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# CURRENT FLUCTUATIONS IN DISCRETE TRANSPORT SYSTEMS FAR FROM EQUILIBRIUM. BREAKDOWN OF THE FLUCTUATION DISSIPATION THEOREM

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A recently developed theoretical approach to transport fluctuations around stable steady states in discrete biological transport systems is used in order to investigate general fluctuation properties at nonequilibrium. An expression for the complex frequency dependent admittance at nonequilibrium is derived by calculation of the linear current response of the transport systems to small disturbances in the applied external voltage. It is shown that the Nyquist or fluctuation dissipation theorem, by which at equilibrium the macroscopic admittance or linear response can be expressed in terms of fluctuation properties of the system, breaks down at nonequilibrium. The spectral density of current fluctuations is decomposed into one term containing the macroscopic admittance and a second term which is bilinear in current. This second term is generated by microscopic disturbances, which cannot be excited by external macroscopic perturbations. At special examples it is demonstrated that this second term is decisive for the occurrence of excess noise e.g. the $1/f^2$-lorentzian noise generated by the opening and closing of nerve channels in biological membranes.

## 1. Introduction

In the last years the analysis of electrical fluctuations in biological membrane transport systems has become an important method (see e.g. [1–5]). Valuable information on the ion transport mechanism in membranes can be obtained from electrical noise measurements. A number of different processes as e.g. the statistical opening and closing of ion channels or the stochastic properties of the ionic movement [6] could be shown to be possible sources of the random current or voltage fluctuations.

Since biological transport systems may be rather complex, a number of papers concerning theoretical concepts for the analysis of noise measurements has been written (see e.g. [7–9] and further references cited in [2–5]). In many cases older methods as e.g. the so-called master equation approach [10,11], developed for the analysis of fluctuation phenomena in physical and chemical systems, could be used. Generally, for systems in thermal equilibrium the Nyquist theorem or fluctuation-dissipation theorem [12–14], relating the current (voltage) noise spectrum to the macroscopic frequency dependent admittance can be applied [8]. We recently have developed a formalism for the treatment of electrical fluctuations around equilibrium and nonequilibrium steady states in discrete transport systems, where the different discrete states may be given by different binding sites for the transported particles (ions) as well as by different, e.g. chemical states [9]. We could demonstrate the universal applicability of this approach to biological transport systems as e.g. ion transport through membrane channels, carrier mediated ion transport, single-file transport and electric fluctuations generated by gating mechanisms [9,12–14].

In this paper we shall use this formalism for the investigation of problems of more general interest concerning general properties of fluctuations in systems around steady states far from thermal equilibrium.

At equilibrium the power spectrum $G_{\Delta J}(\omega)$ of the electric current fluctuations is according to the Nyquist theorem or fluctuation dissipation theorem given by the real part Re $Y(\omega)$ of the frequency dependent complex admittance $Y(\omega)$

$$G_{\Delta J}(\omega) = 4kT \operatorname{Re} Y(\omega), \tag{1.1}$$

($k$ = Boltzmann constant, $T$ = absolute temperature, $\Delta J$ = deviation of current $J$ from stationary current $J^S$).

We shall show in section 4 that generally a relation (1.1) does *not* exist at *nonequilibrium*. Additionally to a first term, which is related to the admittance according to eq. (1.1) and comes from the symmetric part of the flux matrix (c.f. (2.5)–(2.7)), there appears a second contribution to the fluctuations. This second part is generated by the antisymmetric part of the flux matrix, which according to the principle of detailed balance is zero only at equilibrium. In many cases it may easily be interpreted as excess noise and is proportional to the square of the applied voltage. For membrane channels with open-closed kinetic this is just the lorentzian-type noise which is usually measured (c.f. [2–5]). In this connection it is interesting to note that another type of nonequilibrium excess noise, the $1/f$-noise, is proportional to the square of the applied voltage [‡].

In section 2 the concept of current generated in discrete systems is described. The basic assumption is that transitions between discrete states of the system may be connected with measurable current pulses. In section 3 a general expression for the complex admittance is derived using the usual Eyring ansatz (3.5) for the voltage dependence of the rate constants. Though the transport system itself is at non-equilibrium, it is assumed to be in a temperature bath defining the temperature $T$ occurring in the Eyring ansatz. Furthermore a proportionality (3.7) between the voltage difference between two states of the system and the corresponding contribution to the measured current is assumed and made plausible with heuristic arguments in the appendix.

The derivation of the admittance will be done by calculation of the linear current response of the transport systems to small delta-shaped voltage pulses. We shall see that in this way special properties of the frequency dependence of transport fluctuations can be clarified and related to the linear response properties of the systems.

We hope that the decomposition of transport noise into an admittance-term and an excess noise term given below in (4.7) will yield contributions to a better general understanding of fluctuations as e.g. the shape of fluctuation spectra and the problem of minimization of noise at nonequilibrium processes. The latter aspect is discussed in short at the end of this paper. It might be interesting e.g. for the interpretation of biological nonequilibrium transport processes and should be further investigated.

## 2. Current fluctuations in discrete transport systems

We start with a brief summary of the main points and assumptions concerning the treatment of transport fluctuations in discrete transport systems as described previously [9,15,16].

### 2.1. Discrete transport systems

The state of the transport system is described by a set of variables $N_i$, $i = 1, 2, \ldots, n$. The time-dependence of the expectation values $\langle N_i(t)\rangle$ in the vicinity of a stable stationary state $N_i^S$ (linearizable region) is assumed to be given by the linear phenomenological equations

$$\mathrm{d}\langle N_i\rangle/\mathrm{d}t = \sum_{j=1}^{n} M_{ij}\langle N_j\rangle + Y_i. \tag{2.1}$$

The stationary solutions $N_i^S$ of (2.1) are given by the equations

$$\sum_{j=1}^{n} M_{ij}N_j^S + Y_i = 0. \tag{2.2}$$

[‡] After submission of the manuscript of this paper I have got knowledge of the recent work of Procaccia et al. [25,26], concerning the statistical mechanics of nonequilibrium stationary states with application to light scattering experiments. With a completely different approach they also have found (in contradiction to prior studies of steady states) that fluctuations around nonequilibrium stationary states are qualitatively different from equilibrium fluctuations. This difference is caused by a coupling between the fluctuations and the macroscopic fluxes. In our treatment these fluxes correspond to the antisymmetric components ($\phi^S_{\mu\nu} - \phi^S_{\nu\mu}$) of the (unidirectional) fluxes and are also decisive for the occurrence of that part of nonequilibrium transport noise, which is qualitatively different from equilibrium noise. In the cited papers possible light scattering experiments for measuring the nonequilibrium effects are discussed. In the case of electric current fluctuations typical nonequilibrium effects ($1/f$ noise lorentzian noise or carrier noise [17]) have already been measured in agreement with our theoretical results.

Eqs. (2.1) and (2.2) are assumed to describe also the macroscopic behavior of the system, e.g. the time dependent relaxation of $N_i(t)$ after a macroscopic disturbance (Onsager's regression hypothesis).

Introducing the deviations

$$\alpha_i = N_i - N_i^s \tag{2.3}$$

from the stationary state we define the so-called fundamental solutions $\Omega_{ik}(t)$ as solutions $\langle\alpha_i(t)\rangle$ of the phenomenological equations under special initial conditions which distinguish the state $k$

$$\Omega_{ik}(t) = \langle\alpha_i(t)\rangle_{(\alpha_l(0)=\delta_{lk})} \qquad \text{for } Y \neq 0,$$

$$\Omega_{ik}(t) = \langle\alpha_i(t)\rangle_{(\alpha_l(0)+N_l^s\cdot\delta_{lk})} \qquad \text{for } Y = 0, \tag{2.4}$$

where the Kronecker symbol $\delta_{lk} = 1$ for $l = k$ and $\delta_{lk} = 0$ for $l \neq k$.

### 2.2. Fluxes and electric current

Formally the 'fluxes' $\phi_{ik}$, i.e. number of transitions $k \to i$ are introduced. $\phi_{ii}$ is set equal to zero. Because the duration of a transition $k \to i$ is assumed to be infinitely small, $\phi_{ik}$ consists of a sum of delta-shaped pulses, each of which is generated by a transition $k \to i$.

The expectation values of fluxes are given by $\langle N_k(t)\rangle$ and $M_{ik}$

$$\langle\phi_{ik}(t)\rangle = M_{ik}\langle N_k(t)\rangle, \qquad i \neq k \tag{2.5}$$

and the stationary fluxes $\phi_{ik}^s$

$$\phi_{ik}^s = M_{ik}N_k^s. \tag{2.6}$$

In case the system is in contact with $(m - n)$ outer reservoirs, it may be necessary to take into account also the fluxes into, from and between these reservoirs by extending the $(n \times n)$-matrix of fluxes to a $(m \times m)$-matrix $(m > n)$ with the components $\phi_{\mu\nu}$ and introducing the rate constants $M_{\mu\nu}$ $(\mu, \nu > n)$ for the corresponding transitions (compare [9]). E.g.

$$\langle\phi_{\mu i}\rangle = M_{\mu i}N_i(t), \qquad \mu > n, \quad i \leqslant n \tag{2.7}$$

is the expectation value of flux from $i$ to the $(\mu - n)$-th reservoir and the stationary flux $\phi_{\mu\nu}^s$ correspondingly.

We assume that a special transition within the transport system yields a special contribution to the measured electric current $J$. Hence $J$ is given by the linear combination

$$J = \sum_{\mu,\nu=1}^{m} \gamma_{\mu\nu}\phi_{\mu\nu}, \qquad \gamma_{\mu\mu} = 0. \tag{2.8}$$

Obviously the contributions of transitions $\mu \to \nu$ and reverse $\nu \to \mu$ differ only in sign:

$$\gamma_{\mu\nu} = -\gamma_{\nu\mu} \tag{2.9}$$

### 2.3. Autocorrelation function and spectral density of current fluctuations

The derivation of a general expression for the autocorrelation function $C_{\Delta J}(t)$ of the fluctuating part

$$\Delta J = J - J^s \tag{2.10}$$

($J^s$ = stationary current) is done through a determination of the individual correlations $\langle\phi_{\mu\nu}(0)\phi_{\kappa\rho}(t)\rangle$ between the individual fluxes (compare [9,15,16]). Then $C_{\Delta J}(t)$ is a linear combination over all these individual correlations with the general result

$$C_{\Delta J}(t) = \sum_{\mu,\nu=1}^{m} \gamma_{\mu\nu}^2\phi_{\mu\nu}^s\delta(t) + \sum_{\kappa,\nu=1}^{m}\sum_{\mu,\rho=1}^{n} \gamma_{\mu\nu}\gamma_{\kappa\rho}\phi_{\mu\nu}^s M_{\kappa\rho}\Omega_{\rho\mu}(t). \tag{2.11}$$

The spectral density $G_{\Delta J}(\omega)$ of current fluctuations is determined by $C_{\Delta J}(t)$ through the Wiener-Khintchine relations

$$G_{\Delta J}(\omega) = 4\int_0^\infty C_{\Delta J}(t)\cos\omega t\,\mathrm{d}t. \tag{2.12}$$

Hence

$$G_{\Delta J}(\omega) = 2\sum_{\mu,\nu=1}^{m} \gamma_{\mu\nu}^2\phi_{\mu\nu}^s + 4\sum_{\nu,\kappa=1}^{m}\sum_{\rho,\mu=1}^{n} \gamma_{\mu\nu}\gamma_{\kappa\rho}\phi_{\mu\nu}^s M_{\kappa\rho} \times \int_0^\infty \Omega_{\rho\mu}(t)\cos\omega t\,\mathrm{d}t. \tag{2.13}$$

## 3. Admittance

### 3.1. Definition

We assume that additionally to the constant voltage $V^S$ a small (complex) voltage

$$\epsilon(t) = \epsilon_0 \exp(i\omega t) \tag{3.1}$$

is applied to the system. In the linearizable region the corresponding current $J(t)$ is

$$J(t) = J^S + j(\omega, t). \tag{3.2}$$

For the stationary current $J^S$ belonging to the stationary stable state of the transport system the macroscopic conductance $\lambda^S(V^S)$ may be defined by

$$J^S(V^S) = \lambda^S(V^S) \cdot V^S. \tag{3.3}$$

The frequency- and time-dependent current $j(\omega, t)$ can be written as

$$j(V^S, \omega, t) = \epsilon_0 Y(\omega, V^S) \exp(i\omega t), \tag{3.4}$$

where the quantity $Y(\omega, V^S)$ is called the differential complex *admittance* of the system.

### 3.2. Voltage dependence of the rate constants

For the voltage dependence of the rate constants $M_{\mu\nu}$ we can use the Eyring ansatz

$$M_{\mu\nu}(V) = M_{\mu\nu}(V_0)\exp(\alpha_{\mu\nu}u/2),$$

$$u = Ze_0(V - V_0)/kT, \qquad \alpha_{\mu\nu} = -\alpha_{\nu\mu}, \tag{3.5}$$

where $Ze_0$ is the charge being responsible for the generated current pulse during a transition $\nu \to \mu$ in the transport system. The dimensionless number $\alpha_{\mu\nu}$ denotes the fraction $\Delta_{\mu\nu}V/(V - V_0)$ of the voltage difference $\Delta_{\mu\nu}V$ which is seen by the charge $Ze_0$ between states $\nu$ and $\mu$ as consequence of the applied voltage $(V - V_0)$. Naturally $\alpha_{\mu\nu}$ may be zero. The ansatz (3.5) yields the linear expansion of $M_{\mu\nu}$ around $V^S$.

$$M_{\mu\nu}(V^S + \epsilon) = M_{\mu\nu}(V^S)\left[1 + \frac{\epsilon}{2}\frac{\alpha_{\mu\nu}Ze_0}{kT}\right]. \tag{3.6}$$

For energetic reasons it is plausible to assume that the $\alpha_{\mu\nu}$ are directly related to the constants $\gamma_{\mu\nu}$, which according to (2.8) determine the contribution of a transition $\nu \to \mu$ to the measured current $J$ (c.f. also [8]):

$$\alpha_{\mu\nu}Ze_0 = \gamma_{\mu\nu} \tag{3.7}$$

A heuristic derivation of (3.7) is given in the appendix. With (3.7) we get from (3.6)

$$M_{\mu\nu}(V^S + \epsilon) = M_{\mu\nu}(V^S) \times \left[1 + \frac{\epsilon}{2}\gamma_{\mu\nu}\frac{1}{kT}\right]. \tag{3.8}$$

We emphasize that the linear expansion (3.6) of $M_{\mu\nu}$ around $V^S$ and relation (3.7) are explicitely used in the following derivation of a general expression for the admittance.

### 3.3. Linear response and complex admittance

Analogously as spectral density and autocorrelation functions the admittance function $Y(\omega, V^S)$ is connected with the linear current response of the transport system to a small $\delta$-shaped voltage disturbance by Fourier transformation: For

$$(V - V^S) = \xi \cdot \delta(t) \tag{3.9}$$

the resulting curret response is

$$J = J^S + j(t). \tag{3.10}$$

Because of the relation

$$\delta(t) = \int_{-\infty}^{+\infty} e^{i\omega t} d\omega \tag{3.11}$$

and the linear properties of the system, $Y(\omega)$ is given by $j(t)$ through

$$Y(\omega) = \frac{1}{\xi}\int_{-\infty}^{+\infty} j(t)e^{-i\omega t} dt. \tag{3.12}$$

The use of $\delta$-shaped forces is a common method in linear response theory [14]. Naturally a $\delta$-shaped voltage pulse is not small by definition. But "smallness" in this sense means that the disturbances of the variables $N_i$, generated by the pulse, are small and within the linearizable region around $N_i^S$. Furthermore it should be kept in mind that the use of the $\delta$-function in the time domain may be regarded as a special procedure which facilitates the determination of the ex-

pression (3.19) for the admittance in the frequency region. In this sense restriction (3.13) upon the linear expansion of the rate constants is also justified because in the frequency region it leads to the correct linear expansion (3.6).

An expression for the linear response $j(t)$ may simply be derived as follows: With eqs. (2.5)–(2.7) for the macroscopic flux $\phi_{\mu\nu}$ and (3.6), (3.8) for the voltage dependence of the rate constants, the small voltage pulse at $t = 0$ effects a $\delta$-shaped change

$$(M_{\mu\nu} - M_{\mu\nu}(V^s)) = M_{\mu\nu}(V^s) \cdot \frac{\zeta}{2} \cdot \frac{\gamma_{\mu\nu}}{kT} \cdot \delta(t) \qquad (3.13)$$

of the rate constant $M_{\mu\nu}$, which on the other hand is connected with a small macroscopic pulse

$$\tfrac{1}{2}\zeta \frac{\gamma_{\mu\nu}}{kT} M_{\mu\nu} N_\nu^s \delta(t) = \tfrac{1}{2}\zeta \frac{\gamma_{\mu\nu}}{kT} \phi_{\mu\nu}^s \delta(t) \qquad (3.14)$$

in flux $\phi_{\mu\nu}$ at $t = 0$, being proportional to the stationary flux $\phi_{\mu\nu}^s$ itself. Furthermore this macroscopic flux pulse generates a macroscopic disturbance

$$-\tfrac{1}{2}\zeta \frac{\gamma_{\mu\nu}}{kT} \phi_{\mu\nu}^s \qquad (3.15)$$

of the concentration $N_\nu$ at $t = 0$ and naturally a disturbance of opposite sign of $N_\mu$. The total disturbance of $N_\mu$ at $t = 0$ is therefore given by summation over all disturbances generated by the changes of all rate constants $M_{\mu\nu}$ and $M_{\nu\mu}$ ($\nu \neq \mu$). Taking into account (2.9), i.e. $\gamma_{\mu\nu} = -\gamma_{\nu\mu}$, we get

$$(N_\mu(0) - N_\mu^s) = \tfrac{1}{2} \frac{\zeta}{kT} \sum_{\nu=1}^{m} \gamma_{\mu\nu}(\phi_{\mu\nu}^s + \phi_{\nu\mu}^s). \qquad (3.16)$$

The disturbances (3.16) of the $N_\mu$ at $t = 0$, generated by the $\delta$-shaped voltage pulse (3.9), yield the initial condition under which an expression for the linear response $j(t)$ in (3.10) for $t > 0$ may easily be derived with the use of (2.5)–(2.8) and the fundamental solution (2.4):

$$j(t > 0) = \tfrac{1}{2} \frac{\zeta}{kT} \times \sum_{\kappa,\nu=1}^{m} \sum_{\mu,\rho=1}^{n} \gamma_{\mu\nu}\gamma_{\kappa\rho} M_{\kappa\rho}(\phi_{\mu\nu}^s + \phi_{\nu\mu}^s)\Omega_{\rho\mu}(t) \qquad (3.17)$$

Together with (3.14), which determines the response at $t = 0$, we get:

$$j(t \geqslant 0) = \tfrac{1}{2} \frac{\zeta}{kT} \left[ \left( \sum_{\mu,\nu=1}^{m} \gamma_{\mu\nu}^2 \phi_{\mu\nu}^s \right) \delta(t) + \sum_{\kappa,\nu=1}^{m} \sum_{\mu,\rho=1}^{n} \gamma_{\mu\nu}\gamma_{\kappa\rho} M_{\kappa\rho}(\phi_{\mu\nu}^s + \phi_{\nu\mu}^s)\Omega_{\rho\mu}(t) \right], \qquad (3.18)$$

$j(t < 0) = 0.$

The admittance function $Y(\omega)$ is according to (3.12) given by Fourier transformation of $j(t)$. For comparison with the spectral density and in order to investigate the validity or invalidity of the fluctuation dissipation theorem we are especially interested in the real part of $Y(\omega)$:

$$4kT \operatorname{Re} Y(\omega) = 2 \sum_{\mu,\nu=1}^{m} \gamma_{\mu\nu}^2 \phi_{\mu\nu}^s + 4 \sum_{\kappa,\nu=1}^{m} \sum_{\mu,\rho=1}^{n} \gamma_{\mu\nu}\gamma_{\kappa\rho} M_{\kappa\rho} \tfrac{1}{2}(\phi_{\mu\nu}^s + \phi_{\nu\mu}^s) \times \int_0^\infty \Omega_{\rho\mu}(t) \cos \omega t \, dt. \qquad (3.19)$$

## 4. Comparison of the macroscopic admittance with the microscopic fluctuations

### *4.1. Decomposition of spectral density*

In order to investigate how the Nyquist relation (1.1) has to be extended for nonequilibrium fluctuations we slightly manipulate the general expression (2.13) for the spectral density of current fluctuations by decomposing the stationary flux matrix with components $\phi_{\mu\nu}^s$ into its symmetric and antisymmetric parts:

$$G_{\Delta I}(\omega) = 2 \sum_{\mu,\nu=1}^{m} \gamma_{\mu\nu}^2 \phi_{\mu\nu}^s + 4 \sum_{\kappa,\nu=1}^{m} \sum_{\mu,\rho=1}^{n} \gamma_{\mu\nu}\gamma_{\kappa\rho} M_{\kappa\rho} \tfrac{1}{2}(\phi_{\mu\nu}^s + \phi_{\nu\mu}^s) \times \int_0^\infty \Omega_{\rho\mu}(t) \cos \omega t \, dt$$

$$+4\sum_{\kappa,\nu=1}^{m}\sum_{\mu,\rho=1}^{n}\gamma_{\mu\nu}\gamma_{\kappa\rho}M_{\kappa\rho}\tfrac{1}{2}(\phi^{s}_{\mu\nu}-\phi^{s}_{\nu\mu})$$

$$\times\int_{0}^{\infty}\Omega_{\rho\mu}(t)\cos\omega t\,dt. \tag{4.1}$$

By comparison with (3.19) follows:

$$G_{\Delta J}(\omega)=4kT\,\mathrm{Re}\,Y(\omega)$$

$$+4\sum_{\kappa,\nu=1}^{m}\sum_{\mu,\rho=1}^{n}\gamma_{\mu\nu}\gamma_{\kappa\rho}M_{\kappa\rho}\tfrac{1}{2}(\phi^{s}_{\mu\nu}-\phi^{s}_{\nu\mu})$$

$$\times\int_{0}^{\infty}\Omega_{\rho\mu}(t)\cos\omega t\,dt. \tag{4.2}$$

The frequency-dependent contribution to the admittance is connected with the symmetric part $(\phi^{s}_{\mu\nu}+\phi^{s}_{\nu\mu})$ of the stationary fluxes. At thermodynamic equilibrium the principle of detailed balance means

$$\phi^{s}_{\mu\nu}=\phi^{s}_{\nu\mu} \tag{4.3}$$

Hence in this case the second term in (4.2), connected with the antisymmetric part of the stationary fluxes, vanishes and the validity of the Nyquist relation at equilibrium is confirmed.

At nonequilibrium the second term in (4.2) does not vanish in general. The expression

$$J^{s}_{\mu\nu}=\gamma_{\mu\nu}(\phi^{s}_{\mu\nu}-\phi^{s}_{\nu\mu})=J^{s}_{\nu\mu}. \tag{4.4}$$

is symmetric because of (2.9). It is the stationary contribution to $J^{s}$ by transitions $\nu\to\mu$ and $\mu\to\nu$. Furthermore

$$\Delta J_{\mu}(t)=\sum_{\kappa,\mu=1}^{m}\sum_{\rho=1}^{n}\gamma_{\kappa\rho}M_{\kappa\rho}\Omega_{\rho\mu}(t) \tag{4.5}$$

is the time dependent deviation of total current $J$ from the stationary current $J^{s}$ under the initial condition, which distinguishes state $\mu$ at $t=0$ (cf. (2.4)).

Then we get from (4.2)

$$G_{\Delta J}(\omega)=4kT\,\mathrm{Re}\,Y(\omega)$$

$$+2\sum_{\nu=1}^{m}\sum_{\mu=1}^{n}J^{s}_{\mu\nu}\int_{0}^{\infty}\Delta J_{\mu}(t)\cos\omega t\,dt. \tag{4.7}$$

The interpretation of (4.7) is as follows: The first (admittance) term is generated by microscopic disturbances of thesystem which can also be excited macroscopically by an external voltage. It contains no additional information compared with the macroscopic admittance function. On the other hand the second term is generated by microscopic fluctuations which cannot be excited by an external voltage. Because of this term the measurement of nonequilibrium current fluctuations in principal may yield information about the transport system which cannot be obtained from the measurement of macroscopic quantities.

### *4.2. Special examples*

The second term in (4.7) is a bilinear expression in current, and we may expect that its contribution to fluctuations often increases quadratically with current (voltage). Indeed, as is well known this property is typical for nonequilibrium excess noise as e.g. lorentzian noise generated by nerve channels with open-close kinetics [2–5,15] or $1/f$ noise [18,19].

If the channels possess one open state and the ion transport through the channels is fast compared with the opening-closing kinetics of the channels, the current noise spectral density has the general structure [15]

$$G_{\Delta J}(\omega)=\text{shot noise}+\text{lorentzian noise}, \tag{4.8}$$

where the lorentzian noise term is proportional to the square of the current through the single open channel.

Comparison with (4.1) and (4.7) shows that the shot noise is determined by the admittance which in this case is frequency-independent. The lorentzian noise term is excess noise coming from the second term in (4.7) being generated by microscopic channel fluctuations.

The current noise generated by carrier-mediated ion transport through membranes at nonequilibrium and the correponsing decomposition of $G_{\Delta J}(\omega)$ into admittance and excess terms has recently been measured and extensively discussed and is published elsewhere [17].

### *4.3. Permanently open pores with one binding site*

The case of permanently open pores with one binding site within the pore, one ion species and negligible

interactions between the ions and pores [20,21] can serve as a simple example for discussion. The binding sites inside the identical pores are considered to be separated by energy barriers from the reservoirs on the left- and right-hand sides of the pores. The variable $N_1$ denotes the occupation number of ions at this binding site. Its rate of change $\langle \dot{N}_1 \rangle$ with time is described by:

$$\langle \dot{N}_1 \rangle = k_0' N_0 - (k_1' + k_1'')\langle N_1 \rangle + k_2'' N_2. \tag{4.9}$$

$N_0$, $N_2$ are the constant concentrations at the left- and right-hand sides respectively, $k_0'$, $k_2''$ the corresponding rate constants for jumps of the ions into the pores and $k_1'$, $k_2''$ for jumps out of the pores to the right, left respectively.

With

$$\gamma_1 = \gamma_{01} = -\gamma_{10}, \quad \gamma_2 = \gamma_{12} = -\gamma_{21},$$

$$\gamma_1 + \gamma_2 = Ze_0 \tag{4.10}$$

and the stationary solution $N_1^s$ of (4.9)

$$N_1^s = \tau(k_0' N_0 + k_2'' N_2), \quad \tau = 1/(k_1' + k_1''), \tag{4.11}$$

the spectral density of current fluctuations is given by [22,9]

$$G_{\Delta J}(\omega) = 2A_1 + A_2 \frac{4\tau}{(1 + \omega^2\tau^2)}, \tag{4.12}$$

with

$$A_1 = \gamma_1^2(k_0' N_0 + k_0'' N_1^s) + \gamma_2^2(k_1' N_1^s + k_2'' N_2),$$

$$A_2 = (\gamma_1 k_0' N_0 - \gamma_2 k_2'' N_2)(\gamma_2 k_1' - \gamma_1 k_1''). \tag{4.13}$$

For the admittance $Y(\omega)$ holds

$$4kT \operatorname{Re} Y(\omega) = 2A_1 + \frac{2\tau}{1 + \omega^2\tau^2}(\gamma_2 k_1' - \gamma_1 k_1'')$$

$$\times \{\gamma_1(k_0' N_0 + k_1'' N_1^s) - \gamma_2(k_2'' N_2 + k_1' N_1^s)\}. \tag{4.14}$$

And from (4.7) follows with

$$\phi^s = k_0' N_0 - k_1'' N_1^s = k_1' N_1^s - k_2'' N_2,$$

$$J^s = Ze_0 \phi^s \tag{4.15}$$

the decomposition of $G_{\Delta J}(\omega)$:

$$G_{\Delta J}(\omega) = 4kT \operatorname{Re} Y(\omega) + J^s(\gamma_2 k_1' - \gamma_1 k_2'') \frac{2\tau}{1 + \omega^2\tau^2} \tag{4.16}$$

At equilibrium the second term vanishes. The principle of detailed balance means

$$k_1' N_1^s = k_2'' N_2, \qquad k_0' N_0 = k_1'' N_1^s. \tag{4.17}$$

Therefore, for the equilibrium state:

$$G_{\Delta J}(\omega) = 2A_1 - \frac{2\tau}{1 + \omega^2\tau^2} N_1^s(\gamma_2 k_1' - \gamma_1 k_1'')^2. \tag{4.18}$$

The frequency dependent contribution is always negative and the low-frequency white limit is below the high-frequency limit. This "inverse Lorentz-behavior" is typical of transport noise at equilibrium and has recently been measured and discussed at different biological transport systems [6,8,15,16,23]. It is a direct consequence of the fact that at equilibrium the applied voltage disturbance (at $t = 0$) and the current response (for $t > 0$) are in opposite direction. At non-equilibrium the frequency dependent contribution to $4kT \operatorname{Re} Y(\omega)$ may be negative or positive, depending on the response properties of the system. It is positive, e.g. for the special case of pores under very asymmetric conditions

$$\gamma_1 > \gamma_2, \qquad k_1'' = k_2'' = 0, \tag{4.19}$$

where flux can take place only in one direction.

The second term in (4.16) can also be positive and negative, because the sign of $(\gamma_2 k_1' - \gamma_1 k_1'')$ may be equal with or different from the sign of $J^s$, depending on the special choice of the different parameters. Taking the Eyring ansatz (3.5) for the voltage dependence of the rate constants the absolute value of this term becomes greater for higher applied voltages, if it is positive, and smaller, if it is negative. Generally, it is negative in cases where the gradient between concentrations at the left and right pore side is opposite to the direction of the applied voltage. All these properties are in agreement with a general rule, which we have recently proposed [15,16], that the difference

$$G_{\Delta J}(\omega \to \infty) - G_{\Delta J}(\omega \to 0)$$

is always positive at equilibrium and becomes smaller or even changes sign at nonequilibrium.

## 5. Discussion

The results for open channels with one binding site have illustrated some general properties of transport

fluctuations. First, the property of the spectral density at equilibrium to be smaller at low frequencies than at high frequencies as a direct consequence of the fact that the linear current response (for $t > 0$) is in opposite direction to the applied voltage pulse (at $t = 0$). This indicates the impossibility for the occurrence of current excess noise as e.g. $1/f$ noise or nerve channel $1/f^2$ noise at thermal equilibrium. Nevertheless the process itself, which is the actual source of the nonequilibrium excess noise, may be an equilibrium process, as for example the opening and closing of nerve channels, generating $1/f^2$-current noise. Also for $1/f$ noise the recent results of Voss and Clarke [24] seem to indicate that the resistance fluctuations, which are responsable for $1/f$ noise, are there already at equilibrium.

At nonequilibrium under special conditions the current response may be in the same direction as the applied voltage pulse and hence yield an excess noise contribution of the admittance term to the fluctuations.

The bilinear dependence on current of the second term in (4.7), may often result in a quadratic dependence, which is typical of most excess noise sources.

The fact that the sign of both contributions to the fluctuations can be negative for a suitable choice of parameters might include interesting aspects for the problem of minimization of noise in special frequency intervals in amplifyers as well as in biological nonequilibrium transport systems. For the example of pores with one binding site, the minimum noise at low frequency for given curves $J^s$ is reached in those cases of asymmetric pores where the ions can flow only in one direction. Then, as easily may be verified from (4.12) or (4.16) with (4.15), $G_{\Delta J}(\omega = 0)$ is usual shot noise

$$G_{\Delta J}(0) = 2J^s Z e_0. \tag{5.1}$$

The possibilities for a minimization of noise may be much more effective in more complex systems. For biological nonequilibrium systems it should be interesting to investigate, if and how these systems during their evolution have reached states of minimum fluctuations.

## Appendix

*Derivation of relation (3.7)*

We give a heuristic derivation of the relation (3.7) between $\gamma_{\mu\nu}$ and $\alpha_{\mu\nu}$, which is based on an energy balance. We assume the transport system to possess a capacitance $C$ and to be helt under constant voltage $V$ (voltage clamp). Then between the total charge $Q$ and $V$ holds

$$Q = CV. \tag{A.1}$$

If inside the transport system a charge $q$ is transported between points (or states) $\mu$ and $\nu$ with a potential difference $\Delta_{\mu\nu}v$, the energy

$$\Delta_{\mu\nu}E = \Delta_{\mu\nu}v \cdot q \tag{A.2}$$

is lost (by dissipation). As consequence of this energy loss the total voltage $V$ is changed to $(V - \Delta_{\mu\nu}V)$, approximately given by

$$\Delta_{\mu\nu}V = \Delta_{\mu\nu}E/Q. \tag{A.3}$$

Thus with (A.2):

$$\Delta_{\mu\nu}V = \Delta_{\mu\nu}v \cdot q/Q. \tag{A.4}$$

On the other hand, because the system is to be helt under constant voltage, a charge $\Delta_{\mu\nu}q$ must be delivered from outside in order to compensate the change $\Delta_{\mu\nu}V$ in voltage.

With (A.1) $\Delta_{\mu\nu}q$ is given by

$$\Delta_{\mu\nu}q = C\Delta_{\mu\nu}V. \tag{A.5}$$

and hence with (A.4):

$$\frac{\Delta_{\mu\nu}q}{q} = \frac{\Delta_{\mu\nu}V}{V}. \tag{A.6}$$

The fraction $\Delta_{\mu\nu}q/q$ of the charge $q$, which must be delivered from outside and generates a corresponding current pulse, as consequence of the transition of $q$ between $\mu$ and $\nu$, is equal to the fraction $\Delta_{\mu\nu}V/V$ of voltage $V$ between $\mu$ and $\nu$ compared with the total voltage $V$.

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