



Caveat on the Boltzmann distribution function use in biology



Carlos Sevcik Professor *

Laboratory on Cellular Neuropharmacology, Centro de Biofísica y Bioquímica, Instituto Venezolano de Investigaciones Científicas (IVIC), Caracas, Venezuela

ARTICLE INFO

Article history:

Received 3 June 2016

Received in revised form

28 March 2017

Accepted 4 April 2017

Available online 13 April 2017

Keywords:

Boltzmann

Energy states

Probability

Ion channels

ABSTRACT

Sigmoid semilogarithmic functions with shape of Boltzmann equations, have become extremely popular to describe diverse biological situations. Part of the popularity is due to the easy availability of software which fits Boltzmann functions to data, without much knowledge of the fitting procedure or the statistical properties of the parameters derived from the procedure. The purpose of this paper is to explore the plasticity of the Boltzmann function to fit data, some aspects of the optimization procedure to fit the function to data and how to use this plastic function to differentiate the effect of treatment on data and to attest the statistical significance of treatment effect on the data.

© 2017 Published by Elsevier Ltd.

Contents

1. Introduction	34
2. Methods	35
2.1. Monte Carlo Boltzmann functions simulation	35
2.2. Statistical procedures	35
3. Results	35
3.1. The plasticity of the Boltzmann proportion function to fit data	35
3.2. Comparing the theoretical Boltzmann function with values obtained in Monte Carlo simulations	36
4. Discussion	37
Acknowledgments	38
Appendix A	38
A. On rectangular hyperbolas and the Boltzmann function	38
B. Mathematical appendix	39
B.1. How does the Boltzmann function compare with a probability distribution function?	39
B.2. Boltzmann PDF central moments	39
B.3. Boltzmann pdf Hessian and variance	40
B.4. Kolmogorov distribution functions	40
B.5. The Kolmogorov-Smirnov statistics in connection with the Boltzmann function	41
References	41

* IVIC CBB, Apartado 20632, Caracas 1020A, Venezuela.

E-mail addresses: csevcik@ivic.gob.ve, carlos.sevcik.s@gmail.com.

1. Introduction

“When a finger points at the moon, one must not mistake the finger with the moon.”
Old Zen Buddhist advice.

“With four parameters I can fit an elephant and with five I can make him wiggle his trunk.”
Attributed to J. Von Neuman (Dyson, 2004).

Some thoughts and some equations transcending their greatness, also transcend their purpose. During the last quarter of the XIX century Ludwig Boltzmann (Moore (1972), Ch. 9) derived an equation which predicts the proportion N_j particles, in an ensemble of N non interacting particles, that are in a state with particle energy ε_j

$$\frac{N_j}{N} = \frac{e^{-\varepsilon_j/kT}}{\sum_{j=1}^{N_j} e^{-\varepsilon_j/kT}} = \frac{e^{-\varepsilon_j/kT}}{\zeta(T)} \quad (1)$$

where $\zeta(T)$ is called the *particle partition function* or when dealing with molecules, the *molecular partition function*. When only two energy levels are dealt with, the ratio of N_0 particles in energy level ε_0 with N_1 particles in energy level ε_1 predicted by equation (1) is

$$\frac{N_1}{N_0} = e^{-(\varepsilon_1 - \varepsilon_0)/kT}. \quad (2)$$

In an extension of eq. (1) for *degenerate* systems (when more than one states ε_j have the same energy) a statistical weight, g_j equal to the number of superimposed levels, is included. Then

$$\frac{N_j}{N} = \frac{g_j e^{-\varepsilon_j/kT}}{\sum_{j=1}^{N_j} g_j e^{-\varepsilon_j/kT}}. \quad (3)$$

Which is the Boltzmann distribution law in its most general form. The average kinetic energy is

$$\bar{\varepsilon} = \frac{\sum_{j=1}^{N_j} N_j \varepsilon_j}{\sum_{j=1}^{N_j} N_j} = \frac{\sum_{j=1}^{N_j} \varepsilon_j g_j e^{-\varepsilon_j/kT}}{\sum_{j=1}^{N_j} g_j e^{-\varepsilon_j/kT}} = kT^2 \left(\frac{\partial \ln \zeta}{\partial T} \right)_V. \quad (4)$$

The middle term in Eq. (4) includes the *statistical weights* g_j which account for, so called, *degenerate* levels. The molecular partition function is useful only when the system of interest can be considered to be made up of noninteracting particles, molecules with no appreciable intermolecular forces. Only then, can we define and enumerate the states of the system in either terms of quantum mechanical energy states of individual molecules, or classical positions and moments of individual molecules. When interactions between molecules occur, the description of the states of the system must include potential energy terms, such as $U(r_{ij})$, which are functions of intermolecular distances.

Equation (1) may be rewritten for ensembles of interacting particles as

$$p_j = \frac{N_j}{N} = \frac{e^{-E_j/kT}}{\sum_{j=1}^{N_j} e^{-E_j/kT}} = \frac{e^{-E_j/kT}}{Z(T)} \quad (5)$$

where $E_j = \frac{1}{2} m v^2 + U_j$, m is the particle mass, v is velocity and U_j is potential energy. Equation (5) is the *Maxwell-Boltzmann* distribution function. If there are only two possible states in the system Eq. (5) becomes

$$\frac{p_1}{p_1 + p_2} = \frac{e^{-E_1/kT}}{e^{-E_1/kT} + e^{-E_2/kT}} \Rightarrow p_1 = \frac{1}{1 + e^{-(E_2 - E_1)/kT}}. \quad (6)$$

When dealing with cell membranes, a Boltzmann equation is expressed as free energy in voltage units (the electrical potential difference existing across cell membranes) in general the form used looks like

$$B = \frac{1}{1 + e^{-(V_2 - V_1)/\kappa}} \quad (7)$$

where V is used to more clearly specify that we deal with electrical potential differences, κ is customarily referred to as “slope factor” (see for example Peigneur et al. (2012)). Since these situations deal with ensembles of particles the “slope factor” is usually parametrized $\kappa = RT/zF \approx 25.4$ mV, at room temperature if: the ionic valence, $z = 1$, F is the Faraday constant, R is the gas constant and T is the absolute temperature. In electrophysiology, an equation of the form (7) was introduced for the first time by Hodgkin and Huxley (1952a, 1952b) (H&H for brevity), and was used to describe the distribution, inside or outside axons, of hypothetical particles associated with Na^+ and K^+ currents crossing the nerve membrane. Since the Hodgkin and Huxley (1952b) work was seminal for electrophysiology, a plethora of papers have used Boltzmann functions in connection with electrical properties of cells and isolated ionic channels (Sakmann and Neher, 1984). In electrophysiology, however equation (7) is modified (Hodgkin and Huxley, 1952a), V_2 represent *cell trans membrane potential* (*membrane potential* for short) expressed plainly as V and since Eq. (7) takes values between 0 and 1, V_2 is taken as the membrane potential where $B = 0.5$ and is usually termed $V_{1/2}$, Eq. (7) thus becomes

$$B(V|V_{1/2}, \kappa) = \frac{1}{1 + e^{-(V - V_{1/2})/\kappa}}. \quad (8)$$

When Eq. (8) is used in the original fashion of H&H, to represent trans membrane distribution of some charged particle, B is expressed in respect to the potential at which 50% of the particles are in one side of the membrane, and 50% is at the other side. Eq. (8) is thus reduced to a situation where a dependent variable B may be fitted by some nonlinear optimization procedure to an independent variable V (usually expressed in mV) using Eq. (8). The optimization procedure enables to estimate the parameters $V_{1/2}$ and κ . In H&H work (Hodgkin & Huxley (1952a), pg 501, Eq. (1)),

$$h_{\text{steady state}} = \frac{1}{1 + e^{-(V - V_h)/\tau}} \quad (9)$$

which is presented here with post H&H membrane potential sign conventions. V_h was estimated to be close to the resting membrane potential. H&H also used a Boltzmann function to estimate properties of hypothetical particles gating or triggering the mechanism controlling Na^+ conductance in nerve (Hodgkin and Huxley, 1952b), PART I, pp. 503–504] the form of the Boltzmann function in this case was

Download English Version:

<https://daneshyari.com/en/article/5519819>

Download Persian Version:

<https://daneshyari.com/article/5519819>

[Daneshyari.com](https://daneshyari.com)