Modeling the dynamics of polymer chains in water solution. Application to sensor design

V N Starovoitov\textsuperscript{1,2} and B N Starovoitova\textsuperscript{1}
\textsuperscript{1}Lavrentyev Institute of Hydrodynamics, Novosibirsk, Russian Federation
\textsuperscript{2}Novosibirsk State University
E-mail: starovoitov@hydro.nsc.ru, botagoz@hydro.nsc.ru

Abstract. This paper is devoted to a mathematical model of a chaotic dynamics of a polymer chain in water. The model consists of a parabolic equation that is derived according to the self-consistent field approach. This model is employed for the numerical simulation of a biological sensor that detects the presence of a specific protein in the fluid. The sensor is absolutely simple and seems to be new. Besides that, the suggested equation is interesting from the mathematical point of view. It includes a non-local operator of integration not only over the past time interval as in the problems with memory but also over the future time interval. It is unusual for parabolic problems.

1. Introduction
This paper is devoted to modeling and numerical simulations of a biosensor based on the chaotic motion of a polymer molecule in water. The biosensor detect the presence of a specific protein. The polymer chain is equipped with a special atom group (ligand) that can bind this protein. The behavior of the polymer chain changes if it capture the protein which is the spatial restriction for the random motion of the chain. In order to detect this change, we use the average end-to-end distance of the polymer chain. The measurement of this quantity is based on the following principle. Suppose that we have two fluorescent molecules. One of these molecules called donor is excited at its specific fluorescence excitation wavelength. This excited state is then nonradiatively transferred to a second molecule, the acceptor. The transfer occurs if the distance between the molecules does not exceed the so called Förster radius. Thus, the color of the light coming from the acceptor depends on the distance to the donor. If we place the donor and the acceptor at the ends of a polymer chain, we can detect whether the chain is stretched or not. To our knowledge, this principle was suggested in [1]. A possible sensor based on the this principle was considered in [2].

Besides the biological application, the development of the sensor mentioned above is interesting from the mathematical point of view. When modeling the chaotic motion of a polymer chain, we have obtained a parabolic equation whose coefficient depends on the integral of the solution over all the time interval where the problem is considered. In fact, in order to solve the problem we have to know “the future”. Thus, this is a problem with a non-local operator that includes integration not only over the past time interval as in the problems with memory but also over the future time interval.
2. Behavior of polymer chains in water

Here, we describe our approach to modeling of the behavior of polymer chains in water. General facts about polymers chains can be found in the books [3] and [4].

2.1. Ideal chains

The theory of dilute polymer solutions begins with a single linear flexible polymer chain in an infinite solvent medium. Within this simplified system, all intermolecular interactions between solute polymers and between the bonds of one chain are neglected. The only restriction is that the bond \( n \) is linked to the bonds \( n - 1 \) and \( n + 1 \). Besides that, all the bonds have the same length.

The instantaneous configuration of the entire chain can be specified by the coordinates of the elements composing the chain. If each bond is denoted by a vector \( a_j \), then the end-to-end vector of such a chain is \( R = \sum_{j=1}^{N} a_j \), where \( N \) is the number of the segments (see Fig. 1).

It is clear that, for a freely fluctuating chain, the average or mean end-to-end vector \( \langle R \rangle \) will be \( 0 \) as the chain can traverse in all directions with equal probability. Thus, \( \langle R \rangle \) does not serve as a good measure of the chain size since it will be zero irrespective of the number of the monomers. Another measure is the mean of the square of the end-to-end distance, or simply the “mean square end-to-end distance”, denoted by \( R^2 \) = \( \langle R^2 \rangle \). It is not difficult to deduce that \( R^2 = N a^2 \), where \( a \) is the length of the segments.

![Figure 1. General flow pattern in the physical plane.](image)

The most useful characteristic of the chain is the probability distribution of the square end-to-end distance. For ideal chains, this distribution is Gaussian and its density looks as follows

\[
P_N(R) = \left( \frac{2\pi Na^2}{3} \right)^{-3/2} \exp \left( -\frac{3R^2}{2Na^2} \right).
\]

It is not difficult to see that \( R^2 = \int R^2 P_N(R) \, dR \).

Let \( p(x, t) \) be the solution of the Cauchy problem:

\[
\partial_t p - \frac{a^2}{6} \Delta p = 0, \quad p(x, 0) = \delta(x),
\]

where \( \delta(x) \) is the Dirac delta-function concentrated at the origin. Then \( P_N(R) = p(R, N) \). Thus, we can find the density of probability as the solution of the problem above. In a more general case, if the chain is not absolutely free and is influenced by an external field with the potential \( \varphi \), then we should solve the following problem:

\[
\partial_t q - \frac{a^2}{6} \Delta q + \frac{\varphi}{kT} q = 0, \quad q(x, 0) = \delta(x),
\]
where $k$ is the Boltzmann constant and $T$ is the temperature. In this case, $q$ is not the density of probability but the statistical weight. In order to obtain the density of probability $p$, we have to normalize $q$:

$$p = q \left( \int q \, dx \right)^{-1}.$$

For instance, if the motion of the chain is restricted by a body $S$, we take $\varphi$ to be the indicator function of the set $S$: $\varphi(x) = 0$ for $x \notin S$ and $\varphi(x) = +\infty$ for $x \in S$. Thus, the body is considered as an energy barrier.

![Figure 2. The distribution of the density of probability $P_N(x)$ for a free ideal chain (in the left picture) and for a restricted ideal chain (in the right picture).](image)

In Fig. 2 (left), one can see the distribution of the density of probability $p(x)$ for a free ideal chain tethered to the point $x = 0$. We should rotate the picture around the vertical axis in order to obtain the three-dimensional one. The calculations were done for $N = 100$ and $a = 0.4$. Suppose that a spherical body of radius 3 restricts the motion of the chain. For this case, the distribution of the probability is presented on the right picture. The chain is tethered to the point $x = (0, 0, 3)$. The three-dimensional picture can be obtained by rotating around the horizontal axis. Pay attention to the fact that in the first case the maximum of the function $p$ is at the point of tethering and in the second case it is moved approximately two units to the right.

2.2. Real chains

The behavior of real chains differs from that of ideal ones. The bonds composing real chains have non-zero volume and, besides that, interact through the surrounding fluid. Sometimes, the chains whose bonds have non-zero volume are called the chains with excluded volume since the domains occupied by various bonds cannot intersect. We will consider a single chain which does not interact with other chains.

Let us denote by $a$ the length of the Kuhn segment of the chain (see [3, 4]) and by $N$ the number of the Kuhn segments composing the chain. Further, we call them simply segments. One should distinguish the segments and the bonds of the chain. A segment can consist of several bonds. Notice also that in some papers the length of the Kuhn segment is considered as the persistent length of a chain.

In order to describe the behavior of real chains, we apply the self-consistent field approach (see [3, 4]). It is supposed that every segment of the chain produces an energy field in its neighborhood and, in such a way, acts on the other segments. The total energy field $\Phi$ is the
sum of the segment fields. In order to calculate it, we have to know the density of the probability distribution \( \varrho \) of all segments in the space which is defined by the relation:

\[
\varrho(x) = \sum_{k=1}^{N} P_k(x),
\]

where \( P_k(x) \) is the density of probability that \( x \) belongs to the \( k \)-th segment. Due to the excluded volume effect, \( \varrho \) cannot exceed \( \nu^{-1} \), where \( \nu \) is the volume of one segment which can be found experimentally. We define \( \Phi \) by the Flory – Huggins formula:

\[
\Phi = -kT \left( \log(1 - \varrho\nu) + 2\chi\varrho\nu \right),
\]

where \( \chi \) is a constant called the polymer – solvent interaction parameter.

Thus, applying the differential equation approach described in the previous subsection, we obtain the following Cauchy problem:

\[
\partial_t q - \frac{a^2}{6} \Delta q + \frac{\Phi + \varphi}{kT} q = 0, \quad q(x, 0) = \delta(x),
\]

\[
\varrho(x) = \int_0^N p(x, t) \, dt, \quad p = q \left( \int q \, dx \right)^{-1}.
\]

This problem has to be solved for \( t \in (0, N) \) and \( x \in \mathbb{R}^3 \). Here, \( \varphi \) is the energy potential of possible spatial restrictions. We employ this model for numerical simulations of a biological sensor.

It should be noted that the problem above is also interesting from mathematical point of view. The potential \( \Phi \) depends on the values of the solution on the whole interval \( (0, N) \). Thus, in order to solve the problem we have to know the “future”. It is unusual for parabolic problems. The word “future” is enclosed in quotation marks since \( t \) is not the time variable but the arc length parameter on the chain.

3. The sensor design
3.1. General scheme

Let we have a polymer chain with two fluorescent molecules at the ends (see Fig. 3). One of these molecules called donor is excited at its specific fluorescence excitation wavelength. This excited state is then nonradiatively transferred to a second molecule, the acceptor. The transfer occurs if the distance between the molecules does not exceed the so called Förster radius. The color of the light coming from the acceptor depends on the distance to the donor. If we place the donor and the acceptor at the ends of a polymer chain, we can detect whether the chain is stretched or not. At one end, the chain has also a special atom group (ligand) that can bind a specific protein.

Suppose that some amount of such polymer chains is dissolved in water. The solution must be dilute in order to avoid the interaction of the chains, so we can consider the behavior of a single chain. Clearly, the behavior of the chain with captured protein differs from that of the free chain. The difference comes from the fact that the protein represents a spatial restriction for the chaotic motion of the chain and reduces the number of its possible configurations. Therefore, the protein changes the mean distance between the donor and the acceptor. This event can be detected since the color of the light coming from the acceptor depends on the distance to the donor. Thus, it is possible to detect the presence of the protein in the water.

To maximize the effect, we have to choose optimal values of such parameters as the length of the chain and its persistent length, the temperature, the Förster radius of the fluorescent molecules, and some other. Assuming medical and biological applications of the sensor being developed, the temperature must be in the range \( 10^\circ C - 35^\circ C \). Besides that, the polymer has to be non-toxic.
3.2. Numerical simulations

The simulations of the system were done for the polymer chain of polyethylene glycol, whose formula is

\[-(O - CH_2 - CH_2)_n-\]

This polymer is widely applied in biology and in medicine (see [5]). The necessary parameters of aqueous solutions of this polymer were taken from the works [5] – [10]. The following values of parameters were chosen: diameter of the protein 6 nm, the length of the Kuhn segment 0.6 nm, \( \nu = 0.05 \text{ nm}^3 \), the temperature is in the range 25\(^\circ\)C – 28\(^\circ\)C. It is assumed that the protein has the spherical form.

Suppose that the chain end with the ligand is at the point \( x = 0 \). We would like to know the distribution of the density of probability for the other end (for the acceptor). In Fig. 4, the values of this quantity on the ray that starts out at the ligand and goes through the point of its maximum. The calculations were made for the chains of the length 100 (the left picture) and 200 (the right picture) segments. If the chain is free, the distribution of probability is spherically symmetric and depends only on the radial variable. The green dotted line shows this dependence. The red solid line corresponds to the case of the chain with the captured protein and represents the values of the density of probability on the straight line passing through the point orthogonal to the protein surface. The unit of the horizontal axis is nanometer. Notice that the density of probability is equal to zero at the origin due to the excluded volume effect. The first and the last segments of the chain cannot be in the same point simultaneously.

As it was expected, for the chain with the captured protein, the maximum of the probability distribution has moved a few nanometers from the point of tethering. This effect can be detected. However, in order to choose the optimal length of the chain, we have to know another...
characteristics. It is the proportion of the time that the end of the chain (acceptor) is located outside of the sphere of the radius $r$ with the center at $x = 0$. Due to the ergodic theorem, it is exactly the probability of this event. In Fig. 5, the dependence of this probability on $r$ (the horizontal axis) is shown.

Figure 5. The probability of finding the acceptor outside of the sphere of the radius $r$ (the horizontal axis). The graphs correspond to that in Fig. 4.

On the basis of these data, one can evaluate the intensity of the light coming from the acceptor. Assume that the acceptor is blue if the end-to-end distance of the chain does not exceed the Förster radius and is yellow in the other case. If the Förster radius (FR) is equal to 6 nm, we have the following diagrams for the chains consisting of 100 and 200 bonds (Fig 6). We see that for the chain of polyethylene glycol composed of 200 segments and for fluorescent molecules with the Förster radius 6 nm, the intensity of the yellow light coming from the solution increases on 12% if all chains have captured the protein molecules. This effect can be detected. Of course, the sensitivity of this sensor can be improved by a better choose of parameters.

Figure 6. The probability of finding the acceptor outside of the sphere of the radius 6 nm (the yellow bar). The graphs correspond to that in Fig. 5.

References
[1] Hoffmann D and Moske M 2003 Verfahren zum Nachweis eines Analyts mit einem elasto-optischen Biosensor (European Patent EP1363124 24.12.2003)
[2] Botkin N D, Hoffmann K-H, Marx D, Starovoitov V N and Turova V L 2013 Modeling in the development of an elasto-optical biosensor based on nanostructures International Journal of Biomathematics and Biostatistics 2(2) 191-202
[3] Grosberg A Yu and Khokhlov A R 1994 Statistical physics of macromolecules (New York : American Institute of Physics)
[4] Yamakawa H 1971 *Modern theory of polymer solutions* (New York: Harper and Row)
[5] Harris J M 1992 *Poly (ethylene glycol)* (New York)
[6] Kienberger F, Pastushenko V, Kada G, Gruber H, Rienen C, Schindler H and Hinterdorfer P 2000 Static and dynamical properties of single poly (ethylene glycol) molecules investigated by force spectroscopy *Single Mol. 1*(2) 123-128
[7] Zhu P, Yang H, Peng C and Zhang X 2001 The influence of solvent and temperature upon the aggregation of poly (ethylene glycol) *Macromol. Chem. Phys.* 202 1380-1383
[8] Kawaguchi S, Imai G, Suzuki J, Miyahara A, Kitano T and Ito K 1997 Aqueous solution properties of oligo- and poly (ethylene oxide) by static light scattering and intrinsic viscosity *Polymer* 38(12) 2885-2891
[9] Kinugasa S, Nakahara H, Fudagawa N and Koga Y 1994 Aggregative behavior of ploy (ethylene oxide) in water and methanol *Macromolecules* 27 6889-6892
[10] Oesterhelt F, Rief M and Gaub H E 1999 Single molecule force spectroscopy by AFM indicates helical structure of poly (ethylene glycol) in water *New Journal of Physics* 1 6.1-6.11