# A Latent Force Model for Describing Electric Propagation in Deep Brain Stimulation: A Simulation Study

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***Abstract*— Deep brain stimulation (DBS) is a neurosurgical method used to treat symptoms of movement disorders by implanting electrodes in deep brain areas. Often, the DBS modeling approaches found in the literature assume a quasi-static approximation, and discard any dynamic behavior. Nevertheless, in a real DBS system the stimulus corresponds to a wave that changes as a function of time. It is clear that DBS demands an approach that takes into account the time-varying behavior of the input stimulus. In this work, we present a novel latent force model for describing the dynamic electric propagation occurred during DBS. The performance of the proposed model was studied by simulations under different conditions. The results show that our approach is able to take into account the time variations of the source and the produced field. Moreover, by restricting our model it is possible to obtain solutions for electrostatic formulations, here experimental results were compared with the finite element method. Additionally, our approach allows a solution to the inverse problem, which is a valuable clinical application allowing the appropriate tuning of the DBS device by the expert physician.**

## I. Introduction

Parkinson's disease is a progressive disorder of the nervous system marked by tremor, muscular rigidity, and slow, imprecise movement, affecting mainly middle-aged and elderly people. It is associated with degeneration of the basal ganglia of the brain and a deficiency of the neurotransmitter dopamine. On the other hand, deep brain stimulation (DBS) is a neurosurgical method used to treat symptoms of movement disorders by implanting stimulation electrodes in deep brain areas [1]. The clinical successes of DBS have prompted the development of continuously improving scientific techniques to quantify its effects on the nervous system, as well as to provide clinical guidance on the most efficacious electrical parameters for stimulation [2].

Although the method has become a common procedure in many clinical fields like Parkinson's disease, essential tremor, and dystonia, the fundamental mechanisms of DBS remain uncertain [3]. In order to enhance the knowledge about DBS performance and to avoid collateral effects of the treatment, in the last decade many models for predicting the electrical behavior induced by DBS were developed. A suitable stimulation protocol involves not only the accurate placement of the electrode inside the brain, but also the proper configuration of some electrical parameters (pulse width, frequency and the voltage amplitude) for the DBS device. More realistic predictions require reproducing as accurate as possible the medium characteristics and the DBS device behavior.

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In order to model the electrical behavior of the deep brain stimulation some constraints are imposed. Often, in the literature, static (or quasi-static) conditions are assumed: the system is governed by the Poisson's or the Laplace's equation [4]–[6]. Additionally, a realistic geometry of the head is needed for a rigorous representation of the phenomenon, which generates a huge amount of degrees of freedom. A common alternative is to use numerical techniques as the finite element method (FEM) or the finite difference method (FDM) to compute the electric field generated by the DBS. However, in these models, the electric source is represented as a perfect voltage (or current) and its dynamic behavior is discarded, and their effects are ignored. Generally, in a real DBS system, the stimulus waveform corresponds to an square wave train, that is, the stimulus wave changes as a function of the time, which can not be considered by the mentioned methods. The errors induced by this assumption may be significant in the context of brain simulation, where 1mm changes in the spread of activation can have dramatic consequences on the therapeutic effects induced by the stimulation [7].

To account for the dynamics in the electric propagation, a Fourier finite element method (Fourier FEM) was proposed in [7]. The method involves the solution of the Poisson's equation at frequency components to calculate the potential distribution in the tissue medium as a function of the time and space simultaneously for a range of stimulus waveforms. Nevertheless, the Fourier FEM solves for steady state solutions and does not model transients, that is, the effects of the wave propagation are neglected. The results presented in [10] give rise to the conclusion that the quasi-static approximation is valid, however their analysis was done for an infinite domain.

It is clear that the deep brain stimulation demands the study of a dynamical problem, i.e. an approach that takes into account the time-varying behavior of the input stimulus is required. In this work we aim to design and implement a novel latent force model for describing the dynamical electric propagation occurred during deep brain stimulation using Gaussian processes (GP) [8], that takes into account the time variations of the source and the produced field. The main goal is to solve a partial differential equation subject to some boundary constraints (geometry) by using Gaussian processes. In our case, the GP is represented by random variables that correspond to: 1) the excitation

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source at any time and place, and 2) the value of the electric potential at any place of the tissue medium at any time. In particular, we are solving the inhomogeneous wave equation. Our proposal is a general formulation of the electric propagation problem. In fact, by restricting our model it is possible to obtain the Laplace's or Poisson's formulation. Additionally, our approach allows a forward solution to the inverse electric propagation problem, that is, defining the potential distribution it is possible to compute the corresponding input stimulus (and its parameters), which is a valuable clinical application allowing the appropriate tuning of the DBS device by the expert physician.

## II. Materials and Methods

In this work we use a latent force model based on the wave equation for describing the electric propagation in deep brain stimulation. We are particularly interested in computing the electric potential $f$, because once this quantity is calculated, the electric field and the current density can also be obtained. Furthermore, the volume of tissue activated (VTA) is related to the double spatial derivative of the electric potential, and the integration of the current density vector around the electrode provides the total current [9].

### A. Electric potential propagation modeling

Commonly, the electric potential distribution produced during DBS is modeled using the Laplace's [1] [5] [6], or the Poisson's [4] [7] [9] equation, under the assumption that this quantity is a quasi-static field. The quasi-static approximation neglects wave propagation effects and time derivatives in Maxwell's equations, limiting the models to not take into account time variations [10]. This simplifies the wave equation for the electrodynamic scalar potential $f$

$$\nabla^2 f - \frac{1}{c^2}\frac{\partial^2 f}{\partial t^2} = -\frac{\rho}{\varepsilon}, \tag{1}$$

where $f$ is the electric potential, $c$ is the propagation velocity of the electromagnetic wave, $\rho$ denotes the electric space charge density and $\varepsilon$ the permittivity [11]. The quasi-static approximation implies that the second partial derivative with respect to time in (1) can be ignored [12], therefore the wave equation reduces to the Poisson's equation [10] [13],

$$\nabla^2 f = -\frac{\rho}{\varepsilon}. \tag{2}$$

Furthermore, if we consider no sources we get the Laplace's equation, $\nabla^2 f = 0$.

### B. Latent force models using Gaussian processes

The general framework of the latent force models (LFM) is to combine a mechanistic model with a probabilistic prior over some latent function [14]. Here, the mechanistic model corresponds to the wave equation (1), and the latent function represents the source of excitation. We use Gaussian processes for defining a probabilistic prior over the latent function. Formally, a Gaussian process (GP) is a collection of random variables, any finite number of which have a joint Gaussian distribution [15]. The Gaussian process represents the value of the excitation $u(\mathbf{x},t)$ as well as the value of the electric potential $f(\mathbf{x},t)$, at location $\mathbf{x}$ at time $t$.[1] We assume that the latent function follows a Gaussian process prior, with zero mean and covariance function $k_{u,u}(\mathbf{x},t,\mathbf{x}',t')$, i.e. $u(\mathbf{x},t) \sim \mathcal{GP}(0,k_{u,u}(\mathbf{x},t,\mathbf{x}',t'))$. Due to the linearity of the PDE used, its solution $f(\mathbf{x},t)$ also corresponds to a Gaussian process prior with zero mean and covariance function $k_{f,f}(\mathbf{x},t,\mathbf{x},t')$. Furthermore, a covariance function $k_{f,u}(\mathbf{x},t,\mathbf{x}',t')$ between $f$ and $u$ can also be computed.

We are interested in getting the posterior distribution over the function $f$, given an specific source of excitation $u$. This is known as the direct problem. The posterior distribution over $f$ is given by [15],

$$f|u \sim \mathcal{N}\left(K_{fu}K_{uu}^{-1}u \ , \ K_{ff} - K_{fu}K_{uu}^{-1}K_{fu}^{\top}\right), \tag{3}$$

where $K_{ff}$, $K_{fu}$, and $K_{u,u}$ are covariance matrices computed from functions $k_{f,f}(\cdot,\cdot)$, $k_{f,u}(\cdot,\cdot)$, and $k_{u,u}(\cdot,\cdot)$, at particular space points and time instants. We are also interested in the inverse problem, i.e. the posterior distribution over the latent force $u$, given an specific solution $f$,

$$u|f \sim \mathcal{N}\left(K_{fu}^{\top}K_{ff}^{-1}f \ , \ K_{uu} - K_{fu}^{\top}K_{ff}^{-1}K_{fu}\right). \tag{4}$$

We apply latent force models for the direct and inverse problems in deep brain stimulation. In this paper, we restrict the solution domain to have two spatial dimensions $\mathbf{x} = [x \ y]^{\top}$.

### C. A latent force model for the wave equation

Instead of using the quasi-static approximation, we use the general expression for the second order nonhomogeneous wave equation with two space variables in the rectangular Cartesian system of coordinates

$$\frac{\partial^2 f}{\partial t^2} = a^2\left(\frac{\partial^2 f}{\partial x^2} + \frac{\partial^2 f}{\partial y^2}\right) + u(x,y,t), \tag{5}$$

where $f(x,y,t)$ is the unknown function and represents the electric potential, $a$ is a constant coefficient and $u(x,y,t)$ is the excitation source. The exact solution to (5) is dependent on specific boundary and initial conditions. For a boundary value problem in a rectangle domain $0 \le x \le l_1$, $0 \le y \le l_2$, with boundary conditions $f(x=0,y,t)$, $f(x=l_1,y,t)$, $f(x,y=0,t)$ and $f(x,y=l_2,t)$, and initial conditions $f(x,y,t=0)$ and $\partial_t f(x,y,t=0)$, all equal to zero, the solution to the wave equation is given by [16],

$$f(x,y,t) = S\int_0^t\int_0^{l_1}\int_0^{l_2} u(\zeta,\eta,\tau)G(x,y,\zeta,\eta,t-\tau)\mathrm{d}\eta\mathrm{d}\zeta\mathrm{d}\tau,$$

where $S$ is the sensitivity, which accounts for the influence of the latent force over the solution to the partial differential equation. The Green's function $G(x,y,\zeta,\eta,t)$ is [16]

$$\sum_{n=1}^{\infty}\sum_{m=1}^{\infty}\frac{4\sin(p_n x)\sin(q_m y)\sin(p_n\zeta)\sin(q_m\eta)\sin(a\lambda_{nm}t)}{al_1l_2\lambda_{nm}},$$

[1] Location $\mathbf{x}\in\mathbb{R}^D$, with $D = 1, 2$ or $3$ in rectangular Cartesian coordinates.

where $p_n = n\pi/l_1$, $q_m = m\pi/l_2$, and $\lambda_{nm} = \sqrt{p_n^2 + q_m^2}$. We assume that the excitation $u(x,y,t)$ is a Gaussian process with covariance function $k_{u,u}(x,y,t,x',y',t')$ defined as

$$e^{\left(\frac{-(t-t')^2}{\sigma_t^2}\right)} e^{\left(\frac{-(x-x')^2}{\sigma_x^2}\right)} e^{\left(\frac{-(y-y')^2}{\sigma_y^2}\right)}, \tag{6}$$

where $\sigma_t$ represents the length-scale of the time input variable, $\sigma_x$ and $\sigma_y$ represent the length-scale along the $x$ and $y$ spatial input variables, respectively. Since (5) is linear, then the solution $f(x,y,t)$ is also a Gaussian process with zero mean and covariance function $k_{f,f}(x,y,t,x',y',t')$, given by

$$\left(\frac{4}{al_1l_2}\right)^2 \sum_{\forall n}\sum_{\forall m}\sum_{\forall n'}\sum_{\forall m'} \frac{SS' k^t_{f,f}(t,t') k^x_{f,f}(x,x') k^y_{f,f}(y,y')}{\lambda_{nm}\lambda_{n'm'}} \tag{7}$$

where $k^x_{f,f}(x,x')$, $k^y_{f,f}(y,y')$ and $k^t_{f,f}(t,t')$ are kernel functions dependent on the indexes $n$, $n'$, $m$ and $m'$. Finally, the cross covariance $k_{f,u}(x,y,t,x',y',t')$ between the solution $f(x,y,t)$ and the excitation $u(x,y,t)$ is defined by

$$\frac{4}{l_1l_2} \sum_{\forall n}\sum_{\forall m} k^t_{f,u}(t,t') k^x_{f,u}(x,x') k^y_{f,u}(y,y'). \tag{8}$$

Solutions for the kernels in (7) and (8) can be obtained analytically. Particular expressions are not included due to space constrains.

## III. Results and Discussion

The proposed latent force model based on the wave equation (see section II-C) was evaluated under different circumstances. First, we highlight its dynamic properties by calculating the posterior mean over the solution to the wave equation (5), given a time varying source. Second, we find the electric potential produced during deep brain stimulation, using the presented model in a direct problem approach (3). We also compare our outcomes with the electric potential obtained by solving the Poisson equation through the finite element method (FEM). Finally, we show a simulation example where the proposed latent force model is used to solve the inverse model (4), i.e. to find the source of excitation that produced a prescribed electric potential.

In sections III-B and III-C the results obtained by the proposed model are compared with the finite element method. The data set used for these experiments come from coding the solution to the Poisson equation through the Python library FEniCS; a FEM based tool for solving partial differential equations. See [17] for electromagnetic problems solved using FEniCS. The problem specifications were: an uniform mesh of $30 \times 30$ points over a rectangle domain with size $10\text{cm} \times 10\text{cm}$, and all boundary conditions equal to zero. For the LFM, the values of the length-scales of the latent force covariance function (6) were tuned manually.

### A. Time-varying source

We use a time-varying source $u$ to illustrate the dynamic performance of the wave latent force model. Figures 1(a), 1(c) and 1(e) show the source $u$ for the time instants (seconds) [0.5, 0.55, 0.6], respectively. The posterior mean over the solution $f(x,y,t)$ to the wave equation (5), for the same time instants, was obtained by (3), as shown in Figures 1(b), 1(d) and 1(f). Here, the source was of the form $u = A(x,y)B(t)$, where $B(t) = \sin(9\pi t/5)$ and the term $A(x,y)$ is defined as a Gaussian distribution with mean $\boldsymbol{\mu} = [0.75,\ 0.3]^\top$, and an spherical covariance matrix with variance $\sigma^2 = 0.02$.

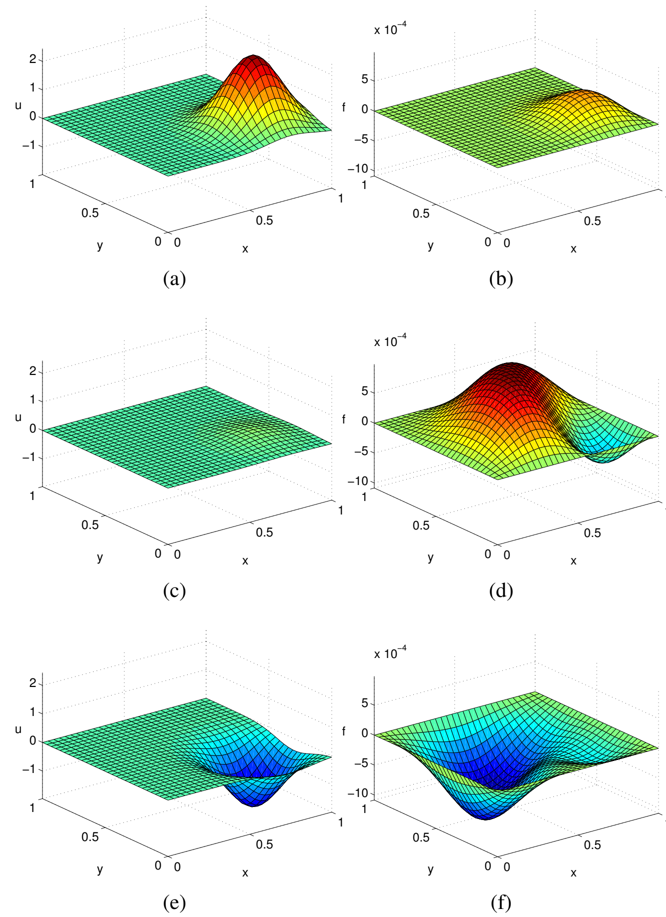


Fig. 1. (a), (c), (e), Illustration of a time-varying source of excitation $u$ at instants (seconds) [0.5, 0.55, 0.6], respectively. (b), (d), (f) Mean of the posterior distribution over the solution $f$ at instants (seconds) [0.5, 0.55, 0.6], respectively.

### B. Direct problem: simulation of deep brain stimulation

In the previous subsection we considered a dynamic source $u$ which results in a posterior over the solution $f$ that also varies in time. We now apply the model in the case where $u$ is static, within the framework of deep brain stimulation. Here, $u$ represents a current source fixed to 1 mA. The source has the form of a piecewise function, defined as $u(x,y,t) = 1 \times 10^{-3}$ at the electrode contact location, and $u(x,y,t) = 0$ elsewhere. Fig. 2(a) shows the corresponding electric potential, calculated using FEM for solving the Poisson equation (2). The posterior mean over the electric potential, obtained through (3) using the latent force model approach (Fig. 2(b)), showed high similarity in shape as well as in magnitude compared with the FEM solution. The quadratic mean error between the results obtained with both methods was $3.3813 \times 10^{-21}$.

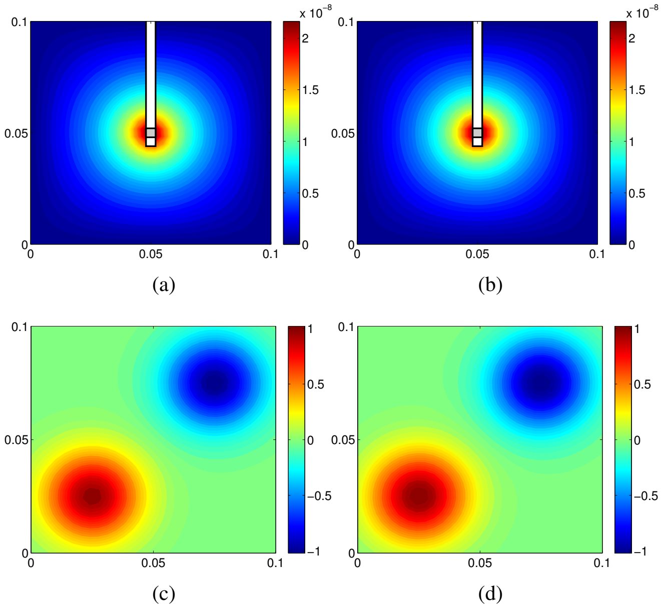


Fig. 2. (a) Electric potential obtained by FEM. (b) Electric potential posterior mean obtained by LFM. (c) Original source to be recovered in the inverse problem. (d) Posterior mean for the source obtained using LFM.

### C. *Inverse problem: Electrostatic field*

So far, we have analyzed the direct problem (3). Specifically, situations where we have knowledge about the source $u$, and wish to found the solution $f$ to the wave equation. The proposed model can also be used for solving the inverse problem, i.e. to recover the source that produced an specific electric potential. To do so, we use FEM to obtain the electric potential generated by the charge density showed in Fig. 2(c), and take these results as input data to the latent force model in (4) to get a posterior distribution over the source $u$. A similar example can be found in [18]. The posterior mean over the recovered source (Fig. 2(d)) exhibited high similarity to the original excitation. The quadratic mean error between the original and recovered source was of $1.3574 \times 10^{-04}$. The variance over the recovered source computed using LFM, as well as the electric potential used as input data, are not showed here due to space limitations.

## IV. CONCLUSIONS

In this paper, we have presented a novel latent force model for describing electric sources and fields, within the framework of deep brain stimulation. We used the partial differential wave equation and Gaussian process priors to model the electric potential as well as its source. The results show that the proposed method can model dynamic electric potentials and sources, as well as electrostatic problems. The electric potential calculated with the latent force model proved to be close to the potential obtained by solving the Poisson equation using the finite element method. Besides, the results show that the inverse problem can be addressed using the proposed model. The latent force model presented in this paper could be extended to make use of more realistic domains, taking into account three spatial dimensions instead of two, and allowing heterogeneous and anisotropic domain properties. Additionally, different boundary and initial conditions can be analyzed. Finally, a partial differential equation that considers the wave propagation in lossy materials might also be considered.


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## REFERENCES


[1] C. Schmidt and U. van Rienen, "Modeling the field distribution in deep brain stimulation: The influence of anisotropy of brain tissue," *IEEE Transactions on biomedical engineering*, vol. 59, no. 6, pp. 1583–1592, 2012.

[2] C. R. Butson, S. E. Cooper, J. M. Henderson, B. Wolgamuth, and C. C. McIntyre, "Probabilistic analysis of activation volumes generated during deep brain stimulation," *NeuroImage*, vol. 54, pp. 2096–2104, 2011.

[3] M. C. Rodriguez-Oroz, M. Rodriguez, J. Guridi, K. Mewes, V. Chockkman, J. L. Vitek, M. R. DeLong, and J. A. Obeso, "The subthalamic nucleus in Parkinson's disease: Somatotopic organization and physiological characteristics," *Brain*, vol. 124, pp. 1777–1790, 2001.

[4] S. Miocinovic, S. F. Lempka, G. S. Russo, C. B. Maks, C. R. Butson, K. E. Sakaie, J. L. Vitek, and C. C. McIntyre, "Experimental and theoretical characterization of the voltage distribution generated by deep brain stimulation," *Experimental Neurology*, vol. 216, pp. 166–176, 2009.

[5] P. F. Grant and M. M. Lowery, "Electric field distribution in a finite-volume head model of deep brain stimulation," *Medical engineering & physics*, vol. 31, pp. 1095–1103, 2009.

[6] M. Liberti, F. Apollonio, A. Paffi, M. Parazzini, F. Maggio, T. Novellino, P. Ravazzani, and G. D'Inzeo, "Fundamental electrical quantities in deep brain stimulation: Influence of domain dimensions and boundary conditions," in *IEEE EMBS*, 2007, pp. 6668–6671.

[7] C. R. Butson and C. C. McIntyre, "Tissue and electrode capacitance reduce neural activation volumes during deep brain stimulation," *Clinical Neurophysiology*, vol. 116, pp. 2490–2500, 2005.

[8] M. Álvarez, D. Luengo, and N. Lawrence., "Latent force models," in *AISTATS*, 2009, pp. 9–16.

[9] G. Walckiers, B. Fuchs, M.-K. Jeong, J.-P. Thiran, J. R. Mosig, and C. Pollo, "Influence of the implanted pulse generator as reference electrode in finite element model of monopolar deep brain stimulation," *Journal of Neuroscience Methods*, vol. 186, no. 5, pp. 90–96, 2010.

[10] C. a Bossetti, M. J. Birdno, and W. M. Grill, "Analysis of the quasi-static approximation for calculating potentials generated by neural stimulation," *Journal of Neural Engineering*, vol. 59, no. 5, pp. 44–53, 2008.

[11] H. Hermann and J. R. Melcher, *Electromagnetic fields and energy*. Prentice-Hall, 1989.

[12] T. Steinmetz, S. Kurz, and M. Clemens, "Domains of validity of quasistatic and quasistationary field approximations," in *15th International symposium on theoretical electrical engineering ISTET*, Lubeck, Germnay, June 2009, pp. 271–275.

[13] M. N. O. Sadiku, *Elements of electromagnetics*. USA: Oxford University Press, 2002.

[14] M. Álvarez, D. Luengo, and N. Lawrence, "Linear latent force models using Gaussian processes," *Pattern Analysis and Machine Intelligence, IEEE Transactions on*, vol. 35, no. 11, pp. 2693–2705, Nov 2013.

[15] C. E. Rasmussen and C. K. I. Williams, *Gaussian processes for machine learning (adaptive computation and machine learning)*. The MIT Press, 2005.

[16] A. D. Polyanin, *Handbook of linear partial differential equations for engineers and scientists*. USA: Chapman & Hall/CRC, 2002.

[17] A. Otto, N. Marais, E. Lezar, and D. Davidson, "Using the fenics package for FEM solutions in electromagnetics," *Antennas and Propagation Magazine, IEEE*, vol. 54, no. 4, pp. 206–223, Aug 2012.

[18] S. Särkkä, "Linear operators and stochastic partial differential equations in Gaussian process regression," in *Artificial Neural Networks and Machine Learning - ICANN 2011*, ser. Lecture Notes in Computer Science. Springer Berlin Heidelberg, 2011, vol. 6792, pp. 151–158.