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Bayesian approach to inverse problem in the case of time-resolved polarized fluorescence investigation of microscopically ordered systems

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ABSTRACT

In the case of fluorescence investigation of systems, which are isotropic in the macro scale but anisotropic in the micro scale, a Bayesian approach to an inverse problem allows finding distributions of model parameters. Next, this approach provides capacity to ascertain, whether the aligning potential alters during an electronic excitation of the fluorescence probe. The usage of the synthetic data set allows to specify an extent of *a priori* information necessary to a description of the data. As a numerical basement for Bayesian calculations the Differential Evolution Markov Chain method is employed.

1. Introduction

The polarized fluorescence measurements are widely used to determine physical properties of ordered systems. The special case of them are systems ordered in the micro scale but macroscopically isotropic, such as vesicles suspensions or solutions/suspensions of labeled macromolecules. The vesicles suspensions are very convenient objects to study properties of the ordered systems, especially lipid layers, due to easiness of a preparation and an investigation by means of the fluorescence depolarization method [1–3]. There can be made out a local director, perpendicular to the surface of the vesicle, describing the local order of the molecules. The rotational motion of the fluorophores inside the membrane gives rise to the depolarization of the fluorescence. Another example is solution or suspension of labeled macromolecules [4,5], where the internal motion of the fluorescence labels and their alignment can be treated in the similar manner. The macroscopic symmetry of such systems allows only three independent components of the polarized fluorescence, $I_{\parallel}(t)$, $I_{\perp}(t)$, and $I_{mag}(t) = 1/3[I_{\parallel}(t) + 2I_{\perp}(t)]$.

In this work the depolarization process is assumed to take place due to the potential restricted rotational diffusion of the fluorophores. The relevant features of the molecular system rendered by this model are (micro) viscosity, related to the diffusion tensor and a probe–mesophase interaction, given by the aligning potential.

An important consideration, discussed in [6–8] states that during the process of the electronic excitation the molecules may undergo changes of their electric properties or even shapes enough radical to change the way they interact with their surroundings. There is experimental evidence for the changes in the polarity and the polarizability of the fluorophores caused by the electronic excitation [3,9–12], so two aligning potentials must be introduced, $V_{gr}(\Omega)$ for the ground state and $V_{ex}(\Omega)$ for the excited one. Consequently, there are two angular equilibrium distributions functions defined as follows:

$$f_{st}(\Omega) = \frac{1}{N_{gr}} \exp\left[-\frac{V_{st}(\Omega)}{k_B T}\right] \quad st = gr,\ ex, \tag{1}$$

where Ω is the angular position of a molecule, k_B is the Boltzmann constant and T is the temperature.

A statistical study of the experimental data meets problems concerning a proper identification of resulting values of model parameters, especially these ones, which are related to the aligning potential. In the case where different interactions in the ground and the excited state are expected, a method consisting in finding the minimum value of the merit function fails, due to a large number of comparably well fitted sets of the parameters.

In order to overcome this problem, the Bayesian probability theory is employed. It makes possible a probabilistic description of the model parameters and provides a tool able to make a comparison between different models. The probability distribution function (pdf) $p(\mathbf{u} \mid D)$ of the model parameters collected in an n dimensional vector $\mathbf{u}$, conditioned on data D is given as follows:

$$p(\mathbf{u}|D) \propto p(D|\mathbf{u})\, p(\mathbf{u}), \tag{2}$$

where $p(D \mid \mathbf{u})$ is the likelihood and $p(\mathbf{u})$ is the prior probability distribution function.

Finding the solution to the inverse problem (2) is, in this case, impossible without a numerical method able to sample the posterior parameters distribution $p(\mathbf{u} \mid D)$. The Differential Evolution

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Markov Chain (DE-MC) method [13] turns out to be a very proficient tool.

The goal of this Letter is twofold. With two models at choice, one allowing the change of the interaction during electronic excitation and one forbidding such a behavior, the one which provides the better description of the synthetic data is to be chosen. Next, within a framework of a given model, the estimates of the model parameters must be calculated.

2. Theory

2.1. Bayesian probability approach

In the least square approximation the inverse problem (2) reads [14]:

$$p(\mathbf{u} \mid D,H) \propto \exp\left[-\frac{1}{2}\chi^2(\mathbf{u})\right] p(\mathbf{u} \mid H), \tag{3}$$

where $\chi^2(\mathbf{u})$ is the merit function and H is the hypothesis concerning an appropriate model.

The probabilistic solution to the inverse problem consists in characterizing the posterior pdf $p(\mathbf{u} \mid D,H)$, which may be achieved by providing mode (s) of the pdf, its mean value, variance and covariance matrix or plotting one- or two-dimensional marginal posterior distributions for chosen parameters.

Passing onto the hypotheses testing, we must calculate the probability $p(H \mid D)$ of the hypothesis H given data D. For two competing hypotheses, H_1 and H_2, a measure how much one of them is superior to the other in the data description is given by the odd-ratio R [15]:

$$R = \frac{p(H_1 \mid D)}{p(H_2 \mid D)}. \tag{4}$$

If we give equal chances to both the hypotheses at the very beginning, so $p(H_1) = p(H_2)$, R reads:

$$R = \frac{p(D \mid H_1)}{p(D \mid H_2)}. \tag{5}$$

The quantity $p(D \mid H)$ is called the marginal posterior likelihood or evidence for the hypothesis H[16] and in our case is given by:

$$p(D \mid H) \propto \int \ldots \int \exp\left[-\frac{1}{2}\chi^2(\mathbf{u})\right] p(\mathbf{u} \mid H) du. \tag{6}$$

We interpret the odd-ratio R as follows: respectively, values $\ln R \leqslant 1$, $1 < \ln R \leqslant 3$, $3 < \ln R \leqslant 5$ and $5 < \ln R$ correspond to 'vague', 'moderate', 'strong' and 'very strong' evidence against the H_2 hypothesis [15].

We assign flat, informative priors to all the parameters. Such a prior bounds the value of the parameter u_i into some interval $[u_i^{min}, u_i^{max}]$. In order to properly assign these bounds, we can use all available knowledge concerning the investigated physical system, results of previous analyzes or theoretical predictions [14].

2.2. Differential Evolution Markov Chain (DE-MC)

This modification of the Markov Chain Monte Carlo (MCMC) [17] method was introduced in [13]. A distribution of interest $\pi(.)$ is sampled by a multichain adoption of the Metropolis algorithm, with N chains, which are ran in parallel. An update to a current state of the given chain originates from differences of the points belonging to different chains. Schematically, for the rth chain a candidate point $\hat{\mathbf{x}}^{(r)}$ is given by:

$$\hat{\mathbf{x}}^{(r)} = \mathbf{x}^{(r)} + \gamma(\mathbf{x}^{(p)} - \mathbf{x}^{(q)}) + \mathbf{b}, \tag{7}$$

where γ is a scaling factor, two chains p and q are randomly chosen and $\mathbf{b}$ is a vector of small random numbers.

Only one adjustable parameter γ is needed by DE-MC. A selection of $\mathbf{b}$ is not critical, its components only need to be small in comparison with components of $\mathbf{x}$. In practical applications, the components of $\mathbf{b}$ can be drawn from the uniform distribution $U(-b, b)$.

DE-MC works because, after the convergence, the vectors of differences $\mathbf{x}^{(p)} - \mathbf{x}^{(q)}$ in the population of the chains render the shape of the underlying distribution of interest. Formally speaking the differences follow the variance–covariance matrix of the target distribution when the number of the chains $N \to \infty$ [13].

An m elements sample $\mathbf{x}_1, \ldots, \mathbf{x}_m$ drawn from the target $\pi(.)$ allows us to calculate MCMC averages of any function $f(\mathbf{x})$ [17]:

$$\langle f(\mathbf{x}) \rangle = \int f(\mathbf{x})\pi(\mathbf{x}) d\mathbf{x} \approx \frac{1}{m}\sum_{i=1}^{m} f(\mathbf{x}_i). \tag{8}$$

In the case of the probabilistic inverse problem the target distribution $\pi(.)$ is the posterior distribution $p(\mathbf{u} \mid D,H)$, and we set $\mathbf{x} = \mathbf{u}$.

2.3. Polarized fluorescence decays

We assume that the fluorescence depolarization is due to the rotational diffusion of the fluorophores, embedded in the uniaxial homogeneous mesophase. The timescale of the rotational or translational motion of the probe carrier should be much greater than all timescales concerning the fluorophores. The photo-physical features of the molecules are described by the absorption and the emission dipole moments, which are assumed to be parallel to the Z axis of the molecular coordinate frame. We consider the radiative depopulation process of the excited state quantified by the constant rate k_F. The aligning potentials are modeled by expansions in the base of the Legendre polynomials $P_j(\beta)$, with only two expansion coefficients $u_{st}^{(2)}$ and $u_{st}^{(4)}$, $st = gr,\ ex$ [18]:

$$V_{st}(\beta) = \sum_{j=2,4} u_{st}^{(j)} P_j(\beta), \tag{9}$$

where β is an angle between the molecular frame Z axis and the local director. The relevant hydrodynamic behavior is quantified by the diffusion tensor component $D_\perp$, related to the 'tumbling' motion of the probe.

The components of the fluorescence intensity $I_\parallel(t)$ and $I_\perp(t)$, are given as follows [3,18]:

$$\begin{aligned} I_\parallel(t) &= Ae^{-k_F t}\left[1 + \frac{4}{5}\sum_{p=-2}^{2}\Phi_p(t)\right], I_\perp(t) \\ &= Ae^{-k_F t}\left[1 - \frac{2}{5}\sum_{p=-2}^{2}\Phi_p(t)\right], \end{aligned} \tag{10}$$

where A is the amplitude of the fluorescence decay and $\Phi_p(t)$ are the correlation functions, obtained from the solution to the equation of motion.

The potential restricted rotational diffusion of the fluorophores is described by the Smoluchowski equation [19] governed by the time-development operator [20,21,18]. The solution to this equation depends on the aligning potential and $D_\perp$ and is expressed by the molecular correlation functions ${}^{22}V_{p0}^{p0}(t)$, $p = -2, .., 2$. Under presented assumptions $\Phi_p(t) = {}^{22}V_{p0}^{p0}(t)$ [18].

The boundary properties of these functions involve the orientational distribution functions in the both states [8]:

$$\begin{aligned} {}^{22}V_{p0}^{p0}(t=0) = (-1)^{-p}\sum_{L=0}^{4} C(22L; p-p) \\ C(22L; 0\ 0)\left\langle D_{0,0}^{(L)}\right\rangle_{gr}\left\langle D_{0,0}^{(L)}\right\rangle_{gr}, \end{aligned} \tag{11}$$