

## Short communication

## Collective Dynamics of Ion Channels in Biological Membranes

P. BABINEC and M. BABINCOVÁ

*Department of Biophysics and Chemical Physics,  
Faculty of Mathematics and Physics, Comenius University,  
Mlynská dolina F1, 842 15 Bratislava, Slovakia*

**Abstract.** Master equation was used to describe the dynamics of coupled ion channels in biological membranes. From the stationary solution it was found that at a critical value of coupling strength the system undergoes phase transition of the second order, which can be of biological relevance.

**Key words:** Biological membranes – Ion channels – Master equation – Phase transition – Collective dynamics

As has been found experimentally, transmembrane ion channels are not functionally independent (Kiss and Nagy 1985; Iwasa et al. 1986, Yeramian et al. 1986). This arises from direct energy interactions between channels embedded in biological membranes of living cells (Houslay and Stanley 1982).

A consistent description of ion channels functioning is only possible on the basis of nonlinear nonequilibrium statistical thermodynamics (Poledna 1989; Valko and Zachar 1989). In this work we use a simple model of interacting ion channels to show that nonlinear effects are important also for the description of collective dynamics.

For the sake of simplicity we consider ion channels as effectively fluctuating two-state elements with one open (conducting) state and one closed (nonconducting) state (Liu and Dilger 1991; French and Horn 1983; Hille 1984).

Let a given configuration of ion channels in a biological membrane consist of  $n_o$  and  $n_c$  open and closed channels, respectively. If the total number of channels  $2N = n_o + n_c$  is constant, then the only relevant variable  $n$  (order parameter) is given by  $n = (n_o - n_c)/2$ .

Transition dynamics of the ion channels is determined by probabilities:

- $p_{co}(n_o, n_c)$  – for transition from open to closed state,
- $p_{oc}(n_o, n_c)$  – for transition from closed to open state.

Let us introduce further probability distribution function  $f(n_o, n_c; t) \equiv f(n; t)$ ,

which expresses the probability that one sample biological membrane has the configuration  $\{n_o, n_c\}$  at time  $t$ .

Time evolution of this function is described by master equation (Davies 1974; Haken 1978; Risken 1984)

$$\begin{aligned} \frac{df(n_o, n_c; t)}{dt} = & (n_o + 1)p_{co}(n_o + 1, n_c - 1) f(n_o + 1, n_c - 1; t) \\ & + (n_c + 1)p_{oc}(n_o - 1, n_c + 1) f(n_o - 1, n_c + 1; t) \\ & - \{n_o p_{co}(n_o, n_c) f(n_o, n_c; t) + n_c p_{oc}(n_o, n_c) f(n_o, n_c; t)\}. \end{aligned} \quad (1)$$

After introducing the functions

$$\begin{aligned} t_{oc}(n) &= n_c p_{oc}(n) = (N - n) p_{oc}(n) \\ t_{co}(n) &= n_o p_{co}(n) = (N + n) p_{co}(n) \end{aligned} \quad (2)$$

the master equation may be rewritten in the form

$$\begin{aligned} \frac{df(n; t)}{dt} = & t_{co}(n + 1) f(n + 1; t) - t_{co}(n) f(n; t) \\ & + t_{oc}(n - 1) f(n - 1; t) - t_{oc}(n) f(n; t). \end{aligned} \quad (3)$$

It is also suitable to introduce probability fluxes

$$\begin{aligned} j_{oc}(n; t) &= t_{oc}(n) f(n; t) \\ j_{co}(n; t) &= t_{co}(n) f(n; t) \end{aligned} \quad (4)$$

and relative flux  $k(n; t)$  between the states  $n$  and  $n + 1$

$$k(n; t) = j_{oc}(n; t) - j_{co}(n + 1; t). \quad (5)$$

The master equation then assumes the following simple form

$$\frac{df(n; t)}{dt} = k(n - 1; t) - k(n; t). \quad (6)$$

The form of transition probabilities may be determined on the basis of experimentally confirmed Ising-like coupling (Liu and Dilger 1993) between ion channels at constant ligand concentration:

$$\begin{aligned} p_{co}(n) &= \nu \exp\left(\frac{g}{NKT}n\right) \\ p_{oc}(n) &= \nu \exp\left(-\frac{g}{NKT}n\right) \end{aligned} \quad (7)$$

where  $\nu$  is transition probability in the uncoupled channel;  $g$  is strength of interaction between ion channels;  $K$  is the Boltzmann constant; and  $T$  is temperature. For the sake of simplicity, the same coupling was considered among all channels, this approximation being similar to all-to-all coupling of the neural network theory (Watkin et al. 1993; Babinová and Babinec 1995).

Using explicit form of transition probabilities we get

$$\begin{aligned} t_{co}(n) &= \nu(N+n) \exp\left(\frac{g}{NKT}n\right) \\ t_{oc}(n) &= \nu(N-n) \exp\left(-\frac{g}{NKT}n\right). \end{aligned} \quad (8)$$

Stationary solution to the master equation (6) may be determined from the condition (Hänggi et al. 1990)

$$\frac{df_{st}}{dt} = 0 \text{ or explicitly } k_{st}(n-1) = k_{st}(n) \quad (9)$$

where  $f_{st}$  is stationary probability and  $k_{st}$  is stationary net flux.

Using natural boundary conditions

$$k(N; t) = k(-N; t) = 0 \quad (10)$$

it follows that

$$k_{st}(n) = 0 \text{ for } -N \leq n \leq N \quad (11)$$

or equivalently

$$t_{oc}(n-1) f_{st}(n-1) = t_{co}(n) f_{st}(n). \quad (12)$$

Eq. (12) may be resolved recursively, which gives

$$f_{st}(n) = f_{st}(0) \prod_{l=1}^n t_{oc}(l-1)/t_{co}(l) \text{ for } 1 \leq n \leq N. \quad (13)$$

The value  $f_{st}(0)$  is determined by normalization condition

$$\sum_{l=-N}^N f_{st}(l) = 1. \quad (14)$$

Using eq. (8) the stationary solution is given by

$$f_{st}(n) = f_{st}(0) \frac{(N!)^2}{(N+n)!(N-n)!} \exp\left(\frac{g}{NKT}n^2\right). \quad (15)$$

This expression may be simplified using Stirling's formula

$$\ln(M!) \simeq M \ln M - M \quad (16)$$

which yields

$$f_{\text{st}}(n) = f_{\text{st}}(0) \exp[N V(x)] \quad (17)$$

where  $x = n/N$  and  $V(x) = \frac{g}{KT}x^2 - [(1+x)\ln(1+x) + (1-x)\ln(1-x)]$ .

The steady-state corresponds to extreme value of  $f_{\text{st}}$ , which may be found from the condition

$$\left. \frac{dV(x)}{dx} \right|_{x=x_{\text{st}}} = \frac{2g}{KT}x_{\text{st}} - [\ln(1+x_{\text{st}}) - \ln(1-x_{\text{st}})] = 0. \quad (18)$$

The solution to eq. 18 is given by

$$x_{\text{st}} = \tanh \left( \frac{g}{KT}x_{\text{st}} \right). \quad (19)$$

There is only one solution  $x_{\text{st}} = 0$  ( $n_c = n_0$ ) to this transcendental equation for  $0 < g < KT$ , which corresponds to the maximum of  $f_{\text{st}}$ . At the critical value of interaction strength  $g_c = KT$  the stationary solution  $x_{\text{st}}$  shows a second order (continuous) phase transition to the two nonvanishing, symmetry breaking ( $n_c \neq n_0$ ), solutions.

In a variety of contexts, physicists have noted the possibility that in the critical state independent microscope fluctuations can propagate so as to give rise to instability on a macroscopic scale (Stanley 1971). In a "noncritical" state, changes in one part of the system have a sufficiently weak effect upon neighboring parts so that the state in different regions of the system is correlated over short distances only. On the other hand, when some parameter of the system is "tuned" to an appropriate value (in our case  $g = KT$ ), a critical globally correlated state may be reached, in which spontaneous macroscopic fluctuations may be observed and arbitrarily small external influences can have strong effects upon the macroscopic state. Moreover, near the critical state the systems are characterized by extreme rapidity with which they respond to external perturbations.

Summarizing, we may say that at appropriate values of interaction strength between ion channels, biological membranes are anomalously sensitive to external influences of various kinds. This effect may be of particular importance in the phenomenon of electrocommunication (Blumenfeld 1983; Bullock and Heiligenberg 1986) where some cells or organisms are able to sense very weak force fields, either electrical, magnetic or mechanical.

**Acknowledgements.** M. B. acknowledges the financial support received from Copernicus Grant CIPA-CT94-0231 and from Slovak Grant Agency (grant 1/2190/95).

## References

- Babincova M, Babinec P (1995) Self-organized criticality of firing dynamics in coupled neuronal systems *Neural Network World* **5**, 121—124
- Blumenfeld L A (1983) *Physics of Bioenergetic Processes* Springer Verlag New York
- Bullock T H, Heiligenberg W (1986) *Electroreception* J Wiley & Sons Chichester
- Davies E B (1974) Markovian master equations *Commun Math Phys* **39**, 91—110
- French R J, Horn R (1983) Sodium channel gating models, mimics and modifiers *Annu Rev Biophys Bioenerg* **12**, 319—356
- Haken H (1978) *Synergetics An Introduction* Springer Verlag, Berlin
- Hanggi P, Talkner P, Borkovec M (1990) Reaction rate theory *Rev Mod Phys* **62**, 251—340
- Hille B (1984) *Ionic Channels of Excitable Membranes* Sinauer, Massachusetts
- Houslay M D, Stanley K K (1982) *Dynamics of Biological Membranes* J Wiley & Sons Chichester
- Iwasa K, Ehrenstein N, Moran N, Jia M (1986) Evidence for interactions between batrachotoxin-modified channels in hybrid neuroblastoma cells *Biophys J* **50**, 531—537
- Kiss T, Nagy K (1985) Interaction between sodium channels in mouse neuroblastoma cells *Eur Biophys J* **12**, 13—18
- Liu Y, Dilger J P (1991) Opening rate of acetylcholine receptor channels *Biophys J* **60**, 424—432
- Liu Y, Dilger J P (1993) Application of the one dimensional and two-dimensional Ising models to studies of cooperativity between ion channels *Biophys J* **64**, 26—36
- Poledna J (1989) Model of calcium channel inactivation. A qualitative analysis *Gen Physiol Biophys* **8**, 11—22
- Risken H (1984) *The Fokker-Planck Equation* Springer Verlag New York
- Stanley H E (1971) *Introduction to Phase Transitions and Critical Phenomena* Oxford University Press Oxford
- Valko L, Zachar J (1989) The steady state criterion of a simple model of calcium channels *Gen Physiol Biophys* **8**, 3—10
- Watkin T L H, Rau A, Biehl M (1993) The statistical mechanics of learning a rule *Rev Mod Phys* **65**, 499—556
- Yeremianian E, Trautmann A, Claverie P (1986) Acetylcholine receptors are not functionally independent *Biophys J* **50**, 253—263

Final version accepted January 22, 1996