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Advances in analytical Modelling for (Nano)medicine

Paolo Di Sia[1-3]

[1] Department of Philosophy, Education, Psychology, University of Padova,
City: Verona, Veneto, Italy

[2] ISEM, Institute for Scientific Methodology, Palermo, Italy

[3] paolo.disia@gmail.com - www.paolodisia.com

Abstract

Efforts in getting advances for nanomedicine benefit of theoretical modelling, which continuously tests current experimental data and brings innovation. The diffusion of nanomaterials in the human body has different characteristics in relation to the effective mass, relaxation times, frequency and other variables of carriers travelling inside a nanostructure. In this paper we consider an interesting analysis of some nanomaterials of increased use in nanomedicine and apply a recently appeared analytical model for transport dynamics at the nanoscale, able both to verify experimental existing data and to do useful previsions. As example of application, variations of transport parameters and the corresponding results are considered in relation to peculiar nanomaterials for nanomedicine, i.e. Fullerenes, Cadmium Selenide, Diamond, Gold.

Keywords: **Medicine, Nanomedicine, Nanomaterials, Nanotechnology, Theoretical Modelling, Nanophysics, Transport Processes, Diffusion.**

1. Introduction

Nanomedicine deals with knowledge and technologies having a medical utilization in the magnitude order of nanometers, where nanotechnology changes the traditional distinction among biology, chemistry and physics and constitutes a rich interdisciplinarity bridge [1,2]. The applications of nanotechnology for medicine span a wide range, from the medical use of nanomaterials to the formulation of new systems for drug delivery, from nanobiosensors to the possible use of molecular nanotechnology and the neuroelectronic interfaces.

Thanks to the “triggered response” drugs, positioned within the organism, there is action only to the appearance of a particular “activator” signal, as nanoparticles which reach the target organ for getting a local release of the drug. Nanometer-sized particles have optical, magnetic, chemical and structural properties that set them apart from bulk solids, with potential amazing applications in medicine. Because of their small sizes, nanoparticles are taken by cells where large particles would be excluded or cleared from the body.

Developments in nanomedicine try to deeply understand the toxicity and the environmental impact of nanomaterials through the sinergy between experiments and mathematical modelling [3,4].

Research is focusing in these years on the development of drug delivery systems for maintaining therapeutic drug levels in small parts of the human body, avoiding generic tissue distribution. Many areas of pure and applied science work with increasing synergy in the same direction.

Nanoparticles have unusual properties able to modify the kinetics of a drug; they have also many advantages, as a high solubility, a longer duration of drugs exposure, a greater therapeutic index, the potential to develop less resistance for chronic use.

In the brain chemical communication and key bio-molecular interactions occur at the nanoscale; nanoscience can help for the deep study of the brain structure and function [5,6].

Nanomedicine can work with high specificity, using in particular two ways:

a) a “passive method”, related to an increase of mass vascularization, which permits a greater presence on target tissues;

b) an “active method”, with the use of probes to which drug molecules are bound.

Advances in these directions lead to interesting improvements, particularly in the field of diagnosis and rapid controlled treatment, if they are supported by a proper theoretical transport modelling. In this paper we use a recent analytical model for the study of dynamics at the nanoscale, able both to confirm known results and to make interesting predictions concerning the characteristics of the used nanomaterials. The model has useful applications in the sector of nanomedicine, from nanoscale to macroscale. In this paper we will focus our attention at the nanolevel.

2. Interesting Nanomaterials for Medicine

The possibility to bind markers to various kinds of nanoparticles, such as nanoshells, dendrimers, liposomes, for recognizing types of cells, as cancer cells, is a primary object of current research. Among the possibility to use peculiar nanomaterials with specific characteristics, particular attention has been directed to gold, fullerenes, diamond, cadmium selenide (CdSe).

a) Gold (silver)-coated nanoshells are metal shells with thickness of few nanometers containing a dielectric core. They have particular chemical and optical properties, can be bound to cancer cells by combining peptide antibodies on their surface. Through laser irradiation, gold is sufficiently heated to cause the death of cancer cells. The variation of the size and the core involves a precise variation of the optical resonance of these particles with precision in a wide range, between ultraviolet and the mid-infrared [7].

b) Fullerenes are "in vivo" a powerful antioxidant with no acute toxicity. It has been shown a protective activity on neurons, in particular a reduction activity of axonal damage in mice with multiple sclerosis. Chemical sensors using nanotubes for the measure of various properties of molecules in the gaseous state have been also designed [8,9].

c) Nanodiamonds can carry drugs inside cells, without producing negative effects, as inflammation; surrounding a drug, they can carry the same drug, preventing the release of healthy cells, thus limiting toxic effects [10].

d) CdSe nanoparticles illuminate when exposed to ultraviolet light; around a cancer their brightness can guide the doctor for a more accurate removal [11].

3. A new analytical Model for Transport Processes

Although the cardiovascular system has features that prevent a precise quantitative description, its functioning can be explained using the physical principles related to the hydrostatics-hydrodynamics laws. It exists an electric standardized symbology for the synthetic representation of resistive phenomena, which well describes the hemodynamics. It is useful and productive the electric analogy for representing phenomena concerning mass (volume) transport, keeping into account of elastic and viscous effects [12,13].

Recently it has been performed a new analytical model, which generalizes Drude-Lorentz, Smith models and effective medium theories (EMTs) for transport processes in solid state physics and soft condensed matter [14-18]. It is based on a complete inversion (complete Fourier transform) of the equation of velocities correlation function on time scale, i.e. considering the entire time axis (-∞,+∞), not the half time axis (0,+∞), as usually considered in literature [19]. This idea is viable considering the real part of the complex conductivity σ(ω). Via contour integration by the residue theorem, the integral is determined by the poles of the real part Reσ(ω) [20]. This leads to an exact formulation and gives a powerful method to describe the velocities correlation function, the mean square deviation of position and the diffusion coefficient in analytical way, getting analytical time-dependent expressions, therefore not time-consuming numerical approaches. Thus:

a) from the velocities correlation function $<\vec{v}(t)\cdot\vec{v}(0)>_T$ at temperature T we obtain the velocity of a nanoparticle at time t;

b) from the mean squared deviation of position $R^2(t)=\left\langle[\vec{R}(t)-\vec{R}(0)]^2\right\rangle$ the position is obtainable;

c) the diffusion coefficient $D(t)=(1/2)(dR^2(t)/dt)$ gives interesting information about the propagation in space and time.

The classical, quantum and relativistic version of the model have been performed [21-25]. It allows both to test experimental known results and to discover new characteristics and details, and contains a gauge factor, which allows its use in a wide range in space and time, from sub-picolevel to macrolevel [26-30]. In this paper we consider nanoscale processes.

In the classical case, i.e. considering non-relativistic velocities of carriers and negligible quantum effects, we have the following expressions for $<\vec{v}(t)\cdot\vec{v}(0)>_T$, $R^2(t)$ and $D(t)$ respectively:

$$\left\langle\vec{v}(0)\cdot\vec{v}(t)\right\rangle=\frac{1}{2}\left(\frac{k_B T}{m^*}\right)\left(\frac{1}{\alpha_I}\right) \tag{1}$$
$$\left[(1+\alpha_I)\exp\left(-\frac{(1+\alpha_I)}{2}\frac{t}{\tau}\right)-(1-\alpha_I)\exp\left(-\frac{(1-\alpha_I)}{2}\frac{t}{\tau}\right)\right]$$

$$R^2(t)=4\left(\frac{k_B T}{m^*}\right)\left(\tau^2\right)\left(\frac{1}{\alpha_I(1+\alpha_I)}\exp\left(-\frac{(1+\alpha_I)}{2}\frac{t}{\tau}\right)-\right.$$
$$\left.-\frac{1}{\alpha_I(1-\alpha_I)}\exp\left(-\frac{(1-\alpha_I)}{2}\frac{t}{\tau}\right)+\frac{2}{\left(1-\alpha_I{}^2\right)}\right) \tag{2}$$

$$D(t)=\left(\frac{k_B T}{m^*}\right)\left(\tau\right)\left(\frac{1}{\alpha_I}\right)\cdot$$
$$\cdot\left[\exp\left(-\frac{(1-\alpha_I)}{2}\frac{t}{\tau}\right)-\exp\left(-\frac{(1+\alpha_I)}{2}\frac{t}{\tau}\right)\right] \tag{3}$$

with $\alpha_I=\sqrt{1-4\omega_0^2\tau^2}\in(0,1)\subset\mathbb{R}$.

α_I is a parameter of the model, k_B the Boltzmann's constant, T the temperature of the system, m^* the effective mass of the carriers, τ the relaxation time, ω_0 the center frequency. The model contains also a second parameter α_R, which keeps in accounts of damped oscillating behaviour of processes [21-25].

4. Applications and Results

As example of application, we have analyzed the dynamical behaviour of carbon nanotubes (CNTs), cadmium selenide (CdSe), Gold, Diamond. About the used parameters, it has been fixed the temperature $T=310K$, the value 0.5 for parameter α_I, an average relaxation time $\tau_{av}=10^{-13}\,s$ and the values of m^* as resumed in Table 1. These values find a justification in the fact that materials constituting the soft condensed matter, as blood, have intermediate properties between solid and liquid, and combine elastic and viscous response.

Material	m^*
CNTs [31]	0.5 m_e
Gold [32]	1.1 m_e
CdSe [33]	0.13 m_e
Diamond [34]	0.94 m_e

Table 1: Values of effective masses m^* for the considered materials (m_e is the electron mass).

We underline, besides the "a-posteriori" verification of known characteristics and behaviors [35-38], the "a-priori" power of the model to give predictions through the use of experimental existing data. This fact justifies the choice of data of Table 1.
In Fig. 1 the time behaviour of the velocity correlation function is considered, from which details related to the velocity of carriers inside the nanostructure can be useful extracted.

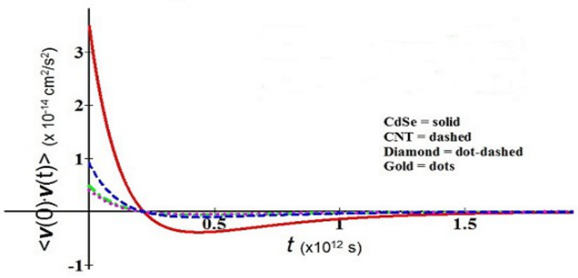

Figure 1: Behaviour of $<\vec{v}(t)\cdot\vec{v}(0)>_T$ vs t for the indicated nanomaterials.

Fig. 2 represents the time behaviour of the mean square deviation of position $R^2(t)$, useful for obtaining informations about the position and the space covered by carriers inside the nanostructure.

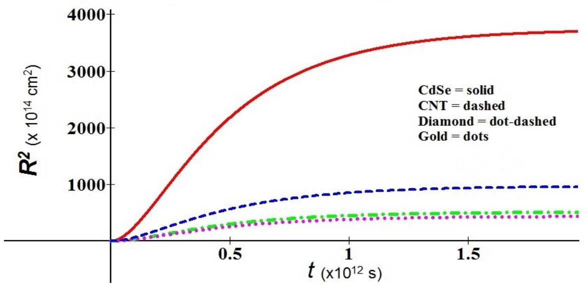

Figure 2: Behaviour of $R^2(t)$ vs t for the indicated nanomaterials.

In Fig. 3 the time behaviour of the diffusion coefficient D is plotted; it is possible to get the peak of diffusion as a function of the used material, as well as the different velocity with which the maximum diffusion value is reached.

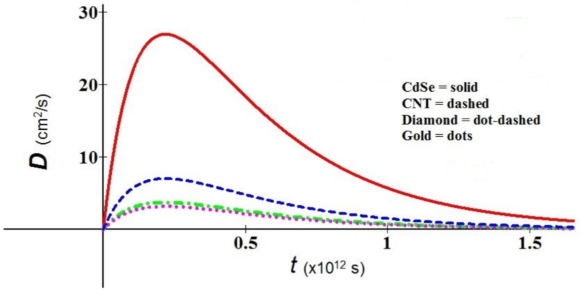

Figure 3: Behaviour of $D(t)$ vs t for the indicated nanomaterials.

About extracting dynamical values from figures, considering three different fixed times, we get:

a) Fig. 1: after $\Delta t_1 = 1.6\times10^{-14}\,s$, the carriers velocity inside the considered nanomaterials is:

- CdSe: $v_{CdSe}=1.73\times10^{7}\,cm/s$;
- CNTs: $v_{CNTs}=0.88\times10^{7}\,cm/s$;
- Diamond: $v_{Diamond}=0.64\times10^{7}\,cm/s$;
- Gold: $v_{Gold}=0.58\times10^{7}\,cm/s$.

b) Fig. 2: after $\Delta t_2 = 10^{-12}\, s$, the space covered by carriers is:

- CdSe: $d_{CdSe} = 57.4\, nm$;
- CNTs: $d_{CNTs} = 29.4\, nm$;
- Diamond: $d_{Diamond} = 21.5\, nm$;
- Gold: $d_{Gold} = 19.6\, nm$.

c) Fig. 3: after $\Delta t_3 = 6 \times 10^{-14}\, s$, the values of diffusion are:

- CdSe: $D_{CdSe} = 15.58\, cm^2 / s$;
- CNTs: $D_{CNTs} = 4.35\, cm^2 / s$;
- Diamond: $D_{Diamond} = 2.46\, cm^2 / s$;
- Gold: $D_{Gold} = 1.7\, cm^2 / s$.

We underline, as scientific novelty of the model, the possibility to naturally get not discrete, but continuous curves, from which accurate informations can be obtained.

5. Conclusions

In this paper we have considered the application of a new analytical model for transport processes related to nanoparticles injectable in the human body; it holds both for the motion of carriers inside a nanostructure, and for the motion of nanoparticles. The model presents interesting novelties for nano-transport, so as the confirmation of existing results.
Interesting considerations are to be underlined:

1) the particular choice of nanomaterial brings to a variation of all transport parameters;

2) for targeted scopes, it is possible to act on the temperature of the system, on the variation of the effective mass through the doping and in connection to the chiral vector, on the variation of the parameters α_I and α_R of the model, which are functions of the center frequency and the relaxation time;

3) the versatility of the model, useful both for helping in the design of new devices with dedicated characteristics, for testing existing experimental data and obtaining new previsions;

4) it is possible to consider all forces acting on a nanoparticle in its precise chemical-physical condition and, through the analytical calculation, to determine its dynamics.

The model has been performed through analytical calculation, therefore provides analytical expressions of the most important transport parameters. This allows to get continuous curves of $<\vec{v}(t) \cdot \vec{v}(0)>_T$, $R^2(t)$ and $D(t)$ and, thanks to a gauge factor in its core, allows a wide range of applicability, from sub-picolevel to macro-level, to every oscillating process.

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Paolo Di Sia is currently Adjunct Professor by the University of Padova, Location Verona (Italy). He obtained a 1st level Laurea in Metaphysics, a 2nd level Laurea in Theoretical Physics, a PhD in Mathematical Modelling applied to Nano-Bio-Technology. He interested in Classical & Quantum Relativistic Nanophysics, Planck Scale Physics, Supergravity, Quantum Relativistic Information, Mind Philosophy, Quantum Relativistic Econophysics, Philosophy of Science, Science Education. He wrote 202 publications at today (papers, books, book chapters, works on scientific web-pages, inner academic publications, in press), is reviewer of 2 mathematics books, reviewer of 12 international academic journals, 8 Awards obtained, included in Who's Who in the World 2015 and 2016. He is member of 7 scientific societies, member of 26 Scientific Committes and International Advisory/Editorial Boards.