10^{-6} \text{ cm}^2 \text{ s}^{-1}$$

The change in sign of the coefficients D_{13} and D_{23} when MA is replaced by ferroin can be explained by combining eqn (26) with data from dynamic light scattering experiments that reveal that the radius of water nanodroplets decreases slightly if we add MA and increases (because of cluster formation) if we add ferroin to pure reverse micelles. These changes in the radius and corresponding changes in the diffusion coefficients of the droplets (D_k^*) result in $\partial D_k^* / \partial c_l$ being positive for MA and negative for ferroin, yielding the observed signs of D_{i3} .

Cross-diffusion on surfaces and in porous materials

There is no direct method to measure cross-diffusion coefficients on surfaces, where many patterns in reaction-diffusion systems have been found.¹¹⁸⁻¹²⁴ Experimental results on cross-diffusion in porous materials or in gels are scarce. For example, Sasaki and Maeda found that cross-diffusion between NaNO_3 (1) and NaCl (2) in porous silica spheres was quite small: $D_{21} = 0$ and $D_{12}/D_{22} = -0.022$. The negative D_{12} was attributed to electrostatic effects (Nernst-Hartley equation). In general, all diffusion coefficients in a porous material are smaller than in the corresponding aqueous solution. There are several studies of self-diffusion coefficients in gels using pulsed NMR. Some of them, for example the diffusion of SDS in a cross-linked gel of ethyl(hydroxyethyl) cellulose, reveal anomalous (non-Gaussian) diffusion, probably due to inhomogeneities in the gel.¹²⁶ There is also considerable evidence that the pore size has a significant effect on diffusion coefficients.^{125,127-129}

Theoretical considerations suggest that there should be large cross-diffusion coefficients as a result of excluded volume effects. For example, if we have two species A and B adsorbed on a surface and the coverage (fraction of the surface occupied) by A, ϕ_A , is significant, it is clear that the diffusion of B must decrease with ϕ_A . An analogous situation must occur in porous materials, for example in the case when the size of the larger species is close to the diameter of the pores. Blocking of the pores by the larger particles will hinder the diffusion of the smaller ones. This effect was recently demonstrated by Shaw *et al.*¹³⁰ in experiments and simulations with a mixture of small

and large spherical particles in a chamber divided by a membrane with asymmetric pores.

Recently, Stojanovic and coworkers have shown that complex molecules containing ribozymes can diffuse along a path covered with immobilized oligonucleotide substrates.¹³¹ These “walkers” do a remarkable job of “keeping to the path” as a result of cross-diffusion due to transient formation of a substrate–enzyme complex.

3. Cross-diffusion in reaction–diffusion systems

A number of theoretical papers discuss pattern formation in reaction–diffusion (RD) systems with cross-diffusion.^{132–142} Almost all these works include nonlinear kinetic terms describing autocatalysis and/or negative feedback in their models. A single study finds that with appropriate cross-diffusion coefficients, linear reaction terms are sufficient to produce pattern formation.¹⁴³ Before analyzing the role of cross-diffusion in actual RD systems, we consider several examples of related systems that can be described by analogous models.

3A “Cross-diffusion” in living systems: chemotaxis and ecology

While the notion that the spatial distribution of one species may affect the motion of other species may seem less than intuitive in chemical systems, such behaviour would appear to be the norm in living systems. Phenomena of this type have been more thoroughly studied in the biological than in the chemical literature, and we mention here a few examples.

Chemotaxis, the phenomenon in which cells direct their motion toward or away from higher concentrations of chemical species, sometimes referred to as chemoattractants or chemorepellants, is perhaps the clearest example of “cross-diffusion” in biology. Bacteria like *E. coli* alternately swim in straight lines and “tumble,” changing their direction in preparation for their next straight-line excursion. The motion resembles a diffusive random walk, and in the absence of chemical gradients, a bacterium obeys the same laws as a diffusing particle. The mechanism of tumbling involves a change in the direction of rotation of the bacterial flagella. When gradients of attractants or repellants are present, the bacterium adjusts its frequency of tumbling, changing direction less often if it senses that it is swimming toward higher attractant or lower repellant concentrations.¹⁴⁴ The result is a net motion, chemotaxis, up a gradient of attractant, for example. Viewed as a form of cross-diffusion, the phenomenon is characterized by a negative $D_{\text{bacterium–attractant}}$ and a positive $D_{\text{bacterium–repellant}}$. Chemotaxis of *E. coli* gives rise to striking patterns like the ones shown in Fig. 3.³² A number of models have been developed and analyzed that describe chemotaxis in terms of diffusion, including cross-diffusion, of cells and chemoattractants.^{145,146}

Ecology provides many examples of pattern formation arising from the motion of one species in response to gradients in the abundance of other species. Meron and coworkers^{147–150} have modeled the development of vegetation patterns in water-limited regions by taking into account cross-diffusive

terms between the biomass density and the groundwater density, where water plays the role of a “chemoattractant” for plants.

As a final example, we observe that predator–prey systems, the inspiration for Lotka’s early model¹⁵¹ of autocatalysis and chemical oscillation, are naturally described in terms of cross-diffusion. Clearly, predators will tend to gravitate toward higher concentrations of prey, while prey will preferentially move toward regions where predators are rare. Models of predator–prey systems with cross-diffusion have been extensively analyzed in the literature, though often with respect to their mathematical properties rather than to provide insight into the kinds of patterns that can emerge.

del-Castillo-Negrete *et al.*^{135,152} examined a two-variable model with cross-diffusion relevant to both plasma physics and predator–prey population dynamics,

$$\partial \varepsilon / \partial t = \varepsilon - \varepsilon^2 - \sigma^2 \varepsilon + \nabla \cdot (d + D\varepsilon) \nabla \varepsilon \quad (27)$$

$$\partial \sigma / \partial t = -\mu \sigma + \alpha \sigma \varepsilon + \nabla \cdot (d + D\varepsilon) \nabla \sigma + \nabla D \sigma \nabla \varepsilon \quad (28)$$

They showed that positive cross-diffusion ($D > 0$) induces instability in one of four homogeneous steady states and can give rise to front propagation between two of the steady states. Two fronts can collide to produce a stationary kink-state. Segregated states, the analog of Turing patterns in chemical systems, were also obtained in this model due to cross-diffusion.

3B “Cross-diffusion” in social systems

Certain interactions between human beings also appear to be determined by behaviours that resemble cross-diffusion. People may prefer to live, for example, near others of the same ethnic group or social class or to avoid members of certain groups. The phenomenon of “white flight,” in which members of the white middle or working classes moved away from

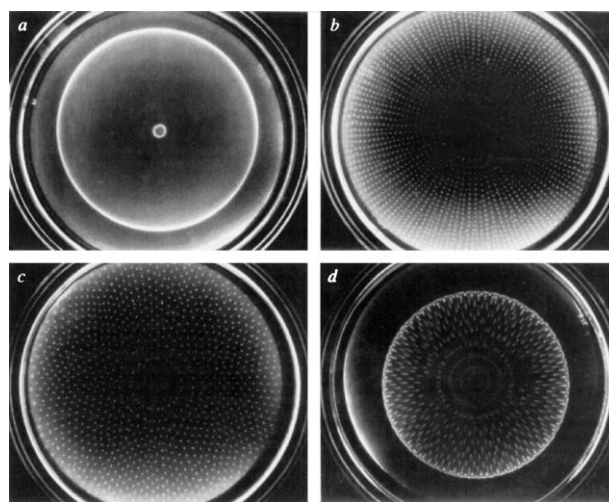


Fig. 3 Patterns generated by chemotactic *E. coli* bacteria in the presence of succinate, a chemoattractant. (a) swarm ring in 1 mM succinate; (b) spots on a pseudo-rectangular lattice in 2 mM succinate; (c) spots on a pseudo-hexagonal lattice in 3 mM succinate; (d) spots with tails on a pseudo-hexagonal lattice in 3 mM succinate with a mutant strain. From ref. 32.

neighborhoods that became racially desegregated in the United States after World War II, causing resegregation, is one example of such behaviour.

Epstein¹⁵³ has examined the illicit drug trade by introducing cross-diffusion terms into a standard model from epidemiology. Defining S as “susceptibles” (ordinary citizens), I as “infectives” (drug users/dealers) and L as law enforcement personnel, he describes the evolution of these three subgroups on a one-dimensional “street” by the set of equations

$$\partial S/\partial t = -\beta SI + \mu S + D_{SS} \partial^2 S/\partial x^2 \quad (29)$$

$$\begin{aligned} \partial I/\partial t = \beta SI - \gamma IL + D_{IS} \partial^2 S/\partial x^2 + D_{IL} \partial^2 L/\partial x^2 \\ + D_{II} \partial^2 I/\partial x^2 \end{aligned} \quad (30)$$

$$\partial L/\partial t = \xi SIL - bL + D_{LI} \partial^2 I/\partial x^2 + D_{LL} \partial^2 L/\partial x^2 \quad (31)$$

D_{IS} and D_{LI} are taken to be negative to capture the fact that infectives gravitate toward susceptibles and police move toward higher concentrations of law-breakers, while D_{IL} is positive, meaning that criminals seek to avoid law enforcement personnel. The model, dubbed “crimo-taxis” by its creator, predicts various kinds of pattern formation, with potential implications for policy makers.

3C Cross-diffusion in physicochemical systems

There are at least three classes of patterns found in physicochemical RD systems that may arise from cross-diffusion. The first group involves phase-separating mixtures of two polymers A and B with which undergo a photoinduced reversible reaction between them.^{154–162} Since phase separation shares key characteristics with cross-diffusion, we will examine these experiments below when we analyze patterns in simple systems.

The second category consists of patterns found in catalytic surface reactions.^{163–169} In general, the competition of species for adsorbed surface sites gives rise to cross-diffusion effects, which have been largely neglected in the literature to date. More specifically, adsorption of non-reactive potassium atoms on a catalytic Rh(110) surface promotes Turing-like patterns in the reaction between adsorbed O₂ and H₂.¹⁶³ Though the authors do not invoke cross-diffusion to explain their patterns, it seems likely that cross-diffusion due to excluded volume effects and/or interactions between K and O atoms plays a major role in generating these patterns. This effect of nonreactive potassium atoms provides an experimental example of the idea we introduce later that nonreactive species can affect the diffusion fluxes of reactive species through cross-diffusion, thereby inducing Turing or wave instabilities.

The third group of patterns occurs in the BZ-AOT system.^{170–172} We recently found that cross-diffusion in BZ-AOT microemulsions is quite significant and may therefore be responsible for many of the wealth of patterns observed in this system.⁹³ A sampling of BZ-AOT patterns is shown in Fig. 4, where we have grouped the most important classes of patterns: wave patterns (upper row and right column), Turing patterns (three left snapshots in the second row), patterns

originating from a wave instability (third row), and localized patterns (three left snapshots in the last row). We will use models of the BZ-AOT system when we analyze the possible role of cross-diffusion in pattern formation in the following sections.

4. Theoretical analysis of cross-diffusion with reactions

We consider a general RD model with the following structure

$$\begin{pmatrix} \partial c_1/\partial t \\ \dots \\ \partial c_n/\partial t \\ \partial s_{n+1}/\partial t \\ \partial s_{n+2}/\partial t \end{pmatrix} = \begin{pmatrix} R_1(c_1, c_2, \dots, c_n) \\ \dots \\ R_n(c_1, c_2, \dots, c_n) \\ 0 \\ 0 \end{pmatrix} + (\nabla) \begin{pmatrix} D_{11} & \dots & D_{1n} & D_{1(n+1)} & D_{1(n+2)} \\ \dots & \dots & \dots & \dots & \dots \\ D_{n1} & \dots & D_{nn} & D_{n(n+1)} & D_{n(n+2)} \\ D_{(n+1)1} & \dots & D_{(n+1)n} & D_{(n+1)(n+1)} & D_{(n+1)(n+2)} \\ D_{(n+2)1} & \dots & D_{(n+2)n} & D_{(n+2)(n+1)} & D_{(n+2)(n+2)} \end{pmatrix} \begin{pmatrix} \nabla c_1 \\ \dots \\ \nabla c_n \\ \nabla s_1 \\ \nabla s_2 \end{pmatrix} \quad (32)$$

which is an extended form of eqn (3). The concentrations c_i and s_{n+j} denote reactive and nonreactive species, respectively. All elements of the matrix \mathbf{D} may depend on the c_i and the s_{n+j} and on the reaction rate constants included in the reaction terms R_i . The dependence of the off-diagonal elements D_{ij} on concentrations was discussed in section 2. In particular, if c_i tends to 0, then $D_{ij} \rightarrow 0$, since there cannot be a flux of species i if $c_i = 0$ regardless of the gradient of species j . Often, D_{ij} depends linearly, or nearly linearly, on c_i .

The notion that D_{ij} may depend on the rate constants is not intuitively obvious, but it does follow from thermodynamic considerations about the chemical potential and the chemical affinity \mathcal{A} .^{86,173} As was shown by Lefever *et al.*,¹⁷³ the Duhem–Jouget theorem implies that \mathcal{A} determines both the diffusion flux and the chemical reaction rate, so that these quantities cannot be independent of each other. We show in the next section that if we assume that D_{ij} and the rate constants k_i in the reversible reaction (33)



can be set independently, then an apparent violation of the second law of thermodynamics can occur. It was also shown theoretically, using a stochastic model of a reactive Lorentz gas, that reaction (33) with a catalyst can induce cross-diffusion between species A and B.¹⁷⁴ This result characterizes exactly how a chemical reaction can affect cross-diffusion. Note that eqn (1) demonstrates the opposite effect, *i.e.*, how diffusion affects rate constants.

4A Simple linear systems

Consider eqn (32) in its simplest form obtained from reaction (33) with rate constants k_1 and k_2 for the forward and reverse reactions, respectively. The matrix \mathbf{D} of

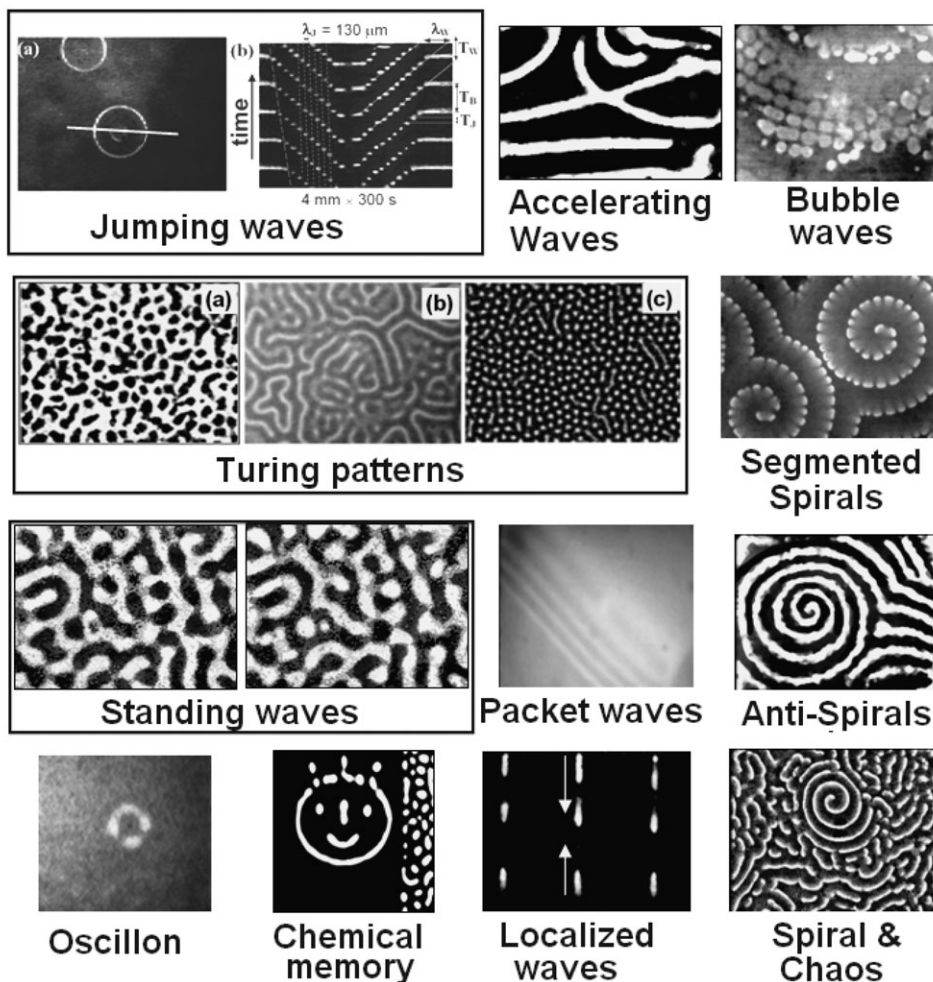


Fig. 4 Several types of patterns found in the BZ-AOT system. Jumping waves are shown as a snapshot (a) and a space-time plot (b) across the white line shown in (a). Turing patterns are represented by three different types of structures: “black spots”, “labyrinth”, and “white spots”. Standing waves are exhibited as two *anti*-phase snapshots. Localized structures are “oscillon”, “chemical memory”, and “localized waves” (arrows show direction of wave propagation).

diffusion coefficients has elements D_{ij} , where 1 corresponds to A and 2 to B. No nonreactive species are present. First, suppose that $k_1 = k_2 = 0$. If we apply a small δ -function perturbation of A at $x = x_0$ in a system with one spatial dimension (1D), then the root mean square displacement of A, $\langle x_A^2 \rangle^{1/2}$ with $D_{12} = D_{21} = 0$ is determined by

$$\langle x_A^2 \rangle = \int_{-\infty}^{\infty} (x - x_0)^2 \frac{1}{2\sqrt{\pi D_{11} t}} \exp\left(-\frac{(x - x_0)^2}{4D_{11} t}\right) dx = 2D_{11} t \quad (34)$$

There is no displacement of B, $\langle x_B^2 \rangle = 0$.

If we allow D_{12} and/or D_{21} to be non-zero, then the solution of the coupled diffusion equations

$$\frac{\partial c_1}{\partial t} = D_{11} \frac{\partial^2 c_1}{\partial x^2} + D_{12} \frac{\partial^2 c_2}{\partial x^2} \quad (35)$$

$$\frac{\partial c_2}{\partial t} = D_{21} \frac{\partial^2 c_1}{\partial x^2} + D_{22} \frac{\partial^2 c_2}{\partial x^2} \quad (36)$$

is⁹³

$$c_1 = A_{11}G_1 + A_{12}G_2 \quad (37)$$

$$c_2 = A_{21}G_1 + A_{22}G_2 \quad (38)$$

where

$$G_i = \frac{1}{2\sqrt{\pi\sigma_i t}} \exp\left(-\frac{(x_0 - x)^2}{4\sigma_i t}\right) \quad (39)$$

σ_1 and σ_2 are the eigenvalues of the matrix \mathbf{D} and

$$A_{11} = [P_1(D_{11} - \sigma_2) + P_2D_{12}]/(\sigma_1 - \sigma_2) \quad (40)$$

$$A_{12} = [P_1(\sigma_1 - D_{11}) - P_2D_{12}]/(\sigma_1 - \sigma_2) \quad (41)$$

$$A_{21} = [P_2(\sigma_2 - D_{22}) - P_1D_{21}]/(\sigma_2 - \sigma_1) \quad (42)$$

$$A_{22} = [P_2(D_{22} - \sigma_1) + P_1D_{21}]/(\sigma_2 - \sigma_1) \quad (43)$$

with initial conditions (at $t = 0$ and $x = x_0$) $A_{11} + A_{12} = P_1$ and $A_{21} + A_{22} = P_2$. Consider the case of $P_2 = 0$, *i.e.*,

a δ -function perturbation of A. The mean square displacements of A ($=c_1$) and B ($=c_2$) are now given by

$$\langle x_A^2 \rangle = \int_{-\infty}^{\infty} (x - x_0)^2 (A_{11}G_1 + A_{12}G_2) dx = 2P_1D_{11}t \quad (44)$$

$$\langle x_B^2 \rangle = \int_{-\infty}^{\infty} (x - x_0)^2 (A_{21}G_1 + A_{22}G_2) dx = 2P_1D_{21}t \quad (45)$$

We see that species B has a displacement proportional to $D_{21}^{1/2}$, while the displacement of A is the same as in the previous case without cross-diffusion (for $P_1 = 1$). Thus, if $P_2 = 0$, then the presence of species B does not affect the diffusion of species A even at non-zero D_{12} .

Consider another limiting case with $D_{12} = 0$, $D_{21} \neq 0$, and arbitrary initial perturbations P_1 and P_2 . Then $\sigma_1 = D_{11}$, $\sigma_2 = D_{22}$, and eqn (40)–(43) give $A_{11} = P_1$, $A_{12} = 0$, $A_{21} = -P_1D_{21}/(D_{22} - D_{11})$, and $A_{22} = P_2 - A_{21}$. The mean square displacements of A and B are then given by

$$\langle x_A^2 \rangle = 2P_1D_{11}t \quad (46)$$

$$\langle x_B^2 \rangle = 2(P_1D_{21} + P_2D_{22})t \quad (47)$$

We see that species B again does not affect species A, now because $D_{12} = 0$. The displacement of B now depends on the sum ($P_1D_{21} + P_2D_{22}$). These simple examples are meant to give some intuitive feeling about the properties of cross-diffusion.

We next introduce rate constants k_1 and k_2 and consider a δ -function perturbation (at $x = x_0$) of the equilibrium steady state ($a_{ss}k_1 = b_{ss}k_2$); for simplicity, we apply an ‘‘equilibrium’’ perturbation, *i.e.*, $P_1k_1 = P_2k_2$. We can calculate the mean square displacements $\langle x_A^2 \rangle$ and $\langle x_B^2 \rangle$ as a function of t to extract the effective diffusion coefficients, $D_A = \langle x_A^2 \rangle / (2P_1t)$ and $D_B = \langle x_B^2 \rangle / (2P_2t)$. For small t , *i.e.*, when $t \ll 1/\max(k_1, k_2)$, the diffusion process proceeds essentially as in the case $k_1 = k_2 = 0$. For large t , however, when $t \gg 1/\min(k_1, k_2)$, the situation is quite different. The effective diffusion coefficients are equal to each other and given by:

$$D^* = D_A = D_B = (D_{21}k_2 + D_{12}k_1 + D_{11}k_2 + D_{22}k_1) / (k_1 + k_2) \quad (48)$$

Note that this result is independent of the type of δ -function perturbation (‘‘equilibrium’’ or not), since at large t equilibrium is established. If D_{12} or D_{21} is negative and $D_{12}/D_{22} < -1$ or $D_{21}/D_{11} < -1$, D^* crosses zero and becomes negative with increasing k_1 or k_2 , respectively. The condition

$$D_k \equiv D_{21}k_2 + D_{12}k_1 + D_{11}k_2 + D_{22}k_1 = 0 \quad (49)$$

marks the onset of Turing instability. Physically, condition (49) can be interpreted as follows. Suppose we start with small perturbation in B and $D_{21} = 0$ (for simplicity), then B tends to diffuse away at a rate that depends on D_{22} , but because $D_{12} < 0$, the perturbation in B also induces a flux of A directed toward the perturbation. If k_1 is large enough and $-D_{12} > D_{22}$ [condition (49) is fulfilled], this incoming A will be converted to B so rapidly that it will negate the outgoing flux of B, and there will be no net diffusion of B away from the perturbation. However D_k cannot be negative, since Turing patterns would then emerge in the closed equilibrium system (33), which is forbidden by

thermodynamics. Condition (49) thus implies that there must be some co-dependence between the diffusion and reaction rate constants for reaction (33). For example, at large k_1 (k_2), D_{22} (D_{11}) must be larger than $-D_{12}$ ($-D_{21}$).

Condition (49) can also be obtained from a linear stability analysis of the system (50)–(51).

$$\partial a / \partial t = -k_1 a + k_2 b + D_{11} \nabla^2 a + \text{div}(D_{12} \nabla b) \quad (50)$$

$$\partial b / \partial t = k_1 a - k_2 b + \text{div}(D_{21} \nabla a) + D_{22} \nabla^2 b \quad (51)$$

where $a = [A]$ and $b = [B]$. To carry out the linear stability analysis, we must, in general, take into account the dependence of the cross-diffusion coefficients on a and b . For example,

$$\text{div}(D_{12} \nabla b) = D_{12} \nabla^2 b + (dD_{12}/da) \nabla a \nabla b \quad (52)$$

However, the last term in eqn (52) does not contribute to the linearized equations. Therefore the characteristic matrix $\mathbf{M} = \mathbf{J} - k^2 \mathbf{D}$ (where \mathbf{J} is the Jacobian for the linearized system, \mathbf{D} is the diffusion matrix, and k is the wavenumber) has the form

$$\mathbf{M} = \begin{pmatrix} -k_1 - k^2 D_{11} & k_2 - k^2 D_{12} \\ k_1 - k^2 D_{21} & -k_2 - k^2 D_{22} \end{pmatrix} \quad (53)$$

Turing instability for system (50), (51) occurs if¹⁷⁵

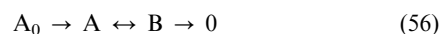
$$\det(\mathbf{M}) < 0 \quad (54)$$

The inequality (54) can be rewritten as:

$$\det(\mathbf{M}) = \det(\mathbf{D})(k^2)^2 + (D_{21}k_2 + D_{12}k_1 + D_{11}k_2 + D_{22}k_1)k^2 + \det(\mathbf{J}) < 0 \quad (55)$$

Since $\det(\mathbf{J}) = 0$ in this case, and $\det(\mathbf{D})$ is always positive, then Turing instability requires $D_k < 0$ (*cf.* eqn (49)).

Note that in open linear systems like



considered by Almirantis and Papageorgiou,¹⁴³ Turing patterns are also impossible, since the parametric region for the required cross-diffusion coefficients is even narrower than that for the corresponding closed system (33) with the same constants k_1 , k_2 , D_{11} , and D_{22} . Indeed, due to the reaction $B \rightarrow 0$ (with rate constant k_0), $\det(\mathbf{J})$ is positive for system (56); and the condition for Turing instability now reads

$$D_{21}k_2 + D_{12}k_1 + D_{11}(k_2 + k_0) + D_{22}k_1 < -2[\det(\mathbf{D})\det(\mathbf{J})]^{1/2} < 0 \quad (57)$$

Comparing (57) to our earlier result (49) without the step $B \rightarrow 0$

$$D_{21}k_2 + D_{12}k_1 + D_{11}k_2 + D_{22}k_1 < 0 \quad (58)$$

we see that D_{12} or D_{21} for system (56) must be even more negative than for system (33) for Turing patterns to occur. So, if Turing patterns can occur in system (56), then they can occur in the closed equilibrium system (33), which would contradict the second law of thermodynamics. Thus, the rate and diffusion coefficients cannot be arbitrarily chosen independently of one another; there must be some co-dependence.

Tran-Cong and collaborators have found Turing patterns experimentally in a system that can be described by eqn (33), where A and B are polymers that can phase separate and can also undergo a reversible photoinduced interconversion.^{159,160,176–178} Phase separation in binary mixtures is related to cross-diffusion in that A molecules tend to diffuse toward A molecules and B toward B (clustering), and clusters A_n diffuse toward regions with lower concentrations of clusters B_n and *vice versa*. Though system (33) is not completely equivalent to a phase-separating system, we can expect Turing patterns in system (33) with appropriate cross-diffusion coefficients when the rate constant k_1 (or k_2) is a function of the light intensity. Note that the system (33) is now an open system with an influx of energy, so no contradiction of thermodynamics is implied.

Consider now what induces the autocatalytic growth of small perturbations in our linear system (33) if $D_k < 0$ (*cf.* eqn (49)). For simplicity, suppose that $-D_{12} > D_{11}k_2/k_1 + D_{22}$ (condition 49 with $D_{21} = 0$). The result of a small perturbation of b_{ss} at $x = x_0$ is plotted as curve “b” in Fig. 5a. Due to the negative cross-diffusion coefficient D_{12} , a flux of species a , $D_{12}\partial b/\partial x$, is directed toward the center of perturbation (horizontal arrow in Fig. 5a) and creates there an excess of a at the expense of a in more remote areas (curve “a”). Since a increases in the center, further increase in b due to the photoinduced reaction $A \rightarrow B$ (term k_1a and vertical arrow in Fig. 5a) occurs. This is a positive feedback loop, which we might call *cross-spatio-chemical autocatalysis*.

The conditions for Turing instability simply imply that the homogeneous steady state is unstable, but say nothing about the state that will eventually emerge. To stabilize an inhomogeneous (Turing) pattern, the system (50), (51) must have one or more nonlinear terms that terminate the exponential growth, $\exp(\text{Re}(\lambda)_{\max} t)$, of the initial small perturbation, where $\text{Re}(\lambda)$ has a positive maximum, $\text{Re}(\lambda)_{\max}$, at wavenumber $k = k_{\max}$. Unlike classical Turing systems, however, our linear reaction system does not contain such chemical nonlinear terms as, for example, $-b^2$. If the cross-diffusion terms (D_{12} and D_{21}) were constants, then the maximum and minimum values of a (or b)

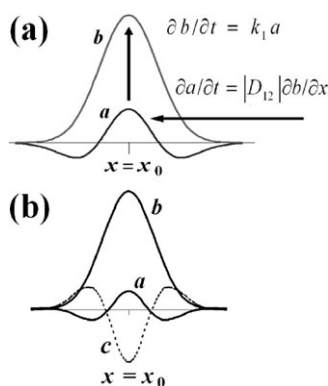


Fig. 5 (a) Schematic explanation of autocatalysis in linear reaction (33). (b) Profiles of species A (curve a), B (b), and C (c) after initial perturbation of B (δ -function at $x = x_0$) without any reaction between A, B, and C. Horizontal axis denotes homogeneous steady state levels for all species. Diffusion coefficients: $D_{12} = D_{21} = D_{31} = D_{23} = 0$, $D_{11} = 1$, $D_{22} = 0.3$, $D_{33} = 0.2$, $D_{32} = 0.2$, and $D_{13} = 0.4$, time $t = 0.3$.

would approach $+\infty$ and $-\infty$, respectively. However, the dependences of D_{12} and D_{21} on a and b , respectively, serve as a brake on the potentially infinite growth of a and b , or, more precisely, these dependences prevent a and b from becoming negative. Indeed, at sufficiently small values of a and b , D_{12} and D_{21} tend to zero, and the condition for Turing instability can no longer be satisfied. Since our system conserves mass, $\int_V a + \int_V b = \text{constant}$ (the subscript V signifies integration over the total volume of the system), *i.e.*, the diffusive terms just redistribute concentrations but cannot change the total amount of matter, the limitation on concentration decrease implies a limitation on growth.

4B Nonreactive species

Consider now the effect of nonreactive species in eqn (32). As the simplest case, we consider the photo-induced reaction (33) and add a nonreactive species C. We know that a sufficiently large negative cross-diffusion coefficient D_{12} can induce Turing instability in reaction (33). But suppose instead that $D_{12} = D_{21} = 0$, *i.e.*, there is no cross-diffusion in the reactive subsystem (A, B). Is it possible to mimic the needed coefficient D_{12} by introducing cross-fluxes between A and C and between B and C? We answer this question in the affirmative by taking a hint from Fig. 5a. We seek cross-diffusion coefficients D_{13} , D_{23} , D_{31} , and D_{32} (where the index 3 corresponds to C) to create a profile of species a analogous to that in Fig. 5a. This task can be accomplished by using the analytical solution of the diffusion equations for three variables (equations and solutions analogous to eqn (35)–(43)).⁹³ Avoiding these cumbersome equations, we first give a qualitative solution of the diffusion equations and then perform linear stability analysis and numerical solution of the corresponding RD system.

A negative coefficient D_{12} would imply that a gradient in B creates a counter-flux of A. Alternatively, if B produces a counter-flux of C (negative D_{32}) and in turn C generates a counter-flux of A (negative D_{13}), the net result should be equivalent to having a negative D_{12} . The same result is obtained if both D_{32} and D_{13} are positive. In Fig. 5b we show this situation schematically for species A, B and C without any reaction. Comparing the profiles of a in Fig. 5a and b, we see that they are similar. Note that a positive coefficient D_{ij} ($i, j = 1, 2, i \neq j$) can be replaced by a combination of positive and negative coefficients D_{kj} and D_{ik} ($k = 3$ for three variables); it does not matter which coefficient is chosen as positive and which as negative.

Consider now the same system more quantitatively by writing the following equations.

$$\partial a/\partial t = -k_1a + k_2b + D_{11}\nabla^2a + \text{div}(D_{AC}\nabla c) \quad (59)$$

$$\partial b/\partial t = k_1a - k_2b + D_{22}\nabla^2b + \text{div}(D_{BC}\nabla c) \quad (60)$$

$$\partial c/\partial t = \text{div}(D_{CA}\nabla a) + \text{div}(D_{CB}\nabla b) + D_{33}\nabla^2c \quad (61)$$

where we specify the concentration dependence of the cross-diffusion coefficients as $D_{AC} = D_{13}a/(a + K_A)$, $D_{BC} = D_{23}b/(b + K_B)$, $D_{CB} = D_{32}c/(c + K_C)$, $D_{CA} = 0$. In Fig. 6 we show the dispersion curves obtained from linear stability analysis of eqn (59)–(61) and the stationary Turing patterns found numerically in 1D for this system. The nonreactive

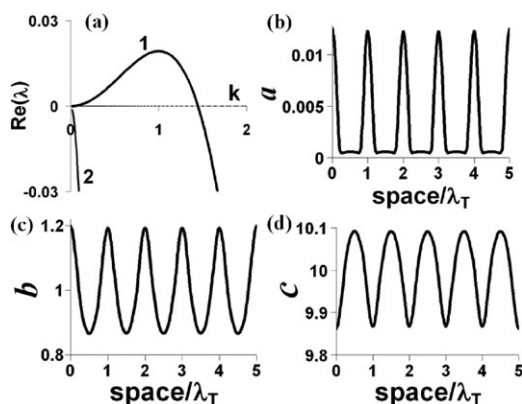


Fig. 6 Dispersion curves and Turing patterns in model eqn (59)–(61). Parameters: $k_1 = 30$, $k_2 = 0.1$, $D_{11} = 2.5$, $D_{22} = 2.5$, $D_{33} = 1$, $D_{12} = D_{21} = D_{31} = 0$, $D_{13} = 1.45$, $D_{23} = 2.7$, $D_{32} = 0.7$, $K_A = 0.0001$, $K_B = 0.1$, $K_C = 0.2$. Turing wavelength $\lambda_T = 6.3$. Curves 1 and 2 in (a) are different real eigenvalues.

variable c (Fig. 6d) becomes spatially periodic like the reactive variables a and b , but 180° out of phase with them in analogy with the initial concentration distribution in Fig. 5b. The average values of all variables are equal to their initial steady state values. In this example we see that the nonreactive species C is an essential ingredient, since without C there are no patterns with $D_{12} = D_{21} = 0$. In a system of this type, sprinkling C into a homogeneous mixture of A and B at equilibrium would result in the formation of Turing patterns.

A similar approach for pattern formation was used in a three-component phase-separating mixture of polymers, $A + B + C$, where the component C is non-reactive.^{162,179,180} However, the notion of cross-diffusion was not explicitly invoked in these works.

4C Bimolecular reaction

Thus far we have considered the role of cross-diffusion only in linear, monomolecular reactions. Consider now the more complex but more common case of bimolecular reactions of the general form



with forward and reverse rate constants k_1 and k_2 , respectively. As we did for reaction (33), we can seek the condition for Turing instability in this equilibrium reaction by applying linear stability analysis. To simplify our investigation and focus on the role of the cross-diffusion coefficients, we introduce just two nonzero cross-diffusion coefficients, D_{12} and D_{13} (where 1, 2, 3, 4 correspond to A, S, B, and P, respectively) between reacting species A and S and between reactant A and product B , since the effect of the other cross-diffusion coefficients can be deduced from an understanding of the role played by these two coefficients.

If only $D_{12} \neq 0$ and all other off-diagonal elements of \mathbf{D} are zero, then linear stability analysis gives the condition for Turing instability as

$$D_{12} > D_{22} + D_{11}[(D_{22}D_{33}/D_{44})k_2b + D_{22}k_2p + D_{33}k_1a]/(D_{33}k_1s) \quad (63)$$

If only $D_{13} \neq 0$, then this condition takes the form

$$-D_{13} > D_{33} + D_{11}[(D_{22}D_{33}/D_{44})k_2b + D_{22}k_2p + D_{33}k_1a]/(D_{22}k_1s) \quad (64)$$

The inequality (64) is similar to the condition (49) obtained for reaction (33) when $D_{21} = 0$:

$$-D_{12} > D_{22} + D_{11}k_2/k_1 \quad (65)$$

Here D_{13} (for reaction 62) is analogous to D_{12} (for reaction 33), D_{33} to D_{22} , k_2b and k_2p to k_2 , and k_1s and k_1a to k_1 .

To obtain Turing patterns in a system described by reaction (62), the coefficient D_{13} must be negative or the coefficient D_{12} positive. Intuitively, positive D_{12} reduces the concentration of S at the site of a positive perturbation of A at $x = x_0$ (opposite of the situation shown in Fig. 5a). This decreases the rate of the forward reaction $A + S$ at $x = x_0$. As a result, a locally increases due to the back reaction $B + P$, the initial positive perturbation δa grows, and we have a positive feedback loop. Similarly, a negative D_{13} implies that a positive perturbation of A draws B toward it, increasing the rate of the back reaction, thereby enhancing the initial perturbation of A . These cross-diffusion-induced effects must exceed the stabilizing effect of the diagonal diffusion terms if instability is to occur.

Again, if neither the forward or the reverse reaction in (62) is photoinduced, then conditions (63) and (64) are cannot hold from a thermodynamic point of view, since Turing patterns could then arise in a closed system. The inequalities (63) and (64) set constraints on the dependence of the mutual diffusion coefficients on the rate constants and equilibrium concentrations for bimolecular reactions. For example, from (63) it follows that at large k_1 , the inequality $D_{12} < D_{22} + D_{11}a/s$ should hold, while at large k_2 , we must have $D_{12} < D_{22} + D_{11}D_{22}(k_2/k_1)(b/D_{44} + p/D_{33})/s$.

If both the coefficients D_{12} and D_{13} for reaction (62) are nonzero, then Turing patterns can occur even if $D_{12} < D_{22}$ and $-D_{13} < D_{33}$. For example, at $k_1 = 10^4 \text{ M}^{-1} \text{ s}^{-1}$, $k_2 = 10^3 \text{ M}^{-1} \text{ s}^{-1}$, $a = 10^{-5} \text{ M}$, $s = 0.1 \text{ M}$, $b = 10^{-4} \text{ M}$, and $p = 0.1 \text{ M}$, a Turing instability exists when

$$(\mathbf{D}) = \begin{pmatrix} 1 & 0.52 & -0.51 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \quad (66)$$

4D Complex systems (with autocatalysis)

At the beginning of section 3, we mentioned several models, typically including autocatalytic reactions or their equivalent, in which introduction of cross-diffusion leads to pattern formation even with equal diagonal elements of the matrix \mathbf{D} .^{132–142} Now we turn to more complex, and chemically realistic, activator–inhibitor systems.

We will look at several models of the well-known Belousov–Zhabotinsky (BZ) oscillatory reaction.^{181,182} Consider first a four-variable model, which is our reduction¹⁸³ of the Field–Körös–Noyes (FKN) model.¹⁸⁴ In the general eqn (32), the four dimensionless reactive species x (1, HBrO_2 , activator),

y (2, Br^- , inhibitor), z (3, oxidized form of the catalyst), and u (4, Br_2) correspond to the following reactive terms:

$$R_1 = (1/\varepsilon_1)(qy - xy + x - x^2) \quad (67)$$

$$R_2 = (1/\varepsilon_2)[-2qy - 3xy + fz - x^2/2 + \alpha u/(y + \gamma)] \quad (68)$$

$$R_3 = x - z \quad (69)$$

$$R_4 = (1/\varepsilon_4)[qy + 2xy + x^2/2 - \alpha u/(y + \gamma)] \quad (70)$$

There are no nonreactive species in this model. All the diagonal elements of the matrix \mathbf{D} are taken to be 1. We search for small cross-diffusion coefficients that strongly affect the stability of the homogeneous steady state [system (67)–(70) has only a single steady state]. Simulations of the BZ reaction typically employ two- or three-variable Oregonator models.¹⁸⁵ We first explore here this four-variable model to demonstrate that other variables, like Br_2 for example, which are usually ignored, can be critical for pattern formation. We find that the system behaviour is quite sensitive to all cross-diffusion coefficients D_{i4} , while all coefficients D_{4j} have negligible effect. *i.e.*, fluxes induced by gradients of bromine are important for pattern formation, while fluxes of bromine induced by gradients of other species are not. For example at the set of parameters ($f = 1.2$, $q = 1 \times 10^{-5}$, $\alpha = 2 \times 10^{-5}$, $\gamma = 0.2$, $\varepsilon_1 = 0.1$, $\varepsilon_2 = 0.004$, $\varepsilon_4 = 10^{-5}$), $D_{14} = -0.000025$ induces Turing instability, $D_{24} = -0.15$ induces wave instability, and $D_{34} = 0.04$ induces both Turing and wave instability, while a negative D_{34} ($D_{34} = -0.001$) induces only wave instability. If we eliminate the fourth variable u from our model, we can seek to capture these effects by incorporating the effects of bromine cross-diffusion into the cross-diffusion coefficients of the remaining variables in the new reduced system. How to do this in a systematic fashion is an open question for the theory of RD systems.

If we are interested in the possibility of dissipative patterns resulting from cross-diffusion in an aqueous BZ solution, it is important to note that negative cross-diffusion coefficients D_{24} between Br_2 and Br^- (due to complex, Br_3^- , formation) as well as between Br_2 and the catalyst $[\text{Ru}(\text{bpy})_3$ or ferriin], D_{34} , can be relatively large at high Br^- or catalyst concentrations, respectively, and at low temperatures.

Consider next the classical three-variable Oregonator model with the chemically reasonable reactions:¹⁸⁵



After rescaling, the reactive terms (1,2,3 = X,Y,Z) are

$$R_1 = (1/\varepsilon_1)(qy - xy + x - x^2) \quad (76)$$

$$R_2 = (1/\varepsilon_2)(-qy - xy + fz) \quad (77)$$

$$R_3 = x - z \quad (78)$$

where $f = 2h$. Again we consider a matrix \mathbf{D} with diagonal elements $D_{ii} = 1$ and search for cross-diffusion coefficients

capable of destabilizing the homogeneous steady state. We find that three cross-diffusion coefficients are important for Turing instability, positive D_{12} and D_{31} , and negative D_{32} (we used $q = 0.002$, $f = 2.5$, $\varepsilon_1 = 0.05$, $\varepsilon_2 = 0.001$, but our conclusions hold for a broad range of other parameter sets). The coefficient D_{12} can originate from reaction (71) or (72), where species X (1) and Y (2) both participate. D_{31} arises from reaction (73), which involves Z and X, and coefficient D_{32} takes its importance from reaction (75).

Recall that positive (negative) cross-diffusion coefficients tend to separate (concentrate) the corresponding species. We know that Y and Z serve as inhibitors, while X is the activator. We note that cross-diffusion processes that separate an activator and an inhibitor (positive D_{12} and D_{31}) or draw together two inhibitors (negative D_{32}) appear to be important. Notice further that, like D_{12} and D_{31} , positive cross-diffusion coefficients D_{21} and D_{13} also separate activator and inhibitor but have little effect; negative D_{23} also has negligible effect on the stability of the steady state. The direction of the chemical reactions: (71) $2 \rightarrow 1$, (73) $1 \rightarrow 3$, and (75) $3 \rightarrow 2$ may explain the difference between the symmetrically related elements of \mathbf{D} ; however, in complex nonlinear systems, such explanations may prove to be illusive.

4E Nonreactive species in complex systems

We now explore briefly the introduction of nonreactive species, described in subsection 4B, to the Oregonator as an example of how addition of a fourth, nonreactive species (reactive term $R_4 = 0$) can mimic important cross-diffusion coefficients. To do this, we set all off-diagonal elements of \mathbf{D} between reactive species to zero and again take all $D_{ii} = 1$. To mimic positive D_{12} and D_{31} and negative D_{32} we test the following pairs of cross-diffusion coefficients between reactive and nonreactive species: D_{42} and D_{14} of opposite sign for positive D_{12} , D_{41} and D_{34} of opposite sign for positive D_{31} , and D_{42} and D_{34} of the same sign for negative D_{32} . In all cases this strategy works quite well, independent of the choice of signs in any pair of cross-diffusion coefficients and even of the values of the individual coefficients. The onset of instability depends only on the *product of coefficients*:

$$D_{42}D_{34} \cong D_{32}^c \quad (79)$$

$$D_{42}D_{14} \cong D_{12}^c \quad (80)$$

$$D_{41}D_{34} \cong D_{31}^c \quad (81)$$

where D_{32}^c , D_{12}^c , and D_{31}^c correspond to the onset of Turing instability in a system without component 4, *i.e.*, system (76)–(78) with a single nonzero cross-diffusion coefficient.

We also find that if we change the sign of one of the cross-diffusion coefficients in the pairs considered above and slightly increase the magnitude of their product, we can obtain wave instability instead of Turing instability. For example, $D_{32} = -0.005$ gives Turing instability for system (76)–(78) (all other cross-diffusion coefficients are 0). At $D_{32} = 0$ and $D_{42} = 0.1$, $D_{34} = 0.05$, we have Turing instability, while at $D_{42} = 0.15$, $D_{34} = -0.2$ (or $D_{42} = -0.15$, $D_{34} = 0.2$), we have wave instability.

If we add a second nonreactive species, more complex combinations of cross-diffusion coefficients can generate instability. Consider, as an example, the two-variable (x and z) Oregonator model¹⁸⁶

$$R_1 = (1/\varepsilon)[x - x^2 - fz(x - q)/(x + q)] \quad (82)$$

$$R_2 = x - z \quad (83)$$

A positive cross-diffusion coefficient D_{21} , which separates activator x and inhibitor z , can induce Turing instability at $D_{11} = D_{22} = 1$ ($q = 0.002, f = 2.5, \varepsilon_1 = 0.05, D_{21}^c = 0.59, D_{12} = 0$). If we add one nonreactive species (3) and set D_{21} to zero, then a combination of coefficients D_{31} and D_{23} with $D_{31}D_{23} = -0.59 = -D_{21}^c$ gives Turing instability. If we add the second nonreactive species, then a combination of D_{31}, D_{43} , and D_{24} such that $D_{31}D_{43}D_{24} = 0.59$ also gives Turing instability. Notice that the product of the three coefficients should be positive. In general, a combination of cross-diffusion coefficients between reactive (i, j) and nonreactive (k, m) species D_{kj}, D_{mk} , and D_{im} can replace the cross-diffusion coefficient D_{ij} between two reactive species i and j , if

$$D_{kj}D_{mk}D_{im} = D_{ij} \quad (84)$$

This result can be extended to larger numbers of nonreactive species, though the likelihood of being able to realize such a system experimentally is small.

Wave instability also can be found in system (82)–(83) with additional nonreactive species ($q = 0.001, f = 2.3, \varepsilon_1 = 0.1, D_{11} = D_{22} = 1, D_{33} = 1.3, D_{44} = 3, D_{13} = -0.1, D_{34} = 13, D_{42} = -60$, other off-diagonal elements of matrix \mathbf{D} are zero). Notice that if we have only reactive species, then wave instability in systems like (2) or (3) requires at least three variables. If additional nonreactive species and cross-diffusion are present, two reactive species are sufficient.

Efforts are currently underway to find species that can be added to the BZ reaction to obtain Turing patterns, standing waves, or other spatiotemporal structures. Researchers have added various surfactants (at levels above the critical micelle concentration) or polymers. What is important to keep in mind in this search that such additives must interact with at least two different species in order to mimic cross-diffusion between them, for example, between the catalyst and Br_2 or between Br^- and HBrO_2 . If the additive interacts only with a single species, cross-diffusion cannot arise. Another strategy, which has not yet been implemented, would be to utilize two additives, each of which interacts with a different BZ species and in turn interact in an appropriate manner with each other, for example *via* excluded volume or electrostatic mechanisms.

5. Conclusion

To date, cross-diffusion has been almost completely ignored in efforts to explain dissipative patterns found in RD systems. Our theoretical analysis shows that this phenomenon has the potential to play an important role in pattern formation, even when the cross-diffusion coefficients are relatively small, if the kinetics are sufficiently nonlinear. At present we know three pattern-forming systems: the CDIMA and FIS reactions, and

the BZ-AOT system, in which stationary patterns have been found, and of course, the BZ reaction itself, where waves are the norm. Recent experiments reveal that cross-diffusion coefficients in the BZ-AOT system are quite significant.⁹³ Therefore cross-diffusion may be an important element in understanding the many types of patterns found in this system. The CDIMA^{5,6} and the FIS¹⁸⁷ reactions probably merit further analysis, since cross-diffusion in these systems can result from electrostatic, excluded volume (diffusion in pores) and complexation effects. Such nonreactive species as starch or polyvinyl alcohol, which are typically added to the CDIMA reaction as indicators, can complex I_3^- and block gel pores to induce cross-diffusion.

We predict that dissipative patterns should occur in photo-induced linear (reversible) reactions with appropriate cross-diffusion coefficients or with additional nonreactive species (like polymers, charged particles or micelles) that can mimic cross-diffusion coefficients between reactive species. The wavelength of these patterns will depend strongly on the rate constants (which can be regulated by the light intensity) and should lie in the range from tens of nanometers to tens of micrometers. This may have practical application.

Further work is needed to elucidate the dependence of cross-diffusion coefficients on concentrations and, especially, on rate constants. As chemists become more aware of the capacity of cross-diffusion to generate patterns, and as they develop better intuition about how such processes occur, they are likely to be able to exploit cross-diffusion as a tool to design systems with desired properties rather than regarding it merely as an exotic phenomenon that cannot be found in textbook treatments of diffusion.

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