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Jump rates for anisotropic particles

Model calculations for the transport of water molecules through membrane channels

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Abstract. A theoretical analysis for site-to-site jump rates for anisotropic molecules is presented. The molecular shape is regarded as a mechanical anisotropy in the form of finite moments of inertia, as well as anisotropy with respect to the interaction potential. The mutual coupling between rotational and translational motion necessarily produces a competitive effect between the equilibrium alignment in the local field and the precession of the figure axis, leading to an increase of the effective activation energy. As a numerical example the jump rate for a water molecule in a gramicidin-like channel has been calculated, and a temperature-independent reduction of some 15% for the rate as compared to the point-like molecule has been found.

Key words: Rate theory, anisotropic particles, generalized Arrhenius law, multi-activation process, water molecules

Introduction

In various recent publications (Schröder 1983a, b, 1985, 1986) a microscopic rate theoretical approach has been used to describe the transport of ions through molecular membrane channels. In the realistic case of a responding channel system the proper discussion of transport properties involves the analytical and numerical evaluation of a multidimensional reaction process. Since a jump rate has to be defined with respect to a certain reaction coordinate, the entire reaction process, involving all dynamic variables, has to be mapped onto one coordinate. This is possible, provided the saddle point configuration of the potential hyper-surface is known. Accordingly, the escape (or reaction) rate can be represented as the projection of the total unidirectional current across the saddle, which follows the reaction path along the steepest descent, onto the selected reaction coordinate. In the case of a transport mediating molecular channel the reaction coordinate is naturally given by the channel axis, whereas the reaction path is determined by the actual topology of the potential hyper-surface. This means that the path depends on the orientation of the ligands as induced by the respective position of the ion. The application of this procedure to a gramicidin-like channel model has been rather successful with respect to the explanation of ion selectivity in such systems (Schröder 1986).

Only ions have been subject to rate theoretical discussions in the previously published calculations. Although general characteristics of the behavior of systems including water can be predicted from known results, a more realistic approach requires the presence of water molecules in the channel, which could be there even in the absence of ions. The inclusion of water on a molecular level, however, poses two different problems, one of which has to do with the many-particle aspect. In principle, the water molecules do not behave very differently from dipolar ligands, but the numerical evaluation will be rather tedious (Kim et al. 1985; Mackay et al. 1984). The other problem is due to the additional rotational degrees of freedom and has to do with the mutual coupling of translational and rotational motion.

For any given position a water molecule within a molecular channel will align its dipole moment parallel to the local field. However, owing to its distinct moments of inertia a water molecule is an asymmetric top spinning in the local field. Since the typical motion of a top in an external field involves precession and nutation of the figure axis, the dipole moment of a rotating water molecule cannot, on the average, be expected to be aligned parallel to the local field. On the contrary it will show an average deviation which depends on the moments of inertia and the coupling of the rotational degrees of freedom to the local field. This effect is of particular importance for the saddle point configuration, since a mean deviation from the equilibrium orientation effectively increases the activation energy.

Accordingly this article consists of two parts. In the first one the expression for the escape rate of a generally anisotropic particle caught in a potential well is derived using the formalism of the transition state method in multi-dimensional systems, as described previously (Schröder 1986). The anisotropy of the respective particle may be reflected in its form as well as by its interaction with the environment. In the second part escape rates are calculated numerically for the example of a water molecule in a model gramicidin-like channel.

I. Escape rates for anisotropic particles

The starting point of the present theoretical discussion is the basic, general definition of the escape rate Γ in a multi-dimensional system (Vineyard 1957):

$$\Gamma = \int \varrho(\dot{\boldsymbol{x}}, \boldsymbol{x}) \cdot (\dot{\boldsymbol{x}}\, d\boldsymbol{S})\, d^n\dot{x}\,, \quad \dot{\boldsymbol{x}}\, d\boldsymbol{S} > 0 \tag{I.1}$$

Γ is the projection of the unidirectional current across the saddle point in the direction of the reaction coordinate, which may be any one of the n components of the position vector

$$\boldsymbol{x} = \{x_\mu\} \quad \mu = 1, \ldots, n\,.$$

With respect to any given decay channel $d\boldsymbol{S}$ is the hyper-surface element of dimensionality $n-1$ with $d\boldsymbol{S} = d^{n-1}x$ cutting through the saddle point parallel to the chosen reaction coordinate. In other words, the integration of the equilibrium distribution function $\varrho(\dot{\boldsymbol{x}}, \boldsymbol{x})$ over $d\boldsymbol{S}$ represents the configurational integral in the subspace orthogonal to the respective reaction coordinate. It was shown (Schröder 1986), that Eq. (I.1) can easily be evaluated if canonical pairs of variables $\{\boldsymbol{p}, \boldsymbol{q}\}$ referring to the saddle point configuration are introduced with the aid of

$$x_\mu = \hat{x}_\mu(q_n) + q_\mu\,, \quad x_n = q_n \tag{I.2}$$

and

$$\dot{x}_\mu = p_\mu / m_\mu\,, \quad \dot{x}_n = \left(p_n - \sum_\mu{}' p_\mu \frac{\partial \hat{x}_\mu}{\partial q_n}\right) / m_n\,,$$

where x_n was chosen to be the reaction coordinate. The set of equilibrium coordinates

$$\hat{\boldsymbol{x}}(x_n) = \{\hat{x}_\mu(x_n)\}\,, \quad \mu = 1, \ldots, n-1\,,$$

determines the saddle point landscape and can be obtained from the roots of $n-1$ equations

$$\frac{\partial V(\boldsymbol{x})}{\partial x_\mu} = f_\mu(\hat{\boldsymbol{x}}(x_n), x_n) = 0\,,$$

where $V(\boldsymbol{x})$ is the interaction potential involving all n degrees of freedom. Then the rate with respect to $q_n = x_n$ is given by

$$\Gamma = \int \dot{q}_n\, d^n\boldsymbol{p} \int d^{n-1}\boldsymbol{q}\, \exp(-\beta \cdot H)/Z\,, \quad \dot{q}_n > 0 \tag{I.3}$$

where

$$Z = \int d^n\boldsymbol{p} \int d^n\boldsymbol{q}\, \exp(-\beta \cdot H)\,,$$

is the sum of states and

$$H = \tfrac{1}{2} \sum_\mu{}' p_\mu^2 / m_\mu + \tfrac{1}{2}\left(p_n - \sum_\mu{}' \frac{\partial \hat{x}_\mu}{\partial q_n} p_\mu\right)^2 / m_n + V(\boldsymbol{q}) \tag{I.4}$$

the Hamiltonian of the system. This procedure can easily be extended to particles with form-anisotropy and anisotropic interaction. Assuming that such a particle possesses three rotational and one translational degree of freedom, the total instantaneous energy may be written as

$$E = \tfrac{1}{2} m\, \dot{z}^2 + \tfrac{1}{2} \sum_{i=1}^{3} I_i\, \omega_i^2 + V(\Omega, z)\,, \tag{I.5}$$

where $V(\Omega, z)$ is the potential energy depending on position z and the set of three Euler angles

$$\Omega = \{\alpha, \beta, \gamma\}\,.$$

The rotational kinetic energy is expressed by cartesian angular velocities, ω_i, in the molecular fixed frame and by three distinct moments of inertia I_i, which reflect the molecular form-anisotropy. The relations between the ω_i and rotations in the laboratory frame are given by (Edmonds 1960):

$$\begin{aligned} \omega_1 &= \dot{\beta} \cdot \sin\gamma - \dot{\alpha} \cdot \sin\beta \cdot \cos\gamma \\ \omega_2 &= \dot{\beta} \cdot \cos\gamma + \dot{\alpha} \cdot \sin\beta \cdot \sin\gamma \\ \omega_3 &= \dot{\alpha} \cdot \cos\beta + \dot{\gamma}\,. \end{aligned} \tag{I.6}$$

For any given position the potential energy may be minimized with respect to the orientations, using the conditions

$$\begin{aligned} \frac{\partial V(\Omega, z)}{\partial \alpha} &= f_\alpha(\hat{\Omega}(z), z) = 0 \\ \frac{\partial V(\Omega, z)}{\partial \beta} &= f_\beta(\hat{\Omega}(z), z) = 0 \\ \frac{\partial V(\Omega, z)}{\partial \gamma} &= f_\gamma(\hat{\Omega}(z), z) = 0 \end{aligned} \tag{I.7}$$

which yield a set of three equilibrium angles

$$\hat{\Omega}(z) = \{\hat{\alpha}(z), \hat{\beta}(z), \hat{\gamma}(z)\}\,.$$

In the next step new independent angular variables are introduced as deviations from equilibrium:

$$\begin{aligned} \alpha &= \hat{\alpha}(z) + \delta\alpha \\ \beta &= \hat{\beta}(z) + \delta\beta \\ \gamma &= \hat{\gamma}(z) + \delta\gamma\,. \end{aligned} \tag{I.8}$$

The substitution of the time-derivatives

$$\dot\alpha = \frac{\partial\hat\alpha}{\partial z}\dot z + \delta\dot\alpha$$
$$\dot\beta = \frac{\partial\hat\beta}{\partial z}\dot z + \delta\dot\beta \tag{I.9}$$
$$\dot\gamma = \frac{\partial\hat\gamma}{\partial z}\dot z + \delta\dot\gamma$$

in Eq. (I.6) leads to the obvious decomposition of the cartesian angular velocities in form of

$$\omega_i = \delta\omega_i + \frac{\partial\hat\varphi_i}{\partial z}\dot z \tag{I.10}$$

and the kinetic energy as

$$E_{\mathrm{kin}} = \tfrac{1}{2} m \dot z^2 + \tfrac{1}{2}\sum_{i=1}^{3} I_i\left(\delta\omega_i + \frac{\partial\hat\varphi_i}{\partial z}\dot z\right)^2, \tag{I.11}$$

where the angular distortion field is defined by:

$$\frac{\partial\hat\varphi_1}{\partial z} = \frac{\partial\hat\beta}{\partial z}\sin\gamma - \frac{\partial\hat\alpha}{\partial z}\sin\beta\cdot\cos\gamma$$
$$\frac{\partial\hat\varphi_2}{\partial z} = \frac{\partial\hat\beta}{\partial z}\cos\gamma + \frac{\partial\hat\alpha}{\partial z}\sin\beta\cdot\sin\gamma \tag{I.12}$$
$$\frac{\partial\hat\varphi_3}{\partial z} = \frac{\partial\hat\alpha}{\partial z}\cos\beta + \frac{\partial\hat\gamma}{\partial z}.$$

Accordingly the angular momenta are obtained as

$$L_i = \frac{\partial E_{\mathrm{kin}}}{\partial(\delta\omega_i)} = I_i\left(\delta\omega_i + \frac{\partial\hat\varphi_i}{\partial z}\dot z\right), \tag{I.13}$$

whereas the translational canonical momentum is given by

$$p = \frac{\partial E_{\mathrm{kin}}}{\partial\dot z} = m\dot z + \sum_{i=1}^{3} L_i\frac{\partial\hat\varphi_i}{\partial z}. \tag{I.14}$$

Thus the desired Hamiltonian is:

$$H = \left(p - \sum_{i=1}^{3} L_i\frac{\partial\hat\varphi_i}{\partial z}\right)^2/(2m) + \tfrac{1}{2}\sum_{i=1}^{3} L_i^2/I_i + V(\Omega,z). \tag{I.15}$$

With the knowledge of the Hamiltonian the evaluation of the rate constant Γ according to Eqs. (I.1) and (I.3) poses no problem. Formally one finds:

$$\Gamma = \frac{\int_0^\infty \dot z\,dp\int d^3L\int d\Omega\,\exp(-\beta H)}{\int dp\int d^3L\int d\Omega\int dz\,\exp(-\beta H)}. \tag{I.16}$$

The integrations of the kinetic and potential contributions, respectively, can be carried out separately. The integral over momentum space in the numerator yields

$$\int_0^\infty \exp(-\beta E_{\mathrm{kin}})\,\dot z\,dp\int d^3L$$
$$= k_B T\cdot\sqrt{(2\pi k_B T)^3\,(m^*/m)}\cdot I_1 I_2 I_3,$$

whereas the corresponding result for the denominator gives

$$\int\exp(-\beta E_{\mathrm{kin}})\,dp\int d^3L = \sqrt{(2\pi k_B T)^4\,m\,I_1 I_2 I_3}.$$

Up to spatial integrations the expression for the rate can be written as:

$$\Gamma = \sqrt{k_B T/(2\pi)}\cdot\frac{\int_c d\Omega\,\exp(-\beta V(\Omega,c))/\sqrt{m^*}}{\int d\Omega\int_a^c dz\,\exp(-\beta V(\Omega,z))}. \tag{I.17}$$

Here $\int_a^c \ldots dz$ denotes the integration between two saddle points.

The quantity m^* would correspond to the effective mass in the case of point-like particles, but for an anisotropic molecule with distinct moments of inertia it is a function which generally depends on the spatial orientation Ω:

$$m^*(\Omega,c) = m + I_1\left(\frac{\partial\hat\varphi_1}{\partial z}\right)^2 + I_2\left(\frac{\partial\hat\varphi_2}{\partial z}\right)^2 + I_3\left(\frac{\partial\hat\varphi_3}{\partial z}\right)^2. \tag{I.18}$$

This is due to the fact that other than for a point-like particle the coefficients in the quadratic form of the kinetic energy are still functions of the generalized coordinates, i.e. of α, β, and γ. The quantity in the denominator of Eq. (I.17) involves the configurational integral

$$Q(z) = \int\exp(-\beta V(\Omega,z))\,d\Omega$$
$$= Q_0\cdot\exp(-\beta V^*(z)),$$

where

$$V^*(z) = -k_B T\cdot\ln\{\int\exp(-\beta V(\Omega,z))\,d\Omega\}$$
$$+ k_B T\cdot\ln Q_0 \tag{I.19}$$

is the potential of the mean force and Q_0 the configurational integral in absence of the molecule, i.e.

$$\lim_{|z|\to\infty} V^*(z) = 0.$$

An analogous decomposition of the numerator is obviously not possible. The explicit angular dependence of the effective mass function is given by Eq. (I.18) with the aid of Eq. (I.12):

$$m^*(\Omega,c) = m + I_1\left(\frac{\partial\hat\beta}{\partial z}\sin\gamma - \frac{\partial\hat\alpha}{\partial z}\sin\beta\cos\gamma\right)^2$$
$$+ I_2\left(\frac{\partial\hat\beta}{\partial z}\cos\gamma + \frac{\partial\hat\alpha}{\partial z}\sin\beta\sin\gamma\right)^2 \tag{I.20}$$
$$+ I_3\left(\frac{\partial\hat\alpha}{\partial z}\cos\beta + \frac{\partial\hat\gamma}{\partial z}\right)^2.$$

Only in the special case of a spherical particle, $I = I_1 = I_2 = I_3$, and independence from the molecular azimuth γ, the effective mass function becomes a constant,

$$m^*(c) = m + I\left[\left(\frac{\partial\hat{\alpha}}{\partial z}\right)^2 + \left(\frac{\partial\hat{\beta}}{\partial z}\right)^2\right],$$

and the rate can be written as:

$$\Gamma = \sqrt{k_B T/(2\pi m^*)} \cdot \frac{\exp(-\beta V^*(c))}{\int_a^c \exp(-\beta V^*(z))\, dz}. \qquad \text{(I.21)}$$

However, it is very instructive to attempt a formulation of Eq. (I.17) as a generalized Arrhenius law, i.e., to use the low temperature approximation. For this purpose we introduce the averaged quantity:

$$\langle 1/\sqrt{m^*(\Omega,c)}\rangle_\Omega = \frac{\int d\Omega \exp(-\beta V(\Omega,c))/\sqrt{m^*}}{\int d\Omega \exp(-\beta V(\Omega,c))}. \qquad \text{(I.22)}$$

The potential of the mean force is expanded around the minimum at the position $z = b$

$$V^*(z) \approx -k_B T \ln\{\int d\Omega \exp(-\beta V(\Omega,c))\} + \tfrac{1}{2}(z-b)^2 \cdot \varkappa(T),$$

where

$$\varkappa(T) = \left\langle \frac{\partial^2 V(\Omega,z)}{\partial z^2}\bigg|_{z=b} \right\rangle_\Omega \qquad \text{(I.23)}$$

is a temperature-dependent quantity. After extending the limits in the Gaussian integral to infinity the jump rate assumes the desired form:

$$\Gamma = \nu_0(T) \cdot \exp\{-\beta \cdot [V^*(c) - V^*(b)]\}. \qquad \text{(I.24)}$$

With:

$$\nu_0(T) = 1/(2\pi) \cdot \left\langle \sqrt{\frac{\varkappa(T)}{m^*(\Omega,c)}} \right\rangle_\Omega. \qquad \text{(I.25)}$$

The expression (I.24) for the rate departs in several respects from the simple Arrhenius law. First, the potential of the mean force, $V^*(z)$, itself is temperature-dependent, so that the activation energy

$$\Delta E^* = V^*(c) - V^*(b)$$

is temperature-dependent.

Secondly, the same indirect temperature dependence is contained in part in the prefactor, namely in $\varkappa(T)$. However, if entropy effects are weak, this temperature dependence can be neglected. Then the main temperature dependence of the prefactor arises through the averaging process involving the orientation Ω. If the anisotropy of the interaction is strong enough and thus leads to distinct pronounced minima with respect to one or several Euler angles, $\varkappa(T)$ is essentially represented by a sum of exponentials.

Thirdly, a similar effect can be expected from a strong form-anisotropy which is reflected in large moments of inertia. The respective sum of exponentials would show up in Eq. (I.22), giving rise, together with Eq. (I.23), to the jump as a multi-activation process, in which the molecule would successively pass through preferred orientations. The obvious criteria for such a process would be the observation of a sequence of different slopes in the Arrhenius plot for sufficiently anisotropic molecules in the corresponding environment.

II. Escape rate for a water molecule

In this section the escape rate for a water molecule in a binding site inside a gramicidin-like channel is calculated according to Eq. (I.21). With a slight modification, considering the head-to-head binding effect of the gramicidin dimer (Pullman and Etchebest 1983; Etchebest and Pullman 1984; Etchebest et al. 1984), the present channel model is identical with the model used previously (Schröder 1985). Accordingly the channel is represented by a helical arrangement of permanent dipoles simulating the carbonyl groups which line the interior of the GA-channel. There are 32 dipoles, 30 of which possess the same moment $p = q'd$ with an effective charge $q' = 0.4e$ and length $d = 1.24$ Å. The two head-to-head dipoles are given half that strength[1]. One helical turn includes 6 dipoles with alternating orientations on a constant radius with $\varrho_0 = 6$ Å. The helical pitch is 6 Å, thus the dimer has a total length of 31 Å with a lattice constant $z_0 = 1$ Å.

The water molecule is assumed to interact with the channel via its dipole moment only. Thus the potential energy is given by

$$V(\vec{r}) = -\vec{p}\vec{E}(\vec{r}), \qquad \text{(II.1)}$$

where $\vec{p}$ is the dipole moment of the water molecule and $\vec{E}(\vec{r})$ is the local field obtained from the contribution of all ligands at their respective positions $\vec{r}_\mu$:

$$E(\vec{r}) = \sum_{\nu=1}^{32}\left\{\frac{\vec{p}_\mu}{|\vec{r}-\vec{r}_\mu|^3} - 3\cdot\frac{(\vec{r}-\vec{r}_\mu)\cdot[\vec{p}_\mu(\vec{r}-\vec{r}_\mu)]}{|\vec{r}-\vec{r}_\mu|^5}\right\}. \qquad \text{(II.2)}$$

With $\vec{r}_\mu = \{\varrho_0 \cdot \cos\vartheta_\mu, \varrho_0 \cdot \sin\vartheta_\mu, \mu \cdot z_0\}$ and $\vec{r} = \{0, 0, z\}$ (for simplicity the water molecule is kept on the channel axis) and the introduction of the dimensionless quantities $\zeta = z/z_0$ and $\Delta = \varrho_0/z_0$ as well as the aid of the auxiliary quantities

$$R_\mu^2 = (\zeta-\mu)^2 + \Delta^2$$

$$Q_\mu = (\zeta-\mu)\cdot\cos\vartheta_\mu - \Delta\cdot\sin\vartheta_\mu,$$

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[1] A. Pullman, private communication

the three components of the local field can be written as:

$$E_1(\zeta) = 1/z_0^3 \sum_{\mu} p_\mu \cdot \cos\varphi_\mu \cdot (\sin\vartheta_\mu + 3\Delta \cdot Q_\mu/R_\mu^2)/R_\mu^3$$

$$E_2(\zeta) = 1/z_0^3 \sum_{\mu} p_\mu \cdot \sin\varphi_\mu \cdot (\sin\vartheta_\mu + 3\Delta \cdot Q_\mu/R_\mu^2)/R_\mu^3$$

$$E_3(\zeta) = 1/z_0^3 \sum_{\mu} p_\mu \cdot [\cos\vartheta_\mu + 3(\zeta-\mu)\, Q_\mu/R_\mu^2]/R_\mu^3 . \tag{II.3}$$

The azimuth angle $\varphi_\mu = \pi \cdot \mu/3$ denotes the position of the ligands in the molecular $x-y$-plane, whereas ϑ_μ accounts for their alternating polar orientation, namely:

$\vartheta_1 = \ \ 200°$

$\vartheta_2 = -20°$

$\vartheta_3 = \ \ 200°$, etc.

The form-anisotropy of water is taken into account by its finite moments of inertia in the ground state (Eisenberg and Kauzmann 1969). The values are:

$I_1 = 2.9376 \cdot 10^{-24}\,\mathrm{g\,Å^2}$

$I_2 = 1.022\mathrm{p} \cdot 10^{-24}\,\mathrm{g\,Å^2}$

$I_3 = 1.9187 \cdot 10^{-24}\,\mathrm{g\,Å^2}$.

The 1-axis is perpendicular to the plane of the molecule, the 3-axis lies in this plane and is the bisector of the bond angle, and the 2-axis is perpendicular to the other two.

Owing to the axial symmetry of a dipole the potential energy depends on the relative orientation only. However, this quantity cannot be used as an integration variable, because the kinetic energy has been parameterized by Euler's angles, which must also be used in the potential energy. Consequently one must write:

$$V = -\vec{p}\vec{E} = -p\,E \cdot [\sin\beta \cdot \sin\beta' \cdot \cos(\alpha - \alpha') + \cos\beta \cdot \cos\beta'] .$$

The minimization procedure, (I.7), simply yields

$$\hat{\alpha} = \alpha' \quad \text{and} \quad \hat{\beta} = \beta' ,$$

where α' and β' determine the direction of the local field, which still depends on the position z:

$$\cos\hat{\alpha} = E_1/E_\perp , \quad \cos\hat{\beta} = E_3/E \tag{II.4}$$

with

$$E_\perp = \sqrt{E_1^2 + E_2^2} \quad \text{and} \quad E = \sqrt{E_1^2 + E_2^2 + E_3^2} .$$

The prefactor, i.e. the effective mass function, does not depend on the azimuth α, whereas the exponential does not depend on the molecular azimuth, γ. Therefore the respective integrals factorize and can be carried out separately. Using

$$V = -p \cdot (E_1 \cdot \sin\beta \cdot \cos\alpha + E_2 \cdot \sin\beta \cdot \sin\alpha + E_3 \cdot \cos\beta)$$

the exponential can be written as:

$$\int_0^{2\pi} \exp(-\beta V)\, d\alpha = \exp(\beta p E_3 \cos\beta) \cdot \int_0^{2\pi} \exp(\beta p \sin\beta) \cdot (E_1 \cdot \cos\alpha + E_2 \cdot \sin\alpha)\, d\alpha$$

$$= 2\pi \cdot \exp(\beta p E_3 \cos\beta) \cdot I_0(\beta p E_\perp \cdot \sin\beta) , \tag{II.5}$$

where I_0 is the modified Bessel function of the first kind. It should be noted that the factorial β in the exponential is $1/k_B T$. After performing all integrations in the denominator and the use of Eq. (II.5) the rate according to Eq. (I.17) is

$$\Gamma = \sqrt{k_B T/2\pi} \cdot \frac{\int_0^{2\pi} m^*(\chi,\gamma)^{-1/2}\, d\gamma \int_{-1}^{1} \exp(\beta p E_3 \chi)\, I_0(\beta p E_\perp \sqrt{1-\chi^2})\, d\chi}{4\pi \int_a^c \sinh(\beta p E)/\beta p E\, dz} \tag{II.6}$$

with $\chi = \cos\beta$. In the next step the integral

$$\int_0^{2\pi} m^*(\chi, \gamma, c)^{-1/2}\, d\gamma$$

has to be evaluated, where m^* is identical with (I.20), except for the fact that $\frac{\partial\hat{\gamma}}{\partial z}$ vanishes, which is due to the axial symmetry of dipole. With respect to form-anisotropy, however, the present effective mass function covers the most general case, because all three moments of inertia are different. After some tedious, but straightforward rearrangements the effective mass function can be written as:

$$m^* = A + B \cdot \cos(2\gamma) + C \cdot \sin(2\gamma) \tag{II.7}$$

The coefficients are:

$$A = m + \tfrac{1}{2} \cdot (I_1 + I_2) \cdot \left[\left(\frac{\partial\hat{\alpha}}{\partial z}\right)^2 + \left(\frac{\partial\hat{\beta}}{\partial z}\right)^2\right] + \tfrac{3}{2} \cdot (I_3 - I) \cdot \left(\frac{\partial\hat{\alpha}}{\partial z}\right)^2 \cdot \chi^2$$

$$B = \tfrac{1}{2} \cdot (I_1 - I_2) \cdot \left[\left(\frac{\partial\hat{\alpha}}{\partial z}\right)^2 \cdot (1-\chi^2) - \left(\frac{\partial\hat{\beta}}{\partial z}\right)^2\right]$$

$$C = -(I_1 - I_2) \cdot \frac{\partial\hat{\alpha}}{\partial z} \cdot \frac{\partial\hat{\beta}}{\partial z} \cdot \sqrt{1-\chi^2}$$

with $I = (I_1 + I_2 + I_3)/3$.

With the aid of Eq. (II.7) the integral over the molecular azimuth, γ, can be converted into the complete elliptic integral of the first kind, $K(k)$ (Abramowitz and Stegun 1965), namely:

$$\int_0^{2\pi} m^{*-1/2}\,d\gamma = 2\cdot\int_0^{\pi}[A+(A^2+B^2)^{1/2} - 2(B^2+C^2)^{1/2}\cdot\sin^2\gamma]^{-1/2}\,d\gamma = 4\cdot[A+(B^2+C^2)^{1/2}]^{-1/2}\cdot K(k)\,. \quad \text{(II.8)}$$

The variable k still depends on the polar orientation $\chi=\cos\beta$ and vanishes in the case of spherical symmetry:

$$k^2=\frac{2\cdot(B^2+C^2)^{1/2}}{A+(B^2+C^2)^{1/2}} = \frac{(I_1-I_2)\cdot\left[\left(\frac{\partial\hat{\alpha}}{\partial z}\right)^2\cdot(1-\chi^2)+\left(\frac{\partial\hat{\beta}}{\partial z}\right)^2\right]}{m+I_1\cdot\left[\left(\frac{\partial\hat{\alpha}}{\partial z}\right)^2+\left(\frac{\partial\hat{\beta}}{\partial z}\right)^2\right]+(I_3-I_1)\cdot\left(\frac{\partial\hat{\alpha}}{\partial z}\right)^2\cdot\chi^2} \quad \text{(II.9)}$$

The derivatives of the dipolar equilibrium angles $\hat{\alpha}$ and $\hat{\beta}$ are easily evaluated with the aid of Eq. (II.4):

$$\frac{\partial\hat{\alpha}}{\partial z}=\left(E_1\cdot\frac{\partial E_2}{\partial z}-E_2\cdot\frac{\partial E_1}{\partial z}\right)/E^2$$
$$\frac{\partial\hat{\beta}}{\partial z}=\left(E_3\cdot\frac{\partial E}{\partial z}-E\cdot\frac{\partial E_3}{\partial z}\right)/(E_\perp E)\,. \quad \text{(II.10)}$$

Finally the resulting expression for the escape rate according to Eqs. (I.17) and (I.19) using Eqs. (II.8)–(II.10) is given by:

$$\Gamma=\sqrt{k_B T/2\pi}\cdot\frac{\int_{-1}^{1}[A+(B^2+C^2)^{1/2}]^{-1/2}\cdot K(k)\cdot\exp(\beta p E_3\chi)\cdot I_0(\beta p E_\perp\sqrt{1-\chi^2})\,d\chi}{\pi/2\int_a^c\exp(-\beta V^*(z))\,dz} \quad \text{(II.11)}$$

The two remaining integrations over χ and z have to be carried out numerically. The potential of the mean force,

$$V^*(z)=-k_B T\cdot\ln[2\cdot\sinh(\beta E p)/\beta E p]\,, \quad \text{(II.12)}$$

involves the summation procedure of (II.3). The numerical result is presented in Fig. 1. Here the potential profile of the present channel model is shown at different temperatures for a single water molecule. The potential of the mean force has been plotted in units of V^*/k_B over the position of the water molecule along the channel axis. The unit of length is 1 Å. As compared to the corresponding channel profile for an ion, the typical energies involved in the present case are one order of magnitude smaller. Since the equilibrium profile as shown here is solely based on the proper equilibrium

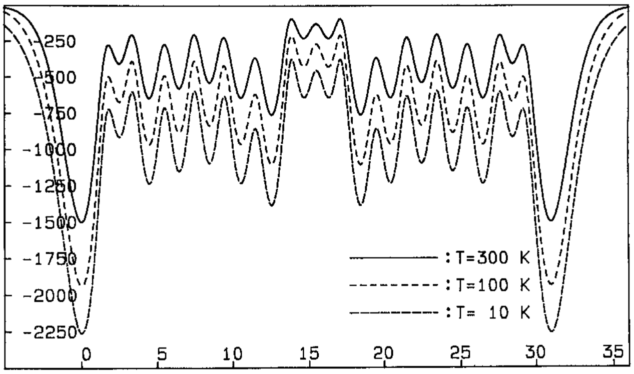

Fig. 1. The potential of the mean force shown for several temperatures. The energy is plotted (in units of V^*/k_B) against the position of the water molecule along the channel axis. The unit of length is 1 Å

orientation of the water dipole for any given position, a finite binding energy can only be obtained as long as the dipole is able to maintain a preferred orientation. For increasing temperature the angular distribution function is "smeared out" and the activation energy decreases drastically. This effect clearly shows up in Fig. 1. The escape rate itself has been evaluated for a typical binding site off the channel ends in the quasi-periodic region and is presented in Fig. 2 in the form of an Arrhenius plot. Here the logarithm of Γ has been plotted against the inverse temperature in the region between 200 and 1,000 K. The full line shows the Arrhenius plot for the actual water molecule, whereas the result represented by the dashed line neglects the finite moments of inertia, i.e. $I_1=I_2=I_3=0$. The rate regarding the form-anisotropy of water is, almost temperature-independent, about 15% less than the corresponding rate for the point-like particle. This is a remarkable, because the moments of inertia are relatively small. On the other hand, however, gain and loss of potential energy essentially depend on the dipolar orientation. Therefore a small average deviation from the equilibrium orientation due to precession of the dipole in the local field causes a significant change in the effective activation energy.

Conclusion

In this article a method developed recently for the calculation of escape rates on the basis of the transi-

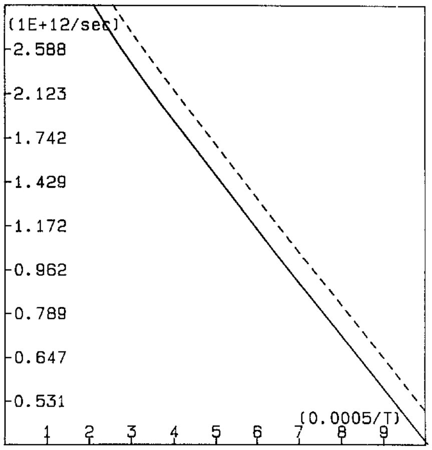

Fig. 2. Plot of $\ln(\Gamma)$ against the inverse temperature for T in the range between 200 and 1,000 K. The full line shows the Arrhenius plot for the actual water molecule, whereas the dashed line shows the same for a point-like water molecule

tion state method in multi-dimensional reaction systems has been extended to anisotropic particles. Such particles are assumed to be subject to translational and rotational motion in an external potential. The particle may be anisotropic with respect to the internal mass distribution and with respect to the interaction with its environment. The latter, for instance, may be reflected by the presence of permanent multi-pole moments or an anisotropic polarizability. For any given position a rigid particle at rest will align in the local field according to its structure, as seen by the interaction, so as to minimize the potential energy. On the other hand the same particle, given some rotational kinetic energy, represents an asymmetric top spinning in the local field. The accompanying precession and nutation, however, produce an average deviation off the equilibrium orientation, thus preventing a minimization as long as the angular momenta do not vanish. Since the equilibrium orientation depends on the position of the particle, a change of the position induces rotation. Thus this competitive effect is present whenever a molecule possesses finite moments of inertia. Moreover, it has been found that the escape rate for a sufficiently large particle, for example, a biaxial molecule, may exhibit a significant deviation from the simple Arrhenius law, because the transition across the saddle point appears as a multi-activation process. Consequently a sequence of successive slopes instead of one should be observed.

An exemplary calculation has been performed for a water molecule in a gramicidin-like channel in the second section. It has been found that the individual escape rates for jumps between two neighboring binding sites are decreased by 15% for a water molecule with the actual moments of inertia. Clearly this correction will have to be taken into account in the calculation of the effective transmembrane current involving ions and water molecules.

The formalism developed here cannot only be used to calculate effective transport rates in any particular environment, but also to study bimolecular reaction rates, where at least one of the reactants could be an anisotropic molecule. A good example is the ion-molecule recombination process, which has been described by means of Monte Carlo methods by other authors (Swamy and Hase 1982). Another example of a possibly successful application could be the rate theoretical analysis of the head-to-head dimerization process of the gramicidin A channel[2] (Venkatachalam and Urry 1983, 1984), which will be the subject of a future communication.

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References

Abramowitz A, Stegun IA (1965) Handbook of mathematical functions. Dover, New York

Edmonds AR (1960) Angular momentum in quantum mechanics. Princeton University Press, London

Eisenberg D, Kauzmann W (1969) The structure and properties of water. Oxford University Press, London

Etchebest C, Pullman A (1984) The gramicidin A channel: II. Role of the ethanolamine end chain on the energy profile for single occupancy by Na^+. FEBS Lett 170:191

Etchebest C, Ranganathan S, Pullman A (1984) The gramicidin A channel: Comparison of the energy profiles of Na^+, K^+ and Cs^+. FEBS Lett 173:301

Kim KS, Vercauteren DP, Welti M, Chin S, Clementi E (1985) Interaction of K^+ ion with the solvated gramicidin A transmembrane channel. Biophys J 47:327

Mackay DH, Berens PH, Wilson KR, Hagler AT (1984) Structure and dynamics of ion transport through gramicidin A. Biophys J 46:229

Pullman A. Etchebest C (1983) The gramicidin A channel: I. The energy profile for single and double occupancy in a head-to-head $\beta^{6.3}$-helical dimer backbone. FEBS Lett 163: 199

Schröder H (1983a) Transit time conception for ion diffusion through membrane channels. J Chem Phys 79:1991

Schröder H (1983b) Rate theoretical analysis of ion transport in membrane channels with elastically bound ligands. J Chem Phys 79:1997

Schröder H (1985) Rate theoretical analysis of ion-selectivity in membrane channels with elastically bound ligands. Eur Biophys J 12:129

Schröder H (1986) Generalized transition state method and continuous diffusion in multi-dimensional systems with relation to ion transport in channels of biological membranes. Eur Biophys J 13:281–290

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[2] I am indebted to F. J. Sigworth for bringing this problem to my attention

Swamy KN, Hase WL (1982) Dynamics of ion-molecule recombination. II. An alkali ion and a water molecule. J Chem Phys 77:3011

Venkatachalam CM, Urry DW (1983) Theoretical conformational analysis of the gramicidin A transmembrane channel. I. Helix sense and energetics of head-to-head dimerization. J Comput Chem 4:461

Venkatachalam CM, Urry DW (1984) Theoretical analysis of gramicidin A transmembrane channel. II. Energetics of helical librational states of the channel. J Comput Chem 5:64

Vineyard GH (1957) Frequency factors and isotope effects in solid state processes. J Phys Solids 3:121