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# Effects of couplings on the optimal desynchronizing control of neuronal networks

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ABSTRACT

Excessive synchronization of neurons in the basal ganglia of the brain is one of the hallmarks for Parkinson's disease (PD). It has been proven that the high-frequency deep brain stimulation (DBS) was an effective treatment for PD patients, and it could alleviate the symptoms of PD by mitigating the pathological synchronous oscillations of neurons. To reduce risks of excessive high-frequency stimulus and improve the DBS treatment, researchers have paid much attention to the optimization strategies of DBS based on neuronal network models. However, the influence of neuronal network models on the control performance has been neglected which significantly affected this optimization. This paper investigated the effects of neuronal network models on the optimal desynchronizing control of synchronized neurons, which was done by applying the discrete time dynamic programming method to reduced phase models for neurons. Numerical simulations show that the coupling types and strengths as well as connection topologies of neuronal networks influence the desynchronizing results greatly. Such as, the neuronal networks with chemical synaptic couplings are more easily to be desynchronized than those with electrotonic couplings, and the networks containing symmetry are very difficult to be desynchronized. This research can contribute to the development and application of the optimal DBS control strategies.



## 1. Introduction

Due to the importance of synchronous firing activities between distant brain regions, and the key role of information processing in brain, synchronization phenomena of neural networks has attracted extensively research interest [1,2]. However, pathological, excessive synchronization of neural networks may impair brain function and is a hallmark of several neurological disorders, such as PD, essential tremor and epilepsy et al. [3]. In PD, for example, excessive synchronous oscillations in β-band frequencies (8–35 Hz) are closely associated with motor symptoms [4,5]. Research shows that reduction of synchronized oscillations by high-frequency DBS is positively correlated with amelioration of motor symptoms [6,7]. Nowadays, DBS has been the standard therapy for medically refractory PD patients. However, the traditional DBS which is in an open-loop fashion could cause excess stimulation and then bring some side effects and risks [8], thus an optimal (feedback-based) approach is attractive from a clinical perspective to minimize side effects and risks by optimizing the timing and energy of the input stimulation.

Motivated by development of improving the DBS treatment, the optimal control has been appropriately applied to neural systems to regulate the spiking timing, frequency and phase of neurons [9–12]. Most previous research devoted to look for the proper control strategies to achieve the effective synchronization or desynchronizing control for neuronal networks, such as the nonlinear delayed feedback control presented by Tass et al. [13,14], and the pinning-impulsive control as well as the matrix measure strategies presented by Cao et al. [15–18]. But in fact, the neuronal systems are very complicated, and there are many other factors, such as size and structure of neuronal networks, types and strengths of the couplings between neurons and so on, which might have their influence on the control performance for synchronizing or desynchronizing neurons. Recently, Schiff have presented that the coupling in a network could have a profound impact on its control [19]. Thus the coupling and network structures present tremendous challenges to our ability to formulate effective control strategies. So figuring out how the desynchronizing control performance can be affected by neuronal network models, especially by the couplings between neurons, could help

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to formulate the more appropriate and preferable control strategies to regulate the dynamic of neural systems.

Brain networks are extremely complicated but can be characterized by highly overrepresented small motifs, and the characteristics of these motifs can provide an implication for the functions of brain. However, even the simplest motifs with only three neurons can have many control variables providing that each neuron is represented by the state-space equations. As we all know that, for periodically spiking neurons, the dynamic of the full state-space model can be described by a limit cycle, and can be characterized by the phase models through phase coordinate transformation together with formal averaging [20,21]. Since then, phase models have been extensively and successfully applied to investigate synchronization phenomena [22], especially the synchronization emerging in networks of interacting oscillators as well as on the response of collections of oscillators to external stimuli [23–25]. And they have also been used to design control strategies for neural systems [26–30], which indicated that the reduced phase models were practical to achieve control objective.

Hence, to explore the effects of couplings and connection structures between neurons on the desynchronizing control performance, we design the optimal desynchronizing control on reduced phase network models. We organize our paper as follows: first, the discrete time dynamic programming method is introduced, and then the phase network models as well as the discrete dynamic programming framework are established, at last, the desynchronizing results and discussions are presented.

## 2. Discrete dynamic programming

The main objective in an optimal control is to find out how a system can be controlled in such a way that its behavior satisfies certain requirements. A very efficient method for solving optimal control problems for discrete-time systems is the recursive dynamic programming technique, introduced by Richard Bellman [31].

Considering a deterministic system in which the state vector at the instant $k$ is denoted as $x_k$, and $k$ satisfies $1 \le k \le K$, then if there exists a control input $u_k$ which is applied at the instant $k$ causing the transition of the system from $x_k$ to $x_{k+1}$, then the evolution of the system can be denoted as:

$$x_{k+1} = f_k(x_k, u_k), x_k \in \chi, u_k \in U \tag{1}$$

where $f_k$ is the state transition function, $\chi$ is the state space and $U$ is the control space. Obviously, the system can be carried from an initial state $x_1$ to the final state $x_{K+1}$ with a sequence of controls $u_1, ..., u_K$ which is named as a policy.

According to the definition of dynamic programming, if the control $u_k$ corresponds to the transition from $x_k$ to $x_{k+1}$, then an elementary cost $g_k(x_k, u_k)$ will be assigned, and then the total costs from $x_1$ to $x_{K+1}$ can be denoted as:

$$J = \sum_{k=1}^{K} g_k(x_k, u_k) + G(x_{K+1}) \tag{2}$$

where $G(x_{K+1})$ denotes the final time cost, then the optimal control policy is to get the minimal or maximal $J$. In dynamic programming framework, we can use the value function $E_m(x_m)$ for state $x_m (1 \le m \le K)$ to describe the cost-to-go from it:

$$E_m(x_m) = \sum_{k=m}^{K} g_k(x_{k,} u_k) + G(x_{K+1}) \tag{3}$$

where $J = E_1(x_1)$. If $E_m^*(x_m)$ denotes the future costs under the optimal control policy starting from state $x_m$, then according to the principle of optimality: whatever the initial state, if the first control decision is contained in an optimal policy, then the remaining control decisions must constitute an optimal policy for the problem with initial state resulting from the first control decision [32], thus we have:

$$\begin{aligned} E_m^*(x_m) &= \min_{u_k \in U, \forall k \ge m} \left( \sum_{k=m}^{K} g_k(x_k, u_k) + G(x_{K+1}) \right) \\ &= \min_{u_k \in U} \left( g_m(x_m, u_m) + E_{m+1}^*(f_m(x_m, u_m)) \right). \end{aligned} \tag{4}$$

here we address the minimal cost as the optimal cost, and Eq. (4) is the base to compute the cost-to-go for a system throughout the time and state domains recursively. After initializing $E_{K+1}(x)$, one can first perform a backward iteration to compute $E_1(x)$ for all states in the state space. Then, given an initial condition $x_1$, a forward iteration loop will yield the optimal control and state trajectories:

$$u_k^* = \arg\min_{u_k \in U} (g_k(x_{k,} u_k) + E_{k+1}{}^*(f_k(x_k^*, u_k))), x_{k+1}^* = f_k(x_k^*, u_k^*), \quad x_1^* = x_1. \tag{5}$$

## 3. Phase network models

Hodgkin–Huxley (HH) model, presented in 1952, was derived to model the loligo squid's giant axon [33]. It was widely used in modeling the dynamic of neurons, and can be denoted as follows:

$$\begin{aligned} \dot{V} &= \frac{1}{C}(-\bar{g}_{Na} h (V - V_{Na}) m^3 - \bar{g}_K (V - V_K) n^4 - \bar{g}_L (V - V_L) + I_b), \\ \dot{m} &= a_m(V)(1-m) - b_m(V) m, \\ \dot{h} &= a_h(V)(1-h) - b_h(V) h, \\ \dot{n} &= a_n(V)(1-n) - b_n(V) n \end{aligned} \tag{6}$$

where

$$\begin{aligned} a_m(V) &= 0.1(V+40)/(1-\exp(-(V+40)/10)), \\ b_m(V) &= 4\exp(-(V+65)/18), \\ a_h(V) &= 0.07\ \exp(-(V+65)/20), \\ b_h(V) &= 1/(1+\exp(-(V+35)/10)), \\ a_n(V) &= 0.01(V+55)/(1-\exp(-(V+55)/10)), \\ b_n(V) &= 0.125\ \exp(-(V+65)/80) \end{aligned}$$

in which $V$ is the voltage across the neuron membrane, $m, h, n$ are the vectors of gating variables which correspond to the states of the membrane's ion channels, $C$ is the constant membrane capacitance and $I_b$ is the baseline current which can be viewed as a bifurcation parameter of the model. The parameters are given as $C = 1\ \mu\text{F cm}^{-2}$, $\bar{g}_{\text{Na}} = 120\ \text{mS cm}^{-2}$, $\bar{g}_{\text{K}} = 36\ \text{mS cm}^{-2}$, $\bar{g}_{\text{L}} = 0.3\ \text{mS cm}^{-2}$, $V_{\text{Na}} = -50$ mV, $V_K = -77$ mV, $V_L = -5.4$ mV. Here we choose $I_b = 10\ \mu\text{A cm}^{-2}$ which corresponds to the periodically spiking state of HH neuron with period $T = 14.63$ ms. The time series and limit cycle of the HH model are shown as Fig. 1.

If we define the state vector $X = [V, m, h, n]^T$, then the Eq.(6) can be denoted as:

$$\frac{dX}{dt} = F(X). \tag{7}$$

thus the $N$ weakly coupled neurons can be in the form:

$$\frac{dX_i}{dt} = F(X_i) + \sum_{j=1}^{N} g_{ij} p(X_i, X_j). \tag{8}$$

$g_{ij}$ is the weak coupling strength between neurons, and $p(X_i, X_j)$ indicates the coupling term between neurons. The coupling term for electronically coupled neurons can take the form:

$$p(X_i, X_j) = V_j - V_i. \tag{9}$$