Optimal control of Piecewise Deterministic Markov Processes with Applications to Optogenetics

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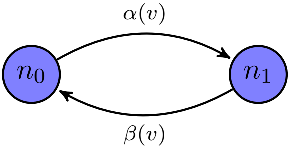
The variables

- $(v_t)_{t\geq 0}$ is the membrane potential along the axon, modelled by the segment $I := [0,1]$. $v_t \in H_0^1(I)$. It is the variable of importance, encodes the neuronal activity, the observable variable.
- $(d_t)_{t\geq 0}$ is the state of the ionic channels distributed along the axon. N channels located at positions $z_i \in I, i = 1, \cdots, N$. $d_t \in \mathcal{D}^N$ with $\mathcal{D}$ the finite set of the possible states.

The ionic channels

- They are gates that can open to let ions flow across the membrane.
- They can be of different types according to the types of ions that go through. In the ML model : K^+ and Ca^{2+}.
- Mathematically: Channels evolve as continuous-time Markov Chains with two kind of states (open and closed states). Their jump rate depends on the membrane potential.



- The state of a channel influences the membrane conductance which dictates the evolution of the membrane potential.

Evolution of the membrane potential at a given conductance

At a given conductance (*i.e.* a given state of the channels) the membrane potential follows the PDE:

$$\partial_t v_t = \kappa \Delta v_t + f_d(v_t), \quad v_t(0) = v_t(1) = 0, \quad v_0 = \zeta \in H_0^1(I).$$

with f_d has the form

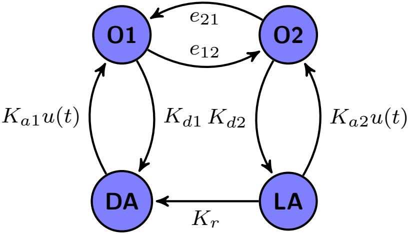
$$\sum_{x \in \mathcal{D}} \sum_{i=1}^{N} w_i^x(d,z)(v_x - v),$$

with

$$w_i^x(d,z) = \bar{w}^x \delta_x(d_i) \delta_{z_i}(z)$$

The Channelrhodopsin-2 (ChR2): an ionic channel opened by light stimulation

The ChR2 is modeled by a controlled Markov Chain where the control u represents the intensity of the light applied to the neuron, $u \in [0, u_{\max}]$. (see [7])



The ML model is modified by adding the conductances corresponding to the ChR2 channels in the term f_d in the PDE.

We get a fully coupled infinite dimensional controlled PDMP where the control acts on the jump rate and the jump measure.

Tracking a given membrane potential repartition

Let $v_{\text{ref}} \in H_0^1(I)$ be a reference signal that you want to mimic over a period of time $[0, T]$, $T > 0$. Let $\mathcal{U}$ be the class of control strategies you consider.

The Control problem $(\mathcal{P})$

Find a control strategy $\alpha \in \mathcal{U}$ that minimizes the cost

$$\mathbb{E}_y^\alpha \left[\int_0^T (||v_t - v_{\text{ref}}||^2_{L^2(I)} + \alpha(t)) \mathrm{d}t \right]$$

for every starting point $y \in H_0^1(I) \times \mathcal{D}^N$.

Existence of an optimal control strategy

Let $A := \{a : \mathbb{R}_+ \to [0, u_{\max}] \text{ measurable}\}$. A control strategy for the ML model is a measurable application $\alpha : \mathbb{R}_+ \times H_0^1(I) \times \mathcal{D}^N \to A$. Let $\mathcal{A}$ be the set of such applications.

Theorem

There exists a control strategy $\alpha^* \in \mathcal{A}$ that solves Problem $(\mathcal{P})$ above in the sense that for all $t \in [T_n, T_{n+1})$, the control applied to the system is $\alpha(T_n, v_{T_n}, d_{T_n})(t - T_n)$ (Piecewise open-loop controls, introduced by Vermes [8]).

Question

For what kind of infinite-dimensional controlled PDMPs can we give such results ?

Contents

The state space and control space

The state space is a product $E \times \mathcal{D}^N$ with

- E a reflexive separable Banach space (with "$E \subseteq H \subseteq E^*$" an evolution triple).
- $N \in \mathbb{N}^*$ and $\mathcal{D}$ a finite set.

The control space U is a Borel subset of a Polish space. Let

$$A := \{a : [0,T] \to U \text{ measurable}\},$$

$T > 0$ the finite time horizon.

The three characteristics of the PDMP

- A family of PDEs defined for $(d, a) \in \mathcal{D}^N \times A$ by

$$\begin{cases} \dot{v}_t = L_d v_t + f_d(v_t, a(t)), \\ v_0 = v, \quad v \in E. \end{cases}$$

  with L_d the infinitesimal generator of a strongly continuous semigroup.
- A jump rate $\lambda : E \times \mathcal{D}^N \times U \to \mathbb{R}_+$.
- A transition measure $\mathcal{Q} : E \times \mathcal{D}^N \times U \to \mathcal{P}(\mathcal{D}^N)$.

See Buckwar and Riedler ([2]) for the case without control.

1. Define an enlarged process and a class of control strategies such that, eventually, optimal controls will be feedback controls.
2. Define a probabilistic space common to every control strategies such that the controlled PDMP is strongly markovian.
3. Consider a proper class of relaxed strategies and prove relaxation theorems.
4. Consider the Markov Decision Process included in the PDMP and show the equivalence of the control problems.
5. Apply dynamic programming on the MDP to characterize the value function of the relaxed control problem as a fixed point of a contracting operator from some space of continuous functions in itself (see Bäuerle and Rieder ([3]) in finite dimension with a constant jump rate).
6. Use a fixed point Theorem to show the existence of an optimal relaxed strategy.
7. Find conditions on the model to obtain existence of a non-relaxed optimal strategy.

Relaxed characteristics

$$\begin{cases} \dfrac{\mathrm{d}}{\mathrm{d}t}\chi_t^{\mu}(z) = -\chi_t^{\mu}(z)\displaystyle\int_U \lambda_d(\phi_t^{\mu}(z),u)\mu_t(\mathrm{d}u), \qquad \chi_0^{\mu}(z)=1, \\ \mathcal{Q}'(\Sigma|z,\mu) = \mathbf{1}_{\{\tau+h\leq T\}}\displaystyle\int_0^{T-\tau-h} \chi_s^{\mu}(z)\mathbf{1}_B(0)\mathbf{1}_G(\phi_s^{\mu}(z))\mathbf{1}_K(\tau+h+s) \\ \qquad\qquad \displaystyle\int_U \lambda_d(\phi_s^{\mu}(z),u)\mathcal{Q}\Big(D|\phi_s^{\mu}(z)d,u\Big)\mu_s(\mathrm{d}u)\mathrm{d}s, \\ \phi_t^{\mu}(z) = S_d(0)v + \displaystyle\int_0^t S_d(t-s)\mathbf{f}_d(\phi_s^{\mu}(z))\mu_s\mathrm{d}s, \end{cases} \tag{1}$$

$\mathbf{f}_d(y)\mu \in E$ such that for all $y^* \in E^*, \langle y^*, \mathbf{f}_d(y)\mu\rangle_{E^*,E} = \int_U \langle y^*, f_d(y,u)\rangle_{E^*,E}\mu(\mathrm{d}u)$, with μ a bounded regular, finetely additive measures on U ($\mu(\cdot) \in L_w^{\infty}([0,T],(BC(U))^*)$, see Fattorini [6]).

The crucial point is to show the continuity of the applications:

$$(t, z, \mu) \to \phi_t^\mu(z)$$

and

$$(t, z, \mu) \to \chi_t^\mu(z).$$

Question

When the existence of an optimal control strategy has been proved, how do you reach it ?

Quantization techniques and approximation of the value function ? Brandejsky, de Saporta, Dufour [1]

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