

Appendix A, Time-dependent reservoir population

After partitioning the energy space the master equation becomes

$$\frac{d}{dt} \begin{pmatrix} \mathbf{p}^r \\ \mathbf{p}^a \end{pmatrix} = \begin{pmatrix} \mathbf{M}^{rr} & \mathbf{M}^{ra} \\ \mathbf{M}^{ar} & \mathbf{M}^{aa} \end{pmatrix} \begin{pmatrix} \mathbf{p}^r \\ \mathbf{p}^a \end{pmatrix} \quad (79)$$

The population vector of the reservoir states \mathbf{p}^r is approximated by the Boltzmann population (with arbitrary normalization) multiplied by a normalization constant, $x(t)$, proportional to the total time-dependent population of the reservoir, $\mathbf{p}^r = x(t)\mathbf{b}^r$. Hence

$$\frac{dx}{dt}\mathbf{b}^r = x\mathbf{M}^{rr}\mathbf{b}^r + \mathbf{M}^{ra}\mathbf{p}^a \quad (80)$$

$$\frac{d\mathbf{p}^a}{dt} = x\mathbf{M}^{ar}\mathbf{b}^r + \mathbf{M}^{aa}\mathbf{p}^a \quad (81)$$

A set of coupled equations is obtained by summing Eq. (80) over all grains in the reservoir, and making the steady-state approximation for the population of the active space in Eq. (81).

$$\frac{dx}{dt}\|\mathbf{b}^r\| = x\|\mathbf{M}^{rr}\mathbf{b}^r\| + \|\mathbf{M}^{ra}\mathbf{p}^a\| \quad (82)$$

$$0 = x\|\mathbf{M}^{ar}\mathbf{b}^r\| + \|\mathbf{M}^{aa}\mathbf{p}^a\| \quad (83)$$

Eq. (83) is equivalent to Eq. (4), and substituting its formal solution into Eq. (82) yields a first-order rate equation for x .

$$\frac{dx}{dt}\|\mathbf{b}^r\| = x [\|\mathbf{M}^{rr}\mathbf{b}^r\| - \|\mathbf{M}^{ra}(\mathbf{M}^{aa})^{-1}\mathbf{M}^{ar}\mathbf{b}^r\|] \quad (84)$$

This result is very close to that of Eq. (7). To show this, note that the column sums of the matrix \mathbf{M} are equal to $\sum_i M_{ij} = -k_j$, which is zero if grain j is in the reservoir space.

$$\|\mathbf{M}^{rr}\mathbf{b}^r\| = -\|\mathbf{M}^{ar}\mathbf{b}^r\| \quad (85)$$

$$\sum_i \mathbf{M}_{ij}^{ra} = -k_j - \sum_i \mathbf{M}_{ij}^{aa} \quad (86)$$

Substituting these into Eq. (84) gives

$$\frac{dx}{dt}\|\mathbf{b}^r\| = x [\|\mathbf{K}^{aa}(\mathbf{M}^{aa})^{-1}\mathbf{M}^{ar}\mathbf{b}^r\|] \quad (87)$$

a result identical to Eq. (7) apart from the exclusion of the active space population in the normalization, which is negligible under most conditions. Note that this method predicts an exponential decay for the population of the reservoir.

Appendix B, Steady-state diagonal Master Equation for isomerization

The main disadvantage with the steady-state method for isomerization described in the main article subsection is the use of an artificial cut-off to separate the Boltzmann-populated reservoirs and the active spaces, in particular the need to check that the results are not sensitive to this cut-off. An alternative formulation of the SSME that does not make this approximation is therefore described for a reversible isomerization reaction. This method also permits the investigation of the analytical relationship between the reversible system and the corresponding truly irreversible reactions in which there is no back reaction.

The coupled isomerization ME is represented in a basis where the matrices \mathbf{M}^A and \mathbf{M}^B have been separately diagonalized to $\mathbf{\Lambda}^A$ and $\mathbf{\Lambda}^B$. $\mathbf{\Lambda}^A$ and $\mathbf{\Lambda}^B$ contain the time constants that would pertain if there were no back-reaction, and determine how the population of each isomer responds to reactive input from the other isomer (or elsewhere). One of these time constants corresponds to k_{uni} for the irreversible reaction. The others all represent fast relaxation processes. Thus there will be a rapid response, governed by the fast components of the eigenvector matrix, and a slow response corresponding to λ_1 . If the time-variation of the reaction is slow then the fast components will rapidly attain a steady state, leaving only the slow components to be considered in detail.

The coupled ME's for a reversible isomerization may be written

$$\frac{d\mathbf{p}^A}{dt} = \mathbf{M}^A \mathbf{p}^A + \mathbf{K}^{AB} \mathbf{p}^B \quad (88)$$

$$\frac{d\mathbf{p}^B}{dt} = \mathbf{M}^B \mathbf{p}^B + \mathbf{K}^{BA} \mathbf{p}^A \quad (89)$$

The matrices \mathbf{M}^A and \mathbf{M}^B are then diagonalized by similarity transforms $\mathbf{\Lambda} = \mathbf{U}^{-1} \mathbf{M} \mathbf{U}$, which bring the equations to the form

$$\frac{d\mathbf{r}^A}{dt} = \mathbf{\Lambda}^A \mathbf{r}^A + \mathbf{J}^{AB} \mathbf{r}^B \quad (90)$$

$$\frac{d\mathbf{r}^B}{dt} = \mathbf{\Lambda}^B \mathbf{r}^B + \mathbf{J}^{BA} \mathbf{r}^A \quad (91)$$

where $\mathbf{r} = \mathbf{U}^{-1} \mathbf{p}$, $\mathbf{J}^{AB} = (\mathbf{U}^A)^{-1} \mathbf{K}^{AB} \mathbf{U}^B$ and $\mathbf{J}^{BA} = (\mathbf{U}^B)^{-1} \mathbf{K}^{BA} \mathbf{U}^A$.

The diagonal matrices $\mathbf{\Lambda}^A$ and $\mathbf{\Lambda}^B$ contain the eigenvalues of the two irreversible reactions, and the vectors \mathbf{r}^A and \mathbf{r}^B contain the projections of the populations onto the eigenvectors of these reactions. Assuming that the projections onto the fast eigenvectors achieve steady-state, the coupled ME's become

$$\frac{dr_1^A}{dt} = \Lambda_{11}^A r_1^A + J_{11}^{AB} r_1^B + \sum_{j \geq 2} J_{1j}^{AB} r_j^B \quad (92)$$

$$\frac{dr_1^B}{dt} = \Lambda_{11}^B r_1^B + J_{11}^{BA} r_1^A + \sum_{j \geq 2} J_{1j}^{BA} r_j^A \quad (93)$$

$$\frac{dr_i^A}{dt} = 0 = \Lambda_{ii}^A r_i^A + J_{i1}^{AB} r_1^B + \sum_{j \geq 2} J_{ij}^{AB} r_j^B \quad (i \geq 2) \quad (94)$$

$$\frac{dr_i^B}{dt} = 0 = \Lambda_{ii}^B r_i^B + J_{i1}^{BA} r_1^A + \sum_{j \geq 2} J_{ij}^{BA} r_j^A \quad (i \geq 2) \quad (95)$$

Because the different parts of the matrix \mathbf{J} appear in different parts of this system of simultaneous and differential equations, it aids clarity to denote each part of \mathbf{J} by a separate symbol. This is illustrated in Eq. (96): $J_{11} = h$, the remainder of the first row of \mathbf{J} is denoted \mathbf{v}^T and its elements are renumbered to start at 1. The remainder of the first column is similarly denoted \mathbf{w} and the cofactor matrix of J_{11} is renumbered and denoted \mathbf{H} . The renumbered \mathbf{r} and Λ matrices are denoted \mathbf{s} and \mathbf{L} , respectively.

$$\mathbf{J} = \begin{pmatrix} h & \mathbf{v}^T \\ \mathbf{w} & \mathbf{H} \end{pmatrix} \quad \Lambda = \begin{pmatrix} \Lambda_{11} & \mathbf{0} \\ \mathbf{0} & \mathbf{L} \end{pmatrix} \quad \mathbf{r} = \begin{pmatrix} r_1 \\ \mathbf{s} \end{pmatrix} \quad (96)$$

The equations may now be rewritten as:

$$\frac{dr_1^A}{dt} = \Lambda_{11}^A r_1^A + h^{AB} r_1^B + (\mathbf{v}^{AB})^T \mathbf{s}^B \quad (97)$$

$$\frac{dr_1^B}{dt} = \Lambda_{11}^B r_1^B + h^{BA} r_1^A + (\mathbf{v}^{BA})^T \mathbf{s}^A \quad (98)$$

$$\frac{ds^A}{dt} = 0 = \mathbf{L}^A \mathbf{s}^A + \mathbf{w}^{AB} r_1^B + \mathbf{H}^{AB} \mathbf{s}^B \quad (99)$$

$$\frac{ds^B}{dt} = 0 = \mathbf{L}^B \mathbf{s}^B + \mathbf{w}^{BA} r_1^A + \mathbf{H}^{BA} \mathbf{s}^A \quad (100)$$

It is now possible to solve formally for the vectors \mathbf{s}^A and \mathbf{s}^B . The matrices \mathbf{H}^{BA} and \mathbf{H}^{AB} cannot be inverted, in fact they need not even be square. However the diagonal matrices \mathbf{L}^A and \mathbf{L}^B may be inverted because their eigenvalues are negative.

\mathbf{s}^A and \mathbf{s}^B therefore obey the following sets of simultaneous equations,

$$(\mathbf{L}^A - \mathbf{H}^{AB}(\mathbf{L}^B)^{-1}\mathbf{H}^{BA})\mathbf{s}^A = \mathbf{H}^{AB}(\mathbf{L}^B)^{-1}\mathbf{w}^A r_1^A - \mathbf{w}^B r_1^B \quad (101)$$

$$(\mathbf{L}^B - \mathbf{H}^{BA}(\mathbf{L}^A)^{-1}\mathbf{H}^{AB})\mathbf{s}^B = \mathbf{H}^{BA}(\mathbf{L}^A)^{-1}\mathbf{w}^B r_1^B - \mathbf{w}^A r_1^A \quad (102)$$

Denoting $\mathbf{Q}^A = \mathbf{L}^A - \mathbf{H}^{AB}(\mathbf{L}^B)^{-1}\mathbf{H}^{BA}$ and $\mathbf{Q}^B = \mathbf{L}^B - \mathbf{H}^{BA}(\mathbf{L}^A)^{-1}\mathbf{H}^{AB}$ we obtain the formal solutions

$$\mathbf{s}^A = (\mathbf{Q}^A)^{-1}\mathbf{H}^{AB}(\mathbf{L}^B)^{-1}\mathbf{w}^A r_1^A - (\mathbf{Q}^A)^{-1}\mathbf{w}^B r_1^B \quad (103)$$

$$\mathbf{s}^B = (\mathbf{Q}^B)^{-1}\mathbf{H}^{BA}(\mathbf{L}^A)^{-1}\mathbf{w}^B r_1^B - (\mathbf{Q}^B)^{-1}\mathbf{w}^A r_1^A \quad (104)$$

These solutions may now be substituted into the differential equations for the slow components, giving

$$\frac{dr_1^A}{dt} = (\Lambda_{11}^A - (\mathbf{v}^{AB})^T \mathbf{Q}^{B-1} \mathbf{w}^A) r_1^A + (h^{AB} + (\mathbf{v}^{AB})^T (\mathbf{Q}^B)^{-1} \mathbf{H}^{BA} (\mathbf{L}^A)^{-1} \mathbf{w}^B) r_1^B \quad (105)$$

$$\frac{dr_1^B}{dt} = (\Lambda_{11}^B - (\mathbf{v}^{BA})^T (\mathbf{Q}^A)^{-1} \mathbf{w}^B) r_1^B + (h^{BA} + (\mathbf{v}^{BA})^T \mathbf{Q}^{A-1} \mathbf{H}^{AB} (\mathbf{L}^B)^{-1} \mathbf{w}^A) r_1^A \quad (106)$$

One of the two time constants for this pair of coupled equations is zero, corresponding to the equilibrium distribution, in which the steady-state approximation is exact. The second time constant may be identified with $-k_{rel}$, and is given by

$$k_{rel} = -(\Lambda_{11}^A + \Lambda_{11}^B) + (\mathbf{v}^{BA})^T (\mathbf{Q}^A)^{-1} \mathbf{w}^B + (\mathbf{v}^{AB})^T (\mathbf{Q}^B)^{-1} \mathbf{w}^A \quad (107)$$

The first term is what would be expected from the simple phenomenological rate equations, and the second and third terms are corrections for the presence of the back reaction.

Appendix C, Diagonal form of the non-linear SSME for reversible association

As argued in Section 4 it is more natural to formulate a steady-state method without any arbitrary cut-off in the state space. Although this is not very fruitful for isomerizations it is more so here. The idea of projecting out the fast components into a steady-state subspace, leaving only the one-dimensional equation for the slow component is similar in spirit to the analysis of Davis and Klippenstein [53].

As in Section 4 the starting point is the diagonalized ME, Eq. (54) and (55). By considering the equilibrium condition this ME may be written as

$$\frac{d\mathbf{s}}{dt} = \mathbf{\Lambda} \left(\mathbf{s} - \frac{x^2}{x_{eq}^2} \mathbf{s}_{eq} \right) \quad (108)$$

$$\frac{dx}{dt} = \left\| \mathbf{K}\mathbf{U} \left(\mathbf{s} - \frac{x^2}{x_{eq}^2} \mathbf{s}_{eq} \right) \right\| \quad (109)$$

Applying the steady-state approximation for all the fast components s_i ($i \geq 2$) gives $s_i = s_{eq,i} x^2 / x_{eq}^2$. Hence

$$\frac{ds_1}{dt} = -|\lambda_1| \left(s_1 - \frac{x^2}{x_{eq}^2} s_{eq,1} \right) \quad (110)$$

$$\begin{aligned} \frac{dx}{dt} &= \left\| \mathbf{K}\mathbf{U}\mathbf{s} \right\| - \frac{x^2}{x_{eq}^2} \left\| \mathbf{K}\mathbf{U}\mathbf{s}_{eq} \right\| \\ &= \left\| \mathbf{K}\mathbf{u}_1 \right\| \left(s_1 - \frac{x^2}{x_{eq}^2} s_{eq,1} \right) \end{aligned} \quad (111)$$

where \mathbf{u}_1 is the first column of \mathbf{U} , containing the eigenvector of M with eigenvalue λ_1 . From the normalization, $\left\| \mathbf{U}\mathbf{s} \right\| = 1 - x$, and the steady-state approximation for all the elements $i \geq 2$ it follows that

$$\left\| \mathbf{u}_1 \right\| \left(s_1 - \frac{x^2}{x_{eq}^2} s_{eq,1} \right) = (1 - x) - \frac{x^2}{x_{eq}^2} (1 - x_{eq}) \quad (112)$$

Furthermore, the conservative nature of the energy transfer matrix \mathbf{P} implies that $\left\| \mathbf{K}\mathbf{u}_1 \right\| = -|\lambda_1| \left\| \mathbf{u}_1 \right\|$, hence

$$\frac{dx}{dt} = |\lambda_1| \left((1 - x) - \frac{4c_0 x^2}{K_c} \right) \quad (113)$$

which is the usual rate equation for x with dissociation rate coefficient $|\lambda_1|$. Hence, the analysis described in this section also justifies the use of the phenomenological rate equation in describing

the kinetics of reversible dissociation / association reactions and permits the identification $k_d = |\lambda_1|$ and $k_a = |\lambda_1|/K_c$ as long as the association is slow relative to the faster time constants of \mathbf{M} , so that the fast components rapidly achieve steady state.

An equivalent analysis can be performed for a pseudo-first order reversible association reaction with the resulting rate equation

$$\frac{dx}{dt} = |\lambda_1| \left((1 - x) - \frac{c_0 x}{K_c} \right) \quad (114)$$

where c_0 is the concentration of the species in excess. It is clear that in both cases the absolute value of the leading eigenvalue of the ME matrix \mathbf{M} can be interpreted as the dissociation rate constant in the reversible system.