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Role and activity of some chosen voltage-gated K+ and Na+ channels mathematical description and analyses.

Ion channels play crucial role in the process of conduction of electrical impulses, particularly in nerve and muscle cells. Channels are integral proteins immersed in the cells lipid bilayer, which itself has usually poor ionic permeation. Channels third order structure creates a transmembrane pore a passage for ions. As comes out from experiments, permeability of ions through channels fluctuates in time, and is determine by varying structure of the channel. Modulation of ionic flux is called gating, which may be driven by different stimuli like chemical species or variation of electric potential. It is interesting that even if channel is subjected to the constant, positive transmembrane voltage that should keep it open, its permeability decreases after short time channel inactivation. It is than clear that the voltage gating is not the only one mechanisms of gating present in ion channels. In this paper we will discuss, so called ball and chain model of inactivation addressed to potassium Shaker channel [1-3]. Polypeptide ball a part of the channels protein that is responsible for inactivation, is treaded as a Brownian particle tethered on polypeptide chain. Its wandering was described by means of diffusion (parabolic and hyperbolic operators) [4,5]. First passage time of the ball was calculated and compared with experimental data [2]. Second part of the paper is devoted to the sodium channel activity in rat prostate cancer cells as well as human breast cancer cells. Fractal methods were used to analyze quantitative differences in secretory membrane activities of two rat prostate cancer cell lines (Mat-LyLu and AT-2) of strong and weak metastatic potential, respectively [6]. Each cells endocytic activity was determined by horseradish peroxidase uptake. Digital images of the patterns of vesicular staining were evaluated by multifractal analyses: generalized fractal dimension (Dq) and its Legendre transform f(a), as well as partitioned iterated function system semifractal (PIFS-SF) analysis. These approaches revealed consistently that, under control conditions, all multifractal parameters and PIFS-SF codes determined had values greater for Mat-LyLu compared with AT-2 cells. This would agree generally with the endocytic/vesicular activity of the strongly metastatic Mat-LyLu cells being more developed than the corresponding weakly metastatic AT-2 cells. All the parameters studied were sensitive to tetrodotoxin (TTX) pre-treatment of the cells, which blocked voltage-gated Na+ channels (VGSCs). Some of the parameters had a simple dependence on VGSC activity, whereby pre-treatment with TTX reduced the values for the MAT-LyLu cells and eliminated the differences between the two cell lines. For other parameters, however, there was a complex dependence on VGSC activity. The possible physical/physiological meaning of the mathematical parameters studied and the nature of involvement of VGSC activity in control

of endocytosis/ secretion are discussed. Basically, the same sort of approach had been used to analyze the endocytic membrane activities of two human breast cancer cell lines (MDA-MB-231 and MCF-7) of strong and weak metastatic potential, respectively, were studied in a comparative approach [7]. Uptake of horseradish peroxidase was used to follow endocytosis. Dependence on ionic conditions and voltage-gated sodium channel (VGSC) activity were characterized. Fractal methods were used to analyze quantitative differences in vesicular patterning. Digital quantification showed that MDA-MB-231 cells took up more tracer (i.e., were more endocytic) than MCF-7 cells. For the former, uptake was totally dependent on extracellular Na+ and partially dependent on extracellular and intracellular Ca2+ and protein kinase activity. Analyzing the generalized fractal dimension (D(q)) and its Legendre transform f(alpha) revealed that under control conditions, all multifractal parameters determined had values greater for MDA-MB-231 compared with MCF-7 cells, consistent with endocytic/vesicular activity being more developed in the strongly metastatic cells. All fractal parameters studied were sensitive to the VGSC blocker tetrodotoxin (TTX). Some of the parameters had a "simple" dependence on VGSC activity, if present, whereby pretreatment with TTX reduced the values for the MDA-MB-231 cells and eliminated the differences between the two cell lines. For other parameters, however, there was a "complex" dependence on VGSC activity. The possible physical/physiological meaning of the mathematical parameters studied and the nature of involvement of VGSC activity in control of endocytosis/secretion are discussed.

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