SUMMARY OF CHANDLER'S REACTIVE FLUX METHOD

I. ONSAGER'S HYPOTHESIS RELATES MACROSCOPIC AND MICROSCOPIC DYNAMICS:

Onsager asserted that for a system near equilibrium, on average the microscopic dynamics of the decay of large fluctuations in a variable (decay of the time correlation function), are the same as the dynamics of relaxation of the variable to its equilibrium value in a macroscopic system.

This hypothesis was proven about twenty years later, during the 1950's, by linear response theory. The hypothesis is valid for systems near equilibrium.

In a macroscopic system, the rate law for a reaction defines a rate constant k associated with description of the progress of the reaction toward equilibrium. For a macroscopic system prepared not far from equilibrium, the rate law will be first order.

For a microscopic system, fluctuations about the equilibrium state are described by a time correlation function. The mathematical structure of a time correlation function is a sum of exponentials. The term corresponding the the slowest first-order decay determines a constant k that characterizes relaxation of a fluctuation to

equilibrium.

By Onsager's hypothesis (or by linear response theory) we may identify the rate constant for relaxation of the macroscopic system with the rate constant for relaxation of the microscopic fluctuation of a relevant variable.

II. MACROSCOPIC PROPERTIES; PHENOMENOLOGICAL DESCRIPTION OF A REACTING SYSTEM:

A. Prepare the system for study:

For convenience, consider a system described by a symmetric double-well potential, like that which characterizes an isomerization such as the ring flip of Tyr-35 of BPTI. The equilibrium constant $K = 1$, and at equilibrium the concentrations of the two isomerizing species $[A]_{eq} = [B]_{eq}$.

Prepare the system slightly perturbed from its equilibrium, such that $[B]_{t=0} > [B]_{eq}$ (and $[A]_{t=0} < [A]_{eq}$ by an exactly equal amount).

B. Measure the rate of reaction (rate of relaxation) as the system returns to equilibrium:

The data are a set of pairs of values:
(time t, concentration $[B]_t$).

C. Analyze the data, to obtain the rate law:

Consider the deviation of the concentration of B at time t from its equilibrium value:

$$\delta B(t) = [B]_t - [B]_{t=0}$$

One will certainly find the relaxation to be first order:

$$\delta B(t) = \delta B(0) e^{-kt}$$

or equivalently,

$$\frac{\delta B(t)}{\delta B(0)} = e^{-kt} \tag{II.1}$$

where for the symmetric double-well potential,

$$k = k_{A \to B} + k_{B \to A} \tag{II.2}$$
$$k_{A \to B} = k_{B \to A}$$

III. MICROSCOPIC DESCRIPTION; DECAY OF FLUCTUATIONS IN AN EQUILIBRIUM SYSTEM:

A. Background:

For the same isomerizing system considered in Part II above, select or construct a particular coordinate, the reaction coordinate q, that represents (follows) for a reacting molecule the transition between states A and B.

The trajectory of a single molecule as it undergoes a transition (reacts) is represented by the function $q(t)$, as in Fig. 5 of Chandler.

Projection of the phase space probability density function $\rho(\Gamma)$ onto the reaction coordinate, q, gives the probability density along q, $\rho(q) = P(q)$, as in Eqn. (7 = 4.1) of Chandler.

The free energy function, $F(q) = -kT \log P(q)$.

The top of the barrier separating states A and B is at $q*$, as in Fig. 4 of Chandler.

B. Construct a function describing the *isomerization* state of the system, and a function describing a *fluctuation* of the isomerization state about the equilibrium state:

At a time t of the trajectory, the state of the system can be described by the population operator defined by Chandler, Eqn. (10 = 5.1) and Fig. 6:

$$h(q(t)) = 1, \quad q(t) > q^* \qquad \text{(III.1)}$$
$$= 0, \quad q(t) < q^*$$

or equivalently,

$$h(q(t)) = \theta(q(t) - q^*) \qquad \text{(III.2)}$$

An instantaneous population fluctuation is given by (Eqn. (11 = 5.2)),

$$\delta h(t) = h(q(t)) - \langle h \rangle \qquad \text{(III.3)}$$

where h **is the population operator for time** $t = 0$**, and** $\langle h \rangle = \langle h(t) \rangle = h_{eq} = x$**, the fraction of time spent in state B.**

C. Analyze the relaxation of the fluctuations:

Fluctuations in a system at equilibrium are described by the normalized time correlation function,

$$C_{\delta h} = \frac{\langle \delta h \delta h(t) \rangle}{\langle (\delta h)^2 \rangle} \qquad \text{(III.4)}$$

where δh **is the fluctuation for time** $t = 0$**.**

Manipulation of Eqn. (III.4) gives

$$C_{\delta h} = \frac{\langle h \delta h(t) \rangle}{\langle h \delta h \rangle} \qquad \text{(III.5)}$$

By Chandler's Eqn. (12 = 5.3) and Eqn. (13 = 5.4),

$$C_{\delta h} = e^{-kt} \qquad \text{(III.6)}$$

D. Identify the rate constant for reaction of the macroscopic system with the rate constant for relaxation of the microscopic fluctuations:

By Onsager's Hypothesis we can identify the microscopic rate constant k of Eqn. (III.6) with the macroscopic rate constant k of Eqn. (II.1). This identification is made implicitly throughout the following discussion.

E. Definition of the reactive flux:

It is convenient to define a reactive flux correlation function, Chandler Eqn. (15 = 5.6),

$$k(t) = -\frac{d}{dt} C_{\delta h} = k\, e^{-kt} \tag{III.7}$$

$$= \frac{1}{x\,(1-x)} < \dot{q}\ \delta(q - q^*)\ h(q(t)) > \tag{III.8}$$

$$= \frac{1}{x\,(1-x)} P(q^*) < \dot{q}\ h(q(t)) >_{q^*} \tag{III.9}$$

where $P(q^*) = <\delta(q - q^*)>$ **and** $<...>_{q^*}$ **means averaging with** q **initially (for** $t=0$**) constrained to** q^***.**

$P(q^*)$ **can be evaluated with umbrella sampling, and the conditional average, with trajectories starting at the barrier top.**

Eqn (III.9), Chandler's Eqn. (17 = 6.2), is the central result of Chandler's reactive flux method.

F. Analysis of the reactive flux for the limit $t \to 0^+$:

From Chandler's Eqn. (18 = 6.3)

$$k^{TST} = k(0^+) = \frac{1}{x\,(1 - x)} P(q^*) \langle \dot{q}\ \theta(\dot{q}) \rangle_{q^*} \quad \text{(III.9)}$$

Eqn. (III.9) is the transition state theory approximation (free flight of the activated complex over the barrier top, no recrossing, equilibrium on the reactant side).

Using $\langle \dot{q}\ \theta(\dot{q}) \rangle_{q^*} = \frac{1}{2} \langle |\dot{q}| \rangle_{q^*}$**, and, for isomerization and a symmetrical two-well potential, evaluating** $P(q^*)$ **and with** $k_{B \to A} = k_{A \to B} = k/2$**,**

$$k^{TST}_{A \to B} = \frac{1}{2} \langle |\dot{q}| \rangle_{q^*} \frac{e^{-\Delta W^*/kT}}{Q} \quad \text{(III.10)}$$

where $\Delta W^* = F(q^*) - F(q_A)$**, the free energy difference between barrier top and reactant well bottom.**

Evaluating Q **and** $\langle |\dot{q}| \rangle_{q^*}$**,**

$$k^{TST}_{A \to B} = \frac{\omega_A}{2\pi} e^{-\Delta W^*/kT} \quad \text{(III.11)}$$

where ω_A **is the frequency corresponding to the shape of the reactant well (force constant; curvature of the energy surface).**

Eqn. (III.10) and (III.11) are familiar statements of

the TST rate: the former is used by Ghosh and McCammon (1987); the latter is derived by Hynes (1988).

G. Analysis of the reactive flux for times $t*$ in the range $\tau_{mol} < t* << \tau_{rxn} = 1/k$:

Transient dynamics over a time $\approx O(\tau_{mol})$ reflect coupling of the reaction coordinate with other degrees of freedom, pictured for a condensed phase as buffeting of the reacting atoms by fast collisions with solvent or other environment atoms, resulting in diffusive motion across the barrier top. After decay of the transient dynamics with characteristic time τ_{mol} (Chandler Fig. 7),

$$k(t*) = k\ e^{-kt*} \qquad \text{(III.12)}$$

Since $t* << \tau_{rxn} = 1/k$, $e^{-kt*} \approx 1$, there is a plateau value of the reactive flux that is the desired estimate of the macroscopic reaction rate:

$$k(t*) \approx k \qquad \text{(III.13)}$$

The familiar factor κ is the factor by which the rate of reaction is below the TST estimate:

$$k = \kappa\ k^{TST} \qquad \text{(III.14)}$$

$$\kappa = \frac{k}{k^{TST}} = \frac{k(t*)}{k(0^+)}$$