Describing the stochastic dynamics of neurons using Hamilton's equations of classical mechanics

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Abstract
We consider the most likely behaviour of neuron models by formulating them in terms of Hamilton's equations. Starting from a Lagrangian for a stochastic system, we describe how Hamilton's equations of classical mechanics can be used to derive an equivalent description in terms of canonical co-ordinates and momenta. We give physical meaning to these generalized momenta; specifically they are linear combinations of the noise terms in the stochastic model. Pseudo-kinetic energy and potential energy terms are also derived. The conjugate momenta can be considered as growing modes, and by implication the most likely noise input to a system will grow exponentially at large times; this surprising prediction agrees with existing experimental work on a single neuron. For many-neuron models, multiple growing modes will exist, and the numerical analysis of these is more complicated; however, the approach may still provide insight on the more detailed dynamics of these systems.

Keywords: Neurons; Modelling; Hamilton's equations; Brain Dynamics

Introduction

Path-integral formulations of dynamical systems have the potential to shed light on the physical understanding of complex systems. Often, a Lagrangian approach is taken, in which the most likely path is the one that minimizes the action. Recently Paninski (2006) has formulated a single integrate-and-fire neuron in terms of a Lagrangian, and demonstrated that this formalism can be used to predict the most likely behaviour of the neuron's membrane potential between firing events. This has been successfully compared with experimental data. Badel *et al.* (2006, 2008) have carried out similar theoretical analyses with generalized integrate-and-fire neuron models. In this work, we go beyond the application of a Lagrangian to the membrane potential, and consider the insights that can be gained regarding the dynamics of the noise process from a consideration of the canonical momenta of the system.

Hamilton's equations are equivalent to Lagrangian dynamics (that is, they contain in principle no new information), but the physics is expressed as a set of coupled first-order differential equations in phase space. The Hamiltonian approach constructs 'canonical momenta' conjugate to each state variable, and in practice these momenta often represent physical quantities, thus providing a framework by which to understand further the system's behaviour (Goldstein 1980). Here we present Lagrangian and Hamiltonian descriptions of a generalized stochastic system. We comment specifically on their physical interpretation and discuss their implications for the modelling of many-neuron systems.

Analysis

Lagrangian
Consider the stochastic process given by the equation:

$$\frac{d\vec{x}}{dt} = \vec{f}(\vec{x}, t) + \vec{v}(t) \tag{1}$$

where $\vec{x}$ is a multi-dimensional state-vector of the system, $\vec{f}$ is an operator, $\vec{v}$ represents the random input to the system and t is time. The statistics of $\vec{v}$ follow:

$$\left\langle \vec{v}(t)\vec{v}^T(t') \right\rangle = \Sigma^2 \delta(t - t'), \tag{2}$$

where Σ^2 is a dimensioned matrix describing the extent of, and correlation in, the noise, δ is the Dirac delta-function, the superscript T denotes the transpose, and the average is taken over time. We can construct a Lagrangian for this system following Paninski (2006). By considering the probability p of a given series of random inputs to the process, we obtain $p \propto \exp(-\int L\, dt)$, where the Lagrangian L is given by:

$$L = \frac{1}{2}\left(\dot{\vec{x}} - \vec{f}\right)^T \Sigma^{-2} \left(\dot{\vec{x}} - \vec{f}\right). \tag{3}$$

Euler-Lagrange equations
We now construct the Euler-Lagrange equations for the most likely path for the system. Using x_k to denote the k-th

element of $\vec{x}$, the N Euler-Lagrange equations are given by:

$$\frac{d}{dt}\left(\frac{\partial L}{\partial \dot{x}_k}\right) = \frac{\partial L}{\partial x_k}; \tag{4}$$

substituting L from Eq. (3) into these equations, and using $\partial \dot{x}_i / \partial \dot{x}_k = \delta_{ik}$, we obtain the N equations:

$$\Sigma_{kj}^{-2}\left(\ddot{x}_j - \dot{f}_j\right) + \left(\ddot{x}_i - \dot{f}_i\right)\Sigma_{ik}^{-2} = -\frac{\partial f_i}{\partial x_k}\Sigma_{ij}^{-2}\left(\dot{x}_j - f_j\right) - \left(\dot{x}_i - f_i\right)\Sigma_{ij}^{-2}\frac{\partial f_j}{\partial x_k} \tag{5}$$

where summation is now assumed over repeated indices, and a dot represents a full differentiation with respect to time. Assuming that the Lagrangian is an explicit function of neither $\dot{\vec{x}}$ nor t (as is often the case for neuron models) — i.e. $\vec{f} = \vec{f}(\vec{x})$, we have by the chain rule $\dot{f}_j = (\partial f_j / \partial x_k)\dot{x}_k$, and so Eq. (5) becomes:

$$\Sigma_{kj}^{-2}\left(\ddot{x}_j - \frac{\partial f_j}{\partial x_l}\dot{x}_l\right) + \left(\ddot{x}_i - \frac{\partial f_i}{\partial x_l}\dot{x}_l\right)\Sigma_{ik}^{-2} = -\frac{\partial f_i}{\partial x_k}\Sigma_{ij}^{-2}\left(\dot{x}_j - f_j\right) - \left(\dot{x}_i - f_i\right)\Sigma_{ij}^{-2}\frac{\partial f_j}{\partial x_k} \tag{6}$$

Small fluctuations

We now consider the case of small fluctuations about an equilibrium state and linearize the function $\vec{f}$ by writing $\vec{x}$ with reference to its long-term average, to give us $\vec{f}(\vec{x}) = M\vec{x}$, where M is a matrix and we have re-positioned our origin to be at the equilibrium point (i.e. $\vec{x} = \vec{0}$ denotes the equilibrium point). In matrix form, the Euler-Lagrange equations (6) then reduce to:

$$Y\ddot{\vec{x}} + \left(-YM + M^T Y\right)\dot{\vec{x}} - \left(M^T Y M\right)\vec{x} = 0, \tag{7}$$

where $Y = \Sigma^{-2} + (\Sigma^{-2})^T$ ($= 2\Sigma^{-2}$, since Σ^2 is symmetric). Furthermore, if we assume solutions of the form $\vec{x} = \vec{c^k}\exp(\lambda^{(k)}t)$ where k denotes the k-th solution, we have $\dot{\vec{x}} = \lambda^{(k)}\vec{x}$ and $\ddot{\vec{x}} = \lambda^{(k)2}\vec{x}$, giving the secular equations:

$$\left(-M^T - \lambda^{(k)}I\right) Y \left(M - \lambda^{(k)}I\right)\vec{c^k} = \vec{0}. \tag{8}$$

where I is the identity matrix.

Solution to the small fluctuations equation

By inspection, one solution of Eq. (8) can be found by solving:

$$\left(M - \lambda^{(k)}I\right)\vec{c^k} = \vec{0} \tag{9}$$

from which we recognize that $\vec{c^k}$ is an eigenvector of the matrix M with eigenvalue $\lambda^{(k)}$. (In general, the eigenvalues can be complex.) We expect N such solutions from an N-dimensional matrix. Further inspection reveals a second set of solution vectors $\vec{C^k}$ exists where $Y(M - \lambda^{(k)}I)\vec{C^k}$ is an eigenvector of M^T with eigenvector $-\lambda^{(k)}$. This implies that the second set of solutions $\vec{C^k}$ are given by:

$$\vec{C^k} = (M + \lambda^{(k)}I)^{-1}Y^{-1}\vec{d^k}, \tag{10}$$

where the set of vectors $\{\vec{d^k}\}$ are the 'reciprocal lattice' vectors of the set $\{\vec{c^k}\}$, that is $\vec{d^i}.\vec{c^j} = 0$ for all $i \neq j$, and $\lambda^{(k)}$ are the *same* eigenvalues as for the matrix M; note, however, it is the negative of these that are the eigenvalues of the second set of solutions.

The solution of the linearized Euler-Lagrange equations (8) is then a linear combination of all the eigensolutions:

$$\vec{x} = \sum_{k=1}^{N} a_k \vec{c^k}\exp\lambda^{(k)}t + \sum_{k=1}^{N} b_k (M + \lambda^{(k)}I)^{-1}Y^{-1}\vec{d^k}\exp(-\lambda^{(k)}t) \tag{11}$$

where $\{a_k\}$ and $\{b_k\}$ are constants describing the amounts of the various modes, and $\{\vec{d^k}\}$ are the 'reciprocal lattice' vectors of the set $\{\vec{c^k}\}$. If the the system has a stable equilibrium, the real parts of all the $\lambda^{(k)}$ will be negative. Therefore the first term of Eq. (11) represents decaying modes, whereas the second term represents growing modes.

Hamilton's equations
The Hamilton formulation uses first order differential equations in time to describe movement of a system through phase space. Formally, we define a *canonical momentum* conjugate to each co-ordinate variable of the Lagrangian, thus doubling the dimensionality of the system but reducing it to first-order in time. Unlike the Lagrangian case, which uses starting and ending conditions, the boundary conditions for the Hamiltonian approach are presented purely as initial conditions. For our case, we start with Eq. (3):

$$L = \frac{1}{2}\left(\dot{q}_k - f_k\right)\Sigma^{-2}_{kj}\left(\dot{q}_j - f_j\right), \tag{12}$$

where we have used $\vec{q} = \vec{x}$ (as is common in classical mechanics). If we assume that $\vec{f} = \vec{f}(\vec{q})$ (i.e. is not an explicit function of $\dot{\vec{q}}$ or t) we obtain our canonical momenta as:

$$p_i = \frac{\partial L}{\partial \dot{q}_i} = \frac{1}{2}\left(\dot{q}_k - f_k\right)\Sigma^{-2}_{ki} + \frac{1}{2}\Sigma^{-2}_{ij}\left(\dot{q}_j - f_j\right) = \Sigma^{-2}_{ij}(\dot{q}_j - f_j), \tag{13}$$

where the last part follows since Σ^2 is symmetric. Our Hamiltonian is then defined by:

$$H = \dot{\vec{q}}^T\vec{p} - L = \dot{q}_i p_i - \frac{1}{2}\left(\dot{q}_k - f_k\right)\Sigma^{-2}_{kj}\left(\dot{q}_j - f_j\right), \tag{14}$$

which in terms of $\vec{p}$ and $\vec{q}$ is:

$$H(\vec{p},\vec{q}) = f_i p_i + \frac{1}{2}p_i\Sigma^2_{il}p_l. \tag{15}$$

The second term on the right-hand-side of Eq. (15), which varies as canonical momentum squared, we identify as a pseudo-kinetic energy. This leaves the first term as a pseudo-potential energy. In this case, since there is no explicit time dependence of the Hamiltonian, we would expect the pseudo-energy to be a conserved quantity. The $2N$ equations of motion for the system are now given by:

$$\dot{q}_i = \frac{\partial H}{\partial p_i} = f_i + \Sigma^2_{il}p_l, \quad \dot{p}_i = -\frac{\partial H}{\partial q_i} = -\frac{\partial f_k}{\partial q_i}p_k. \tag{16}$$

We now have the full dynamics of Eq. (1) described in terms of Hamilton's equations. We have in particular identified the canonical momenta p_k and described their dynamics. Implications for neuron models are now discussed.

Discussion
We find that the canonical momenta $\vec{p}$ have a physical interpretation. Comparing Eq. (16) with the original equation of motion (1), we see that (in matrix form):

$$\Sigma^2\vec{p} = \vec{v}; \tag{17}$$

i.e. $\vec{p}$ is simply $\Sigma^{-2}\vec{v}$. This is non-intuitive since $\vec{v}$ represents the noise process, yet the Hamilton equation for the time-derivative of $\vec{p}$ is well defined. These facts are reconciled when we recall that the Lagrangian and Hamiltonian approaches represent the *most likely* path of the system; so the relationship between $\vec{p}$ and $\vec{v}$ can be viewed as a statement of what the most-likely noise input $\vec{v}$ is for given starting and ending conditions.

In the case of small fluctuations about an equilibrium point $\vec{q} = 0$, we can define $\vec{f}(\vec{q}) = M\vec{q}$, or, in components, $f_k = M_{kj}q_j$, and so Eq. (16) becomes:

$$\dot{p}_i = -M_{ki}p_k = -M^T_{ik}p_k. \tag{18}$$

Note the negative sign. Recall that, for a stable equilibrium, M is a negative definite matrix, so the real parts of its eigenvalues are negative. Clearly if $\vec{p}$ is initially an eigenvector of M^T, it will remain as an eigenvector and so *grow* exponentially in time according to the corresponding eigenvalue.(The eigenvalues of M and M^T are the same.) Therefore, we can consider the growing canonical momenta as giving rise to the growing modes of Eq. (11). The time-constants for the growth in $\vec{p}$ depends upon the eigenvalues of M, rather than the extent of the noise Σ.

Implications
The Hamiltonian description predicts that the modes associated with canonical momenta will grow exponentially with time, without bound. This may seem non-sensical, but we must limit our discussion to situations where starting and finishing points are known. In the Lagrangian method this is done by selecting the coefficients $\{a_k\}$ and $\{b_k\}$ in

Eq. (11) appropriately; with Hamilton's equations one can choose the correct initial values of the state variables q_i and their canonical momenta p_i. As an example, we consider the firing of a single neuron. Of particular relevance are the questions of what causes a neuron to fire (Rudolph *et al.* 2007), and whether we can predict the imminent firing of a neuron from an easily measurable quantity such as membrane potential. The Hamiltonian theory suggests that at late times the behaviour will be dominated by the exponential growth of the canonical momenta. This growth will be manifested through an increasing trend in the state variables (e.g. membrane potential) away from their equilibrium values. This agrees with what has been found experimentally (Pospischil *et al.* 2007, Rudolph *et al.* 2007); we have also demonstrated this numerically with a two-component model of a single neuron (Wilson and Steyn-Ross 2008). Moreover, since the canonical momenta are associated with the noise inputs through Eq. (17), there will be exponentially increasing bias to the noise on the build-up to a spike; indeed, one could say that it is an increased bias in the noise that is what causes a neuron to fire. This may be testable experimentally.

Secondly, we consider the case of many-neuron models, for example the well-used mean-field approach in two spatial dimensions (e.g. Robinson *et al.* 1997, Steyn-Ross *et al.* 2004, Bojak and Liley 2005). These models can also undergo transitions from one state to another (Steyn-Ross *et al.* 2004, Wilson *et al.* 2005). In this case the effective dimensionality N of the system is very high, and so there will be multiple exponential modes. One would expect that, during a transition away from an equilibrium state, the most rapidly *growing* conjugate modes are those associated with the eigenvalue $\lambda^{(k)}$ with most *negative* real part, through Eq. (11). In mean-field models, these modes are generally those with high spatial frequency (e.g. Wilson *et al.* 2005). This means that the high spatial frequencies will appear very quickly just before the transition, i.e. for most of the approach to transition the low frequency modes dominate. In some models, e.g. when gap junction connectivity is included (Steyn-Ross *et al.* 2007), there can be spatial frequencies where the real part of an eigenvalue is positive and spatial structures (Turing patterns) emerge naturally. In these cases one would expect the momenta conjugate to these modes to *decay* with time; i.e. the bias in the noise needed to drive the system into these structures decreases with time, and, once they start forming, they are likely to continue.

Conclusions

We have developed Lagrangian and Hamiltonian descriptions of a stochastic process in N dimensions. The canonical momenta are linear combinations of noise input to the system; the theory predicts that the magnitudes of these will increase exponentially with time — e.g. on the approach to a transition in state such as an action potential. From a Hamiltonian viewpoint, a transition between states of a neural system is the result of an exponentially growing canonical momentum pulling the system away from a stable equilibrium into a different regime.

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