Biochimica et Biophysica Acta, 553 (1979) 326—341
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BBA 78354

THEORY OF SINGLE-FILE NOISE

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(Received August 14th, 1978)

Key words Current noise, Single file diffusion, Membrane channel, Damped oscillation

Summary

A general theoretical approach to the analysis of electric fluctuations generated by the so-called single-file diffusion through narrow channels is presented. The formalism is a slight extension of an approach to electric fluctuations in discrete transport systems with negligible interactions between the particles recently developed by one of the authors. In the single-file transport mechanism interactions between the particles must be taken into account. Three main results of principal interest are: (a) the electric fluctuations around stationary states (at equilibrium and non-equilibrium) are determined by the time-dependent solutions of the macroscopic single-file transport equations, (b) as a direct consequence of the interactions between the ions in the single-file transport the macroscopic time-dependent current and the autocorrelation function of the microscopic current fluctuations can exhibit damped oscillatory behavior, and the current noise spectrum can show peaking, (c) the number of binding sites for the ions within the pores seems to have a strong influence on the oscillatory behavior: with increasing number of binding sites the damping of the oscillations decreases and the peaking of the spectrum becomes stronger.

(1) Introduction

More than 20 years ago the so-called single-file mechanism for ion transport through narrow channels in biological membrane has been proposed by Hodgkin and Keynes [1] to explain non-linear stationary current voltage characteristics of the potassium channel. Since that time a number of theoretical investigations of stationary single-file transport have been published (e.g. refs. 2—6). The essential property of single-file diffusion is that the movement of the ions is constrained to one dimension and the ions cannot overtake each other. The usual way of describing mathematically the single-file movement is to regard the ion channel (pore) as a sequence of binding sites separated by energy barriers over which the ions have to jump (jump diffusion).

In this paper we have developed the first general theoretical approach to the treatment of the electrical fluctuations related to the single-file transport mechanism. We recently have presented a general theory of transport noise in discrete transport systems under the assumption of negligible interactions between the transported particles [7]. The single-file mechanism includes interactions between the ions in so far as each binding site can be occupied by only one particle and the rate constants for jumps of ions over the energy barriers can be dependent on the occupation state of the pore. We shall show that our approach to electric transport noise can easily be extended to single-file transport. The essential assumption is that interactions between different pores may be neglected. The calculation of current noise spectra is based on the solution of the macroscopic time-dependent single-file transport equations.

Apart from the presentation of the general approach to single-file noise the aim of this paper is to investigate the principal consequences of the single-file mechanism for the electrical transport fluctuations. As long as the ionic movement through the channels is so fast that the characteristic transport times affect the spectral density of electrical fluctuations at rather high frequencies, it seems difficult to measure these effects with presently available experimental methods.

We shall explicitly discuss the simplest case of pores with two binding sites and one ion species. One result of principal interest is, that at non-equilibrium as a consequence of the interaction between the ions the eigenvalues of the matrix of coefficients of the kinetic transport equations can be complex numbers. Hence the macroscopic time-dependent transport and the autocorrelation function can show a damped oscillatory behaviour and the current noise spectrum may have peaks. In the case of negligible interactions between the ions the eigenvalues are always real (and negative), i.e. there are no oscillatory transport phenomena. The occurrence of damped oscillations in reaction schemes containing closed loops and violating the Wegscheider conditions (non-equilibrium) is well known (see e.g. refs. 8—10). Recently Chen [11] has pointed out that as a consequence the spectra of the steady-state fluctuations in concentrations can show peaking.

The general formalism is developed in the sections 2 and 3. In section 4 the application to the special case of pores with two binding sites is given. For comparison one example of pores with three binding sites is calculated. The results of the numerical calculations show that in general the dependence of the spectral density on different parameters such as the potential profile within the channel or the dielectric properties seems to be rather complicated. We have tried to work out some typical dependences due to variation of the magnitude of electrostatic interactions between the ions, of an applied voltage and of the number of binding sites. All numerical calculations are restricted to the frequency domain (spectral density). The general formula for the corresponding autocorrelation function of current fluctuations in the time domain is given in Eqn. 3.5.

In order to investigate the typical single-file effects we have restricted our calculations to open channels. The theoretical treatment of channels with more than one conductance state, i.e. open-close kinetics, makes necessary only slight extensions of the approach in this paper and will be presented elsewhere.

We finally emphasize that in the present paper we have developed a theory of single-file fluctuations around equilibrium and non-equilibrium steady states. According to the Nyquist relation in equilibrium states the microscopic fluctuations are related to the small signal impedance. In ref. 7 we have shown that a similar relation is valid for transport noise in open pores also at non-equilibrium states in the case of vanishing interactions between the ions. We believe that with the approach to transport fluctuations developed in ref. 7 and the present paper the validity of a corresponding relation at non-equilibrium can be investigated more generally. This will be subject to future work.

(2) The single-file transport model

(a) General equations

Before deriving a general theoretical approach to single-file noise we give a description of the model of single-file transport through membranes which shall be used. The transport system consists of a membrane separating two ionic solutions and containing a number N_{p} of identical narrow channels (pores). The concentrations of the ionic species in both solutions are assumed to be held constant. The basic assumptions underlying the single-file movement of the ions through the pores are:

(1) There are no interactions between different pores, i.e. the state of one pore does not influence the movement of ions within the other pores.

(2) The individual pore contains a certain number of binding sites for the ions, i.e. the ions must pass across a sequence of energy barriers to cross the membrane.

(3) The ions are not permitted to pass each other within the pores.

We do not want to go into the details of single-file transport theory which has been developed in a number of papers by Heckmann et al. [2–5]. We briefly describe the main structure of the transport equations which determine the time-dependent single-file transport: The individual channel or pore can be found in a certain number of different states depending on whether the binding sites are occupied by an ion of a certain species or not. If the pore contains n binding sites and may take up p different ion species this number of states is

$$N = (1 + p)^n \tag{2.1}$$

These N different states can be numbered by $i = 1, 2, ..., N$. If the transport system contains many identical pores the (macroscopic) time dependence of the occupation numbers n_i of state i, i.e. number of pores in state i, is given by the following homogeneous set of linear first-order differential equations:

$$\frac{\mathrm{d}N_i}{\mathrm{d}t} = \sum_{k=1}^{N} M_{ik} N_k \tag{2.2}$$

The matrix elements M_{ik} of M contain the transition rates (rate constants) $k_{i,k}$ for transitions from state k to state i in the following way:

$$M_{ik} := k_{i,k} \quad \text{for } i \neq k \tag{2.3}$$

$$M_{ii} := -\sum_{k=1}^{N} k_{k,i}$$

We emphasize that the Eqns. 2.2 are linear because according to the first basic assumption interactions between different pores are neglected. On the other hand interactions between the ions can be included in Eqn. 2.2 through the special choice of the transition rate constants $k_{i,k}$. The structure of the matrix $\underset{\sim}{M}$ in Eqn. 2.2 is determined by certain rules for the movement of ions, e.g. only jumps of ions between adjacent binding sites are possible, and at one instant only one jump can occur.

The number of independent equations in Eqn. 2.2 can be drastically reduced if interactions between the particles are neglected, because at any time only a small fraction of pores is occupied by one or more ions [8]. In this case and for one ionic species Eqn. 2.2 can be replaced by an inhomogeneous system of n equations [8]:

Microscopically the occupation numbers statistically fluctuate around mean values usually called the (ensemble averaged) expectation values of N_i denoted by $\langle N_i \rangle$. Because he deterministic Eqns. 2.2 are linear, they hold also for the expectation values of occupation numbers [14]. Hence:

$$\frac{\mathrm{d}\langle N_i \rangle_{\underset{\sim}{\mathrm{N}}(0)}}{\mathrm{d}t} = \sum_{k=1}^{N} M_{ik} \langle N_k \rangle_{\underset{\sim}{\mathrm{N}}(0)} \tag{2.2a}$$

or in matrix notation with $\langle \underset{\sim}{\tilde{N}} \rangle$ as the transpose of $\langle \underset{\sim}{N} \rangle$

$$\frac{\mathrm{d}}{\mathrm{d}t} \langle \underset{\sim}{N} \rangle_{\underset{\sim}{\mathrm{N}}(0)} = \underset{\sim}{M} \langle \underset{\sim}{\tilde{N}} \rangle_{\underset{\sim}{\mathrm{N}}(0)} \tag{2.2b}$$

The index $\underset{\sim}{\mathrm{N}}(0)$ denotes the initial state at time zero.

The total number of pores N_{p} is assumed to be constant. This yields the conservation relation

$$\sum_{i=1}^{N} N_i = N_{\mathrm{p}} \tag{2.4}$$

Hence the N equations (Eqns. 2.2) are not independent. This admits the existence of at least one non-trivial time-independent steady-state solution $\underset{\sim}{N}^{\mathrm{s}}$ of the linear equations:

$$\sum_{k=1}^{N} M_{ik} N_k^{\mathrm{s}} = 0 \tag{2.5}$$

In the following we assume the existence of exactly one steady-state solution $\underset{\sim}{N}^{\mathrm{s}}$ of Eqn. 2.2, describing the final state $\lim_{t\to\infty} \underset{\sim}{N}(t)$ of Eqn. 2.2 for arbitrary initial states $\underset{\sim}{N}(0)$. The deviations from the steady state are

$$\alpha_i := N_i - N_i^{\mathrm{s}} \tag{2.6}$$

$\langle \underset{\sim}{\alpha} \rangle$ satisfies as well the Eqns. 2.2

$$\frac{\mathrm{d}}{\mathrm{d}t} \langle \underset{\sim}{\alpha} \rangle_{\underset{\sim}{\mathrm{N}}(0)} = \underset{\sim}{\mathrm{M}} \langle \underset{\sim}{\tilde{\alpha}} \rangle_{\underset{\sim}{\mathrm{N}}(0)} \tag{2.7}$$

but now with the conservation relation

$$\sum_{i=1}^{N} \alpha_i = 0 \tag{2.7a}$$

(b) The fundamental solutions

As in ref. 7 the treatment of fluctuations will be based upon the fundamental solution matrix $\underset{\sim}{\Omega}(t)$ for $\langle \underset{\sim}{\alpha} \rangle$ of Eqn. 2.7: The elements $\Omega_{ik}(t)$ of $\underset{\sim}{\Omega}$ are defined as solutions

$$\Omega_{ik}(t) := \langle \alpha_i(t) \rangle_{\left(\alpha_j(0) + N_j^s = \begin{cases} 1 & \text{for } j = k \\ 0 & \text{otherwise} \end{cases}\right)} \tag{2.8}$$

i.e. $\Omega_{ik}(t)$ is the expectation value of the deviation $\alpha_i(t)$ from the steady state for one pore, which at $t = 0$ is in the state k. The general solution of Eqn. 2.7 and hence also of Eqn. 2.2 is given by the fundamental matrix through

$$\langle \underset{\sim}{\alpha}(t) \rangle_{\underset{\sim}{\alpha}(0)} = \underset{\sim}{\Omega}(t) \cdot (\underset{\sim}{\tilde{\alpha}}(0) + \underset{\sim}{\tilde{N}}^s) \tag{2.9}$$

We emphasize that often in the standard literature (e.g. ref. 12) the fundamental matrix includes the stationary solution $\underset{\sim}{N}^s$, which is omitted in our definition of $\underset{\sim}{\Omega}(t)$.

(c) Fluxes and electric current

At this point, before we discuss the fluxes and the electric current generated by the transport system, we should make a remark concerning the reaction scheme represented by Eqn. 2.2: As pointed out, each pore can be found in N different occupation states, which in the Eqns. 2.2 are distinguished. One state is the empty pore. The conservation relation Eqn. 2.4 is a consequence of the fact that at any time each pore is in exactly one of these states. Reaction schemes described by homogeneous equations and satisfying conservation relations are often called closed systems. But we emphasize that the single-file transport system itself, described by such a closed reaction scheme, is open in the sense that ions may enter and leave the pores. As will be made clear below at the special example of pores with two binding sites the reaction scheme may contain closed loops.

In ref. 7 we have considered transport systems, where the occupation numbers were assumed to be the numbers of particles at the binding sites. The fluxes were built up by jumps of particles from one binding site to another one. On the other hand in this paper in Eqn. 2.2 the occupation number N_i is the number of pores in state i. Nevertheless also in the single-file model a transition of a pore from state k to state i is connected with a jump of a particle from a binding site to an adjacent one. These jumps build up the individual fluxes, consisting of a sum of δ-functions. This connection of a transition $k \rightarrow i$ with an individual unidirectional flux of a particle makes possible an analogous treatment of fluctuations in fluxes.

Formally as in ref. 7 we introduce a 'flux' matrix $\underset{\sim}{\phi}$ with the elements ϕ_{ik} denoting the 'flux' (number of transitions $(k \rightarrow i)$ from state k to state i). ϕ_{ii} is set equal to zero. Microsopically ϕ_{ik} consists of a sum of identical δ-pulses, each pulse generated by a transition $k \rightarrow i$ of one special pore. Because interactions between different pores are neglected the probability per unit time of a transition $k \rightarrow i$ is proportional to the number N_k of pores in state k and the jump rate M_{ik}. Hence the ensemble averaged expectation values $\langle \phi_{ik} \rangle$ of ϕ_{ik} are given by

$$\langle \phi_{ik}(t) \rangle = M_{ik} \langle N_k(t) \rangle \quad \text{for} \quad i \neq k \tag{2.10}$$

The stationary expectation values are indicated by $\langle \phi^{\mathrm{s}}_{ik} \rangle$

$$\langle \phi^{\mathrm{s}}_{ik} \rangle := M_{ik} \cdot (\lim_{t \rightarrow \infty} \langle N_k(t) \rangle) \tag{2.11}$$

For the calculation of fluctuations in fluxes we need the 'fundamental' expected fluxes

$$\langle \varphi^{\mathrm{k}}_{ij}(t) \rangle := M_{ij} \Omega_{jk}(t) \tag{2.12}$$

The $\langle \varphi^{\mathrm{k}}_{ij} \rangle$ describe the deviation from the stationary flux $\langle \phi^{\mathrm{s}}_{ik} \rangle$ for one single pore under the initial condition Eqn. 2.8 that the pore at $t = 0$ is in state k.

As already pointed out, a transition $k \rightarrow i$ of one pore is connected with a jump of an ion from a binding site to an adjacent one and yields a contribution to the electric current J in the outer circuit. Hence the observable quantity electric current J is given by a linear combination

$$J = \sum_{i,k=1}^{N} \gamma_{ik} \phi_{ik} \tag{2.13}$$

Obviously the contributions of transitions $i \rightarrow k$ and $k \rightarrow i$ to J differ only in sign and $\underset{\sim}{\gamma}$ is an antisymmetric matrix

$$\gamma_{ik} = -\gamma_{ki} \tag{2.14}$$

(3) Autocorrelation function and spectral density of the electric current

Analogously as in ref. 7 we can calculate the fluctuations of the electric current around steady states by a treatment of the correlations between transitions individual fluxes $i \rightarrow k$ and $j \rightarrow l$ at different times. We introduce a fourth order correlation matrix $\underset{\sim}{C}(t)$ with elements $C_{ik,jl}(t)$ representing the ensemble averaged correlations between ϕ_{ik} at one time and ϕ_{jl} at the same time or later. Because we consider fluctuations around steady states, the correlations can be referred to time zero. In $C_{ik,jl}(t)$ only the contributions of the fluctuating part of fluxes are taken into account. Hence

$$\begin{aligned} C_{ik,jl}(t) &:= \langle (\phi_{ik}(0) - \langle \phi^{\mathrm{s}}_{ik} \rangle)(\phi_{jl}(t) - \langle \phi^{\mathrm{s}}_{jl} \rangle) \rangle \\ &= \langle \phi_{ik}(0) \phi_{jl}(t) \rangle - \langle \phi^{\mathrm{s}}_{ik} \rangle \langle \phi^{\mathrm{s}}_{jl} \rangle \end{aligned} \tag{3.1}$$

for $i \neq k$, $j \neq l$ and $C_{ik,jl} = 0$ otherwise

We derive a general expression for $C_{ik,jl}(t)$ with the following arguments. Non-zero contributions to the ensemble average $\langle \phi_{ik}(0) \cdot \phi_{jl}(t) \rangle$ can only occur when just at $t = 0$ a pore makes a transition $k \rightarrow i$. This means that we have to take the ensemble average only over the subclass of realizations with the initial condition (see Eqn. 2.8) for one pore to be in state i. One pore is correlated only with itself, because the pores act independently of each other. The time-independent part of $\langle \phi_{ik}(0) \cdot \phi_{jl}(t) \rangle$ cancels the second part of the right-hand side of Eqn. 3.1. Hence we can write for $C_{ik,jl}(t)$

$$\begin{aligned} C_{ik,jl}(t) &= \langle \phi_{ik}(0) \cdot (\delta_{ik,jl} \cdot \delta(t) + M_{jl}\Omega_{li}(t)) \rangle \\ &= \langle \phi_{ik}(0) \rangle \cdot (\delta_{ik,jl} \cdot \delta(t) + M_{jl}\Omega_{li}(t)) \end{aligned} \tag{3.2}$$

with

$$\delta_{ik,jl} = \begin{cases} 1 & \text{for} \quad (i, k) = (j, l) \\ 0 & \text{otherwise} \end{cases} \tag{3.2a}$$

The first δ-like term in the bracket on the right-hand side of Eqn. 3.2 contains the correlation of a transition $k \rightarrow i$ with itself at time zero. This term yields a shot noise contribution to the current noise spectrum Eqn. 3.7 below. The second term takes into account the ensemble averaged, i.e. expectation value of the contribution of transitions (flux) $l \rightarrow j$ as consequence of the transition $k \rightarrow i$ at time zero (see Eqns. 2.8 and 2.12).

Because we consider fluctuations around steady states, $\langle \phi_{ik}(0) \rangle$ is given by

$$\langle \phi_{ik}(0) \rangle = \langle \phi^{s}_{ik} \rangle = M_{ik} N^{s}_{k} \quad \text{for} \quad i \neq k \tag{3.3}$$

With Eqns. 3.3 and 3.2 the correlations are

$$C_{ik,jl}(t) = M_{ik} N^{s}_{k} \cdot (\delta_{ik,jl}\, \delta(t) + M_{jl}\Omega_{li}(t)) \tag{3.4}$$

for $i \neq k$, $j \neq l$ and

$$C_{ik,jl} = 0 \quad \text{for} \quad i = k \quad \text{or} \quad j = l$$

The autocorrelation function of the fluctuating part ΔJ of the electric current J is with Eqn. 2.13 given by a linear combination of the elements of $\underset{\sim}{C}$ (compare Eqn. 3.5 in ref. 7):

$$\begin{aligned} \langle \Delta J(0) \cdot \Delta J(t) \rangle := &\sum_{i,k,j,l=1}^{N} \gamma_{ik} \gamma_{jl} C_{ik,jl}(t) \\ = &\sum_{i,k,j,l=1}^{N} \gamma_{ik} \gamma_{jl} M_{ik} N^{s}_{k} (\delta_{ik,jl} \delta(t) + M_{jl}\Omega_{li}(t) \end{aligned} \tag{3.5}$$

The noise spectrum G_J of J is given by the Wiener-Khintchine relations:

$$G_J(\omega) = 4 \int_0^{\infty} \langle \Delta J(0) \Delta J(t) \rangle \cos \omega t \, \mathrm{d}t \tag{3.6}$$

Hence with Eqn. 3.5

$$G_J(\omega) = \sum_{i,k,j,l=1}^{N} \gamma_{ik} \gamma_{jl} M_{ik} N^{s}_{k} \times (2\delta_{ik,jl} + 4M_{jl} \int_0^{\infty} \Omega_{li}(t) \cos \omega t \, \mathrm{d}t) \tag{3.7}$$

(4) Pores with two binding sites, one ion species

(a) Single-file equations, comparison with usual jump diffusion

We apply the general theoretical approach to the most simple example of pores with two binding sites and one ion species. In this case an individual pore can be found in four different states: As shown in Fig. 1 the empty pore is characterized by $|00|$, the pore with one ion at the first binding site by $|10|$, etc. The transition $|00| \rightarrow |10|$ is determined by the rate constant k^{10}_{00}, the number of pores in state $|00|$ is N_{00} etc. Then the time dependence for the expectation values is given by the following homogeneous set of equations:

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}\langle N_{00}\rangle &= -(k^{10}_{00} + k^{01}_{00})\langle N_{00}\rangle + k^{00}_{10}\langle N_{10}\rangle + k^{00}_{01}\langle N_{01}\rangle \\
\frac{\mathrm{d}}{\mathrm{d}t}\langle N_{01}\rangle &= -(k^{00}_{01} + k^{10}_{01} + k^{11}_{01})\langle N_{01}\rangle + k^{01}_{00}\langle N_{00}\rangle + k^{01}_{10}\langle N_{10}\rangle + k^{01}_{11}\langle N_{11}\rangle \\
\frac{\mathrm{d}}{\mathrm{d}t}\langle N_{10}\rangle &= -(k^{00}_{10} + k^{01}_{10} + k^{11}_{10})\langle N_{10}\rangle + k^{10}_{00}\langle N_{00}\rangle + k^{10}_{01}\langle N_{01}\rangle + k^{10}_{11}\langle N_{11}\rangle \\
\frac{\mathrm{d}}{\mathrm{d}t}\langle N_{11}\rangle &= -(k^{01}_{11} + k^{10}_{11})\langle N_{11}\rangle + k^{11}_{01}\langle N_{01}\rangle + k^{11}_{10}\langle N_{10}\rangle
\end{aligned} \tag{4.1}$$

These four equations are not independent. If N_p is the total number of pores, they satisfy the conservation relation:

$$N_{00} + N_{10} + N_{01} + N_{11} = N_p = \text{constant} \tag{4.2}$$

We number the four states in the following way (see Fig. 1)

$$|10| \leftrightarrow 1, \quad |01| \leftrightarrow 2, \quad |11| \leftrightarrow 3, \quad |00| \leftrightarrow 4 \tag{4.3}$$

Then we can write Eqn. 4.1 in the form

$$\frac{\mathrm{d}}{\mathrm{d}t}\langle N_i\rangle = \sum_{k=1}^{4} M_{ik}\langle N_k\rangle \quad \text{for} \quad i = 1, 2, 3, 4$$

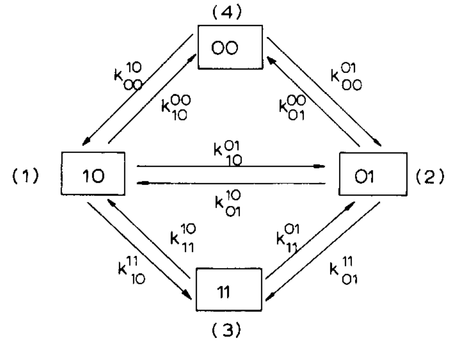

Fig. 1. State diagram for single-file diffusion in pores with two binding sites and one ion species.

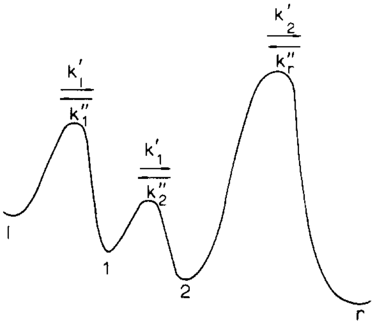

Fig. 2. Potential profile and jump rates for jump diffusion in pores with two binding sites. l and r denote the reservoirs of constant concentrations on the left and right pore mouths, respectively.

with

$$\underset{\sim}{M} = \begin{pmatrix} -(k^{00}_{10} + k^{01}_{10} + k^{11}_{10}) & k^{10}_{01} & k^{10}_{11} & k^{10}_{00} \\ k^{01}_{10} & -(k^{00}_{01} + k^{10}_{01} + k^{11}_{01}) & k^{01}_{11} & k^{01}_{00} \\ k^{11}_{10} & k^{11}_{01} & -(k^{01}_{11} + k^{10}_{11}) & 0 \\ k^{00}_{10} & k^{00}_{01} & 0 & -(k^{10}_{00} + k^{01}_{00}) \end{pmatrix} \tag{4.4}$$

The time dependence of the occupation numbers N_i is determined by the eigenvalues of $\underset{\sim}{M}$. Because of the conservation relation Eqn. 4.2, at least one eigenvalue is zero, i.e. Eqn. 4.1 has a non-trivial stationary solution N_i^s. For a better understanding of the meaning of the rate constants appearing in Eqns. 4.1 and 4.4 it is useful to consider the simple transport model for pores with two binding sites and negligible interactions between the ions (see Fig. 2). Obviously interactions may be neglected if at all times the number of empty pores is great compared with the number of pores occupied by one or two ions. In this case the phenomenological transport equations for the expectation values of the total numbers n_1, n_2 of ions at the first and second binding site are

$$\begin{aligned} \frac{\mathrm{d}}{\mathrm{d}t}\langle n_1\rangle &= k'_l \cdot n_l - (k'_1 + k''_1)\langle n_1\rangle + k''_2\langle n_2\rangle \\ \frac{\mathrm{d}}{\mathrm{d}t}\langle n_2\rangle &= k'_1\langle n_1\rangle - (k'_2 + k''_2)\langle n_2\rangle + k''_r n_r \end{aligned} \tag{4.5}$$

n_l and n_r are constant concentrations (reservoir) at the left and right pore mouths, respectively.

The rate constants k'_i, k''_i $(i = 1, 2)$ in Eqn. 4.5 are related to the rate constants in Eqn. 4.1 for those transitions between different states of the pores which are not dependent on ionic interactions. These transitions are between the states $|00|$, $|01|$ and $|10|$.

One finds easily

$$\begin{aligned} &k^{01}_{10} = k'_1, \quad k^{10}_{01} = k''_2, \\ &k^{00}_{01} = k'_2, \quad k^{00}_{10} = k''_1 \end{aligned} \tag{4.6a}$$

and

$$k_{00}^{10} N_{\mathrm{p}} = k_l' n_l, \quad k_{00}^{10} N_{\mathrm{p}} = k_{\mathrm{r}}'' n_{\mathrm{r}}. \tag{4.6b}$$

As already emphasized in section 2, the single-file Eqns. 4.1 determine the time dependence of the occupation numbers of the four possible states of the pores, while Eqns. 4.5 are transport equations describing the time dependence of the numbers of binding sites 1 or 2 which, summed over all pores, are occupied by an ion.

Clearly, one gets approximately the jump diffusion Eqns. 4.5 from Eqn. 4.1 in the limit

$$\begin{aligned} k_{00}^{10} &<< k_{10}^{00}, \quad k_{00}^{01} << k_{01}^{00}, \\ k_{10}^{11} &<< k_{11}^{10}, \quad k_{01}^{11} << k_{11}^{01}, \end{aligned} \tag{4.7a}$$

and with Eqn. 4.6. If Eqn. 4.7a is valid, the number of pores occupied by one or two ions is small compared with the number N_{00} of empty pores and the number N_{11} of pores occupied by two ions is small compared with the number N_{10} or N_{01} of pores occupied by only one ion. Hence

$$N_{10} \approx n_1, \quad N_{01} \approx n_2, \quad N_{11} \approx 0 . \tag{4.7b}$$

Another important limiting case contained in Eqn. 4.1 is the case where the state $|11|$ is forbidden. It has been proposed [12] that possibly in some cases for electrostatic reasons a single pore can be occupied by only one ion. Clearly, in this case N_{10} is equal to the number of ions at binding site 1 and N_{01} at binding site 2:

$$N_{10} = n_1, \quad N_{01} = n_2. \tag{4.7}$$

In this case one can get from Eqn. 4.1 two transport equations for n_1 and n_2 by setting $N_{11} = 0$ and replacing N_{00} by $(N_{\mathrm{p}} - n_1 - n_2)$

$$\begin{aligned} \frac{\mathrm{d}}{\mathrm{d}t} \langle n_1 \rangle &= k_l \left(1 - \frac{\langle n_1 \rangle + \langle n_2 \rangle}{N_{\mathrm{p}}}\right) n_l - (k_1' + k_1'')\langle n_1 \rangle + k_2'' \langle n_2 \rangle \\ \frac{\mathrm{d}}{\mathrm{d}t} \langle n_2 \rangle &= k_{\mathrm{r}} \left(1 - \frac{\langle n_1 \rangle + \langle n_2 \rangle}{N_{\mathrm{p}}}\right) n_{\mathrm{r}} - (k_2' + k_2'')\langle n_2 \rangle + k_1' \langle n_1 \rangle \end{aligned} \tag{4.8}$$

in agreement with ref. 12.

In the following model calculations of spectra for special examples we shall include both limiting cases.

(b) Numerical calculations of spectra

We have performed a number of explicit calculations of current noise spectral densities generated by single-file ion transport in pores with two binding sites. According to the general formula Eqns. 3.5—3.7 the fluctuations are calculated with the use of the fundamental solution matrix $\underset{\sim}{\Omega}$. The explicit way of calculation of $\underset{\sim}{\Omega}$ and of spectral density G_J is described in the appendix for both cases of real or real and complex eigenvalues of $\underset{\sim}{M}$. The dependence of the spectral density on different parameters as the transition probabilities or the constants γ_{ik} determining the contributions of the individual transitions to the measured current seems to be rather complicated. We have tried to work out some typical dependences and properties. In order to investigate possible effects of the number of binding sites especially on the oscillatory behavior we have done one calculation for a simple case of pores with three binding sites.

(1) Equilibrium. Calculations of spectra of current noise at equilibrium ($J = 0$), are presented in Fig. 3: Cases a and c simulate the two limiting cases of very strong electrostatic interactions between the ions and negligible interactions given by Eqns. 4.8 and 4.5, respectively. In the latter example where the probabilities for entrance of ions into the pores are small (see Eqn. 4.6), we have taken into account this fact by multiplying G_J with a factor 100, assuming that the number of pores in this case is a hundred times greater as in the other cases. Hence the results for G_J in Fig. 3, though in arbitrary units, are normalized to the condition that the average number of ions within all pores is approximately equal. The shape of the three spectra shows no essential differences.

The state diagrams in cases a and b show closed loops. In case a, where the state $|11|$ may be neglected, the number of closed loops is one and in case b three. At equilibrium the rate constants for closed loops satisfy the so-called Wegscheider conditions (see e.g. refs. 8—10) which are equivalent to the principle of microscopic reversibility [8]. In this case it can generally be shown that all eigenvalues of $\underset{\sim}{M}$ according to Eqn. 4.2 are real and non-positive. For the case c of negligible interactions between the ions it can generally be shown (e.g. ref. 7) for arbitrary numbers of binding sites within the pores and at equilibrium as well as at non-equilibrium, that all eigenvalues are real. Hence at

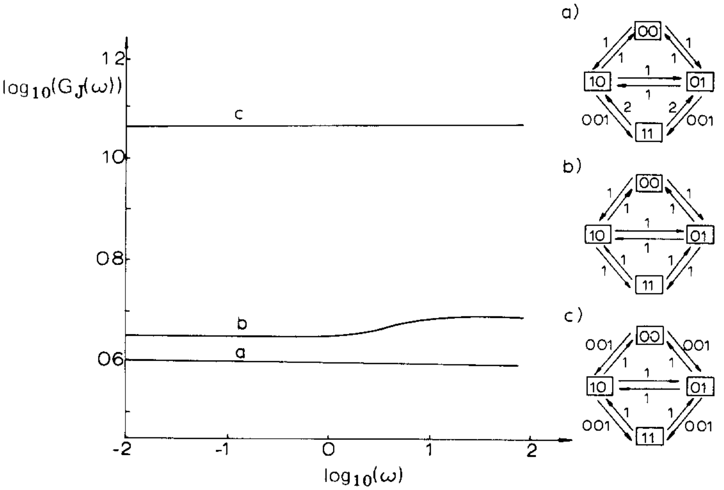

Fig. 3. Spectra G_J of current noise at equilibrium ($J = 0$) for different transport models (arbitrary units). The state diagrams illustrate the different model situations being calculated (compare Fig. 1). (a) One ion case: the probability that a pore contains more than one ion, i.e. to be in state $|11|$, is very small, because k_{01}^{11} and k_{10}^{11} are small. (b) General single-file model with equal transition probabilities between all four states. (c) Usual jump diffusion case (Eqn. 4.5): the probability of pores being empty (state $|00|$) is great compared with the probability of pores being occupied. The contributions of the individual transitions to the measured current, which are determined by the constants γ_{lk} (see Eqn. 2.13), are set equal $\gamma_{41} = \gamma_{12} = \gamma_{24} = \gamma_{23} = \gamma_{31} = -\gamma_{14} = -\gamma_{21} = -\gamma_{42} = -\gamma_{32} = -\gamma_{13}$.

equilibrium the single-file transport is non-oscillatory and the spectra show no peaks.

(2) Non-equilibrium. Away from equilibrium in cases a and b the eigenvalues of $\underset{\sim}{M}$ may be complex (see e.g. refs. 8—10), because the Wegscheider conditions are no longer satisfied and the state diagrams represent driven cycling steady states. This means that the single-file transport may possibly exhibit damped oscillatory behavior (compare ref. 12). As consequence the resulting spectra may show peaks. Probably the weakest damping of oscillations occurs in those cases where transitions in only one direction are possible [8—10,12]. In this case the effect of oscillatory transport is expected to have the greatest influence on the spectra. This may be seen from the structure of G_J in Eqn. A.8b which is similar to resonance curves of the forced oscillations of a damped harmonic oscillator. The minimum damping can be achieved by applying high voltage, forcing the ions to jump in only one direction.

Some typical features of non-equilibrium single-file noise are demonstrated by the numerical results in Fig. 4. In case b the spectrum shows a peak as consequence of the oscillatory behavior of solutions of Eqn. 4.1. In case a the spectrum is white, though two eigenvalues of $\underset{\sim}{M}$ are complex and hence the fundamental solution matrix $\underset{\sim}{\Omega}$ has an oscillatory time dependence. Nevertheless the oscillatory terms in G_J cancel each other because of the special choice of the constants γ_{ik}. Generally, in addition to the structure of the solution of the single-file transport equations, the behavior of electric current and spectrum are strongly dependent on the γ_{ik} and hence, e.g. on the dielectric and

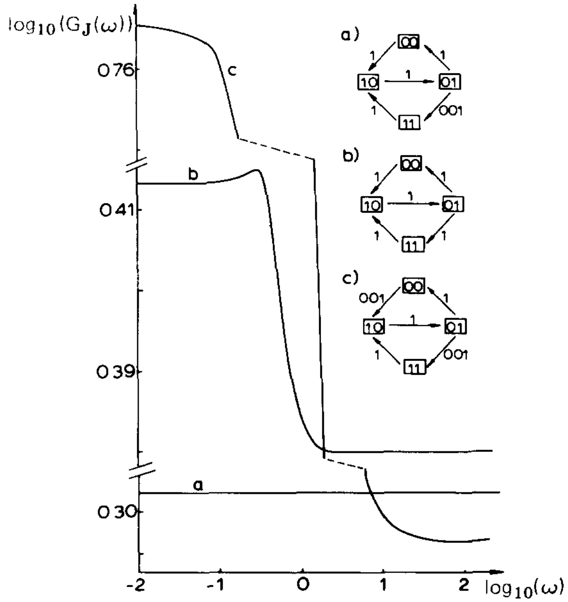

Fig. 4. Spectra G_J of current noise for different transport models at non-equilibrium ($J \neq 0$). The state diagrams illustrate the different calculated model situations, which correspond to Fig. 3. The applied voltage is assumed to be high, so that jumps of ions take place only in one direction.

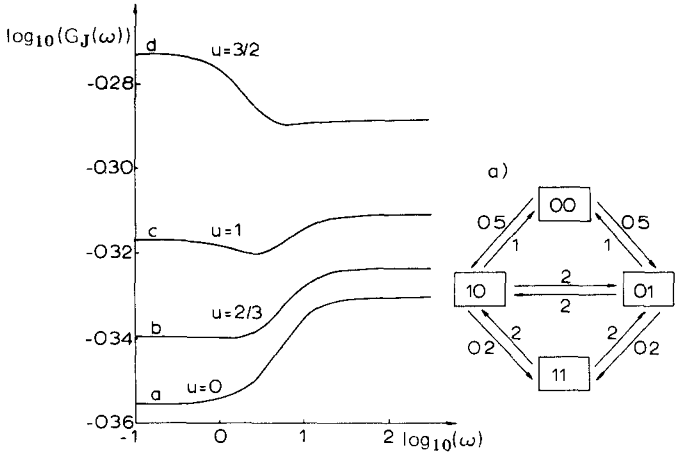

Fig. 5. The effect of an applied voltage on the spectrum G_J of current noise generated by a single-file transport model. The change of jump constants under the influence of different applied voltages is taken into account by different values of u (see Eqn. 4.9).

geometric properties of the transport system. In case c of negligible interactions the spectrum exhibits a Lorentz-type behavior.

(3) The effect of an applied voltage. A typical effect of an applied voltage on the spectra of single-file noise is demonstrated in Fig. 5. At equilibrium (case a) the low frequency limit of G_J is lower than the high frequency limit. This inverse Lorentz spectrum behavior seems to be typical of equilibrium transport noise and has recently been observed by Kolb and Läuger [16,17]. It may possibly be explained by the influence of long-time correlations.

The state diagram in Fig. 5 shows a special choice of rate constants at equilibrium (case a). With the onset [18] for the rate constants

$$k_{ik} = \bar{k}_{ik}\, e^{\gamma_{ik}\, u} \qquad (4.9)$$

(k_{ik}, equilibrium value of rate constant for transitions $k \rightarrow i$; $u = Ve_0/kT$; V, applied voltage; e_0, elementary charge; k, Boltzmann's constant; T, absolute temperature) an increasing applied voltage can be taken into account by increasing u. The absolute values of all γ_{ik} are assumed to be equal (=1/3). For transitions connected with jump of ions to the right (left) γ_{ik} is chosen positive (negative). As shown by Fig. 5 with increasing applied voltage the low frequency limit increases. In cases b and c the spectra show (weak) minima.

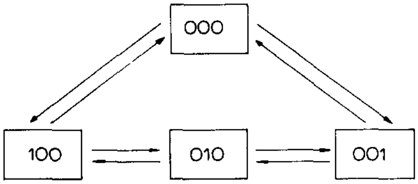

Fig. 6. State diagram for single-file transport in pores with three binding sites under the restriction that the single pore contains not more than one ion.

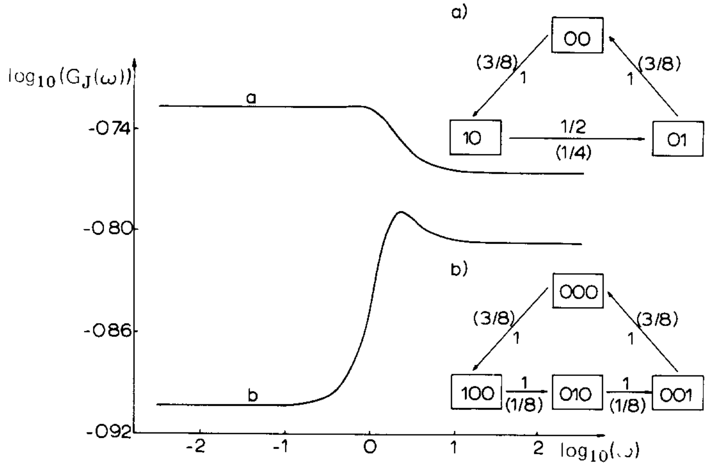

Fig. 7. Peaking of current noise spectra due to oscillatory behavior of single-file diffusion at high applied voltage in pores with two (case a) and three (case b) binding sites. The single-file model is restricted to the case where the single pore contains no more than one ion. According to the state diagrams the steady states are driven cycling steady states violating the Wegscheider conditions. The chosen values of γ_{ik} are set in brackets.

(4) The effect of the number of binding sites on the damping of the oscillations. Even in the theoretically most favorable case the damping of the oscillations is very strong in pores with two binding sites. This means that peaks in the spectrum are very weak. For several reasons one expects the damping to become weaker in pores with more binding sites resulting in stronger peaks in G_J. We have calculated the current noise spectrum for the simple example of pores with three binding sites in the one-ion case and compared it with the corresponding results for pores with two binding sites.

Fig. 6 shows the state diagram for the case where the pores cannot be occupied by more than one ion. The transport equations in this case are easily derived analogously as Eqn. 4.8 and the spectral density is calculated similarly as described in Appendix. Indeed in the case calculated and shown in Fig. 7 the damping of the oscillatory term is weaker, about by a factor 10, than for the corresponding pore with two binding sites where the two transitions $|100| \rightarrow |010| \rightarrow |001|$ with jump constants = 1/2 are replaced by one jump $|10| \rightarrow |01|$ with jump constant = 1. As consequence the peak in G_J becomes stronger. This result indicates that the number of binding sites within the pores strongly influences the oscillatory single-file transport phenomena.

Appendix

In this appendix we describe the derivation of the fundamental solution matrix $\underset{\sim}{\Omega}$ of Eqns. 4.1 and give an explicit formula for the spectral density of the electric current. For simplicity, we assume that the coefficient matrix $\underset{\sim}{M}$ according to Eqn. 4.2 has distinct eigenvalues (both real or complex). Under this assumption $\underset{\sim}{M}$ is diagonalizable with the eigenvalues λ_k as diagonal elements. Moreover we have four linearly independent eigenvectors $\underset{\sim}{v}_k$, which satisfy the relation

$$\underset{\sim}{M}\underset{\sim}{v}_k = \lambda_k \underset{\sim}{v}_k \quad \text{for} \quad k = 1, 2, 3, 4\,. \tag{A1}$$

In general the eigenvalues λ_k may be complex numbers. Therefore they can be written as $\lambda_k = \zeta_k + i \cdot \vartheta_k$. The related eigenvectors $\underset{\sim}{v}_k$ are complex column matrices, i.e. they can be written as $\underset{\sim}{v}_k = \underset{\sim}{r}_k + i\ \underset{\sim}{\omega}_k$ with $\underset{\sim}{r}_k$, $\underset{\sim}{\omega}_k$ as real column matrices. With the λ_k and $\underset{\sim}{v}_k$ also the complex conjugates λ and $\underset{\sim}{v}_k$ are eigenvalues and eigenvectors of $\underset{\sim}{M}$, respectively.

The functions

$$\underset{\sim}{X}_k(t) := \underset{\sim}{v}_k\ e^{\lambda_k t} \quad \text{for} \quad k = 1, 2, 3, 4, \tag{A2}$$

are solutions of Eqn. 4.1 and may be complex. To get real solutions we take any complex solution X_l, $1 \leqslant l \leqslant 4$, and write it in the form

$$\underset{\sim}{X}_l = (\underset{\sim}{r}_l \cdot \cos \vartheta_l t - \underset{\sim}{w}_l \cdot \sin \vartheta_l t)\, e^{\zeta_l t} + i(\underset{\sim}{r}_l \cdot \sin \vartheta_l t + \underset{\sim}{w}_l \cdot \cos \vartheta_l t)\, e^{\zeta_l t}$$

Since λ_l and $\bar{\lambda}_l$ are distinct, the eigenvectors v_l and $\bar{v}_l$ are linearly independent, and consequently the vectors $\underset{\sim}{r}_l$ and $\underset{\sim}{w}_l$ too. That means, the real and the imaginary part of X_l form two linearly independent real solutions of Eqn. 2.2 and we do not need $X_k = v_l\ e^{\lambda_l t}$ to get four linearly independent solutions.

In order to form the fundamental matrix of the differential Eqn. 4.1 we distinguish between two cases: (a) all eigenvalues of $\underset{\sim}{M}$ are real and (b) there are also complex eigenvalues. In case (a) let $\underset{\sim}{W}(t)$ be the four-dimensional matrix

$$\underset{\sim}{W}(t) := (\underset{\sim}{r}_1\ e^{\lambda_1 t}, \underset{\sim}{r}_2\, e^{\lambda_2 t}, \underset{\sim}{r}_3\, e^{\lambda_3 t}, \underset{\sim}{r}_4), \tag{A3a}$$

and in case (b) we set

$$\underset{\sim}{W}(t) := (\underset{\sim}{r}_1\, e^{\lambda_1 t}, (\underset{\sim}{r}_2 \cdot \cos \vartheta_2 t - \underset{\sim}{w}_2 \cdot \sin \vartheta_2 t)\, e^{\zeta_2 t}, (\underset{\sim}{r}_2 \cdot \sin \vartheta_2 t + \underset{\sim}{w}_2 \cdot \cos \vartheta_2 t)\, e^{\zeta_2 t}, \underset{\sim}{r}_4) \tag{A3b}$$

Therein, λ_1 denotes a real eigenvalue, λ_2 and λ_3 are both real, complex (with $\lambda_2 = \bar{\lambda}_3$), respectively. The eigenvector $\underset{\sim}{r}_4$ belongs to the eigenvalue $\lambda_4 = 0$. Since all eigenvectors are linearly independent the inverse matrix $\underset{\sim}{H}$ with the elements h_{ij} of $\underset{\sim}{W}(0)$ exists, and we are able to define

$$\underset{\sim}{\overline{\Omega}}(t) := \underset{\sim}{W}(t) \cdot \underset{\sim}{H} \tag{A4}$$

The functions $\overline{\Omega}_{li}$ are defined for all real t. In the limit $t \to \infty$ one gets

$$\Omega_{li}(\infty) := r_{14} h_{4i} \tag{A5}$$

because apart from $\lambda_4 = 0$ all eigenvalues of $\underset{\sim}{M}$ are real negative or have a negative real part [13]. We call the matrix

$$\underset{\sim}{\Omega}(t) := \underset{\sim}{\overline{\Omega}}(t) - \underset{\sim}{\overline{\Omega}}(\infty) \tag{A6}$$

a fundamental solution matrix of the differential Eqn. 4.1. This definition is consistent with Eqn. 2.9.

Finally we obtain the spectral density of the electric current by carrying out the integration in formula 3.7:

$$G_J(\omega) = 2 \cdot \sum_{i,k=1}^{4} \gamma_{ik}^2 M_{ik} N_k^s + 4 \cdot \sum_{i,k,j,l=1}^{4} \gamma_{ik} \gamma_{jl} M_{ik} M_{jl} N_k^s \cdot I_{li} \tag{A7}$$

For which in case (a)

$$I_{li} := - \sum_{n=1}^{3} \frac{\lambda_n}{\lambda_n^2 + \omega^2} \cdot r_{ln} h_{ni} \tag{A8a}$$

and in case (b)

$$I_{li} := - \frac{\lambda_1}{\lambda_1^2 + \omega^2} \cdot r_{l1} h_{1i} + \{(-w_{l2} h_{2i} + r_{l2} h_{3i}) \cdot \vartheta_2 \cdot (\zeta_2^2 + \vartheta_2^2 - \omega^2)$$

$$- (w_{l2} h_{3i} + r_{l2} h_{2i}) \cdot \zeta_2 \cdot (\zeta_2^2 + \vartheta_2^2 + \omega^2)\}/R \tag{A8b}$$

with

$$R := (\omega^2 - |\lambda_2|^2)^2 + 4\zeta_2^2 \omega^2$$

Acknowledgements

We wish to thank Professor P. Läuger for interesting discussions and Beatrix Kleutsch for assistance in the numerical calculations. This work has been supported by the Deutsche Forschungsgemeinschaft.

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