*Bulgarian Chemical Communications, Volume 47, Number 4 (pp. 000 – 000) 2015*

# Numerical simulation of the transport process of biomolecules and ions at molecular level in parallel carbon-wall nanofluidic channels

K. Liu[1*], Y. C. Ning[1], D. C. Ba[1*], S. W. Xiao[2], X. L. Zhang[3], D. Y. Wang[1], G. Y. Du[1], Y. S. Ba[1]

[1]*School of Mechanical Engineering and Automation, Northeastern University, Shenyang, 110089, China;*
[2]*Institute of High Energy Physics Chinese Academy of Sciences, 100049 Beijing, China;*
[3]*Capital Aerospace Machinery Company, Beijing, 100076, China,*

Received April 4, 2015;

The manipulation of biomolecules in nano-scale channels is quite interesting but full of challenge. One of the preconditions is to understand the transport process of biomolecules and ions in nanofluidic channels. In this issue, numerical simulations were carried out at a molecular level. The model of polypeptide GNNQQNY was introduced as a protein molecule under different conditions varying the driving factors like channel height, solution concentration and electric field intensity. The simulated results were discussed and analysed by comparing the molecular distribution, protein molecules' movement amplitude and potential energy. The decreasing channel height greatly influences the movement of proteins due to the more obvious electric double layer (EDL) effect. The increasing ionic concentration helps the passage of protein molecules while the layered concentration phenomenon of molecules and ions nearby the channel wall aggravates with the average ionic density. The electric field strength was also found to be an effective tool to control the passage of protein molecules. The results were helpful to understand the transport of biomolecules in nanofluidic channels.

**Keywords:** Molecular simulation, nanofluidic channel, protein molecules, transport process, GROMACS

## INTRODUCTION

Nanofluidic chips are widely used in the detection [1], separation [2] and manipulation [3] of biomolecules in solutions with the rapid progress of nanoscale fabrication [4]. Due to the complex structure and high surface activity, it is quite difficult to control the movement of biomolecules in nanofluidic research [5]. Researchers focus their interest on electrophoresis and electroosmotic flow in the research of the electrokinetic phenomenon in parallel plates. Qiao and Aluru [6, 7] simulated the electric double layer (EDL) structure and electroosmotic flow in nanoscale channels. R. Karnik [8, 9] manipulated the concentration and transport of ions and biomolecules on changing the wall surface charge of 35 nm high nanofluidic diodes. Kun Liu and Dechun Ba [10] built a 1-D model of ion transport in rectangular nanofluidic channels using the Poisson-Boltzmann equation, which proves that potential control is an effective way to manipulate the movement of protein molecules.

## MODEL AND SIMULATION DETAILS

The simulation system is built in the channel between two parallel plates, supposed with nanoscale distance and unlimited length. Assume that the solution between the parallel plates is sufficient and free without any initial external pressure gradient. The geometrical model is built as shown in Fig.1.

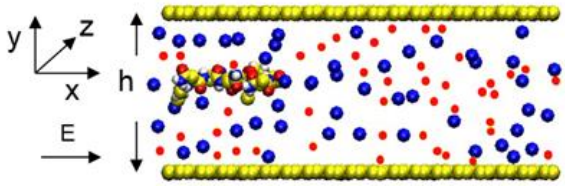


**Fig.1.** The geometrical model of biomolecules and ions transport in nanoscale channels.

The direction along the height is marked as *y* axis and the direction along the biomolecules' flow is marked as *x* axis. The channel is full of electrolyte solution mixed with protein molecules, the polypeptide *GNNQQNY*. For the sake of a clear display, the water molecules are hidden in Fig.1. The channel along the *x* and *y* axes is divided into tiny units with the scale of 7.60 nm×2.34 nm. The channel wall per unit is composed of 72 monolayer carbon atoms in every unit. One protein molecule is initially located in the left side of the channel. Larger (blue) and smaller (red) spheres represent $Na^+$ and $Cl^-$ ions, respectively.

The flow in the channel is limited along the *y* axis. Periodic boundary conditions are brought to the flow along the x and z axis. The wall is charged with an average density of 0.05C/m$^2$. The water molecular model is simplified as a SPC model [13-15]. In the simulation system, two kinds of potential energy are mainly considered, Lenard-

* To whom all correspondence should be sent:
E-mail: kliu@mail.neu.edu.cn (K.Liu);
dchba@mail.neu.edu.cn (D.C.Ba)

 

Jones (LJ) interaction and electrostatic interaction. LJ atomic model is adapted to the charged ions in the channel. All LJ parameters are derived from Gromos96 force field.

GROMACS program packages are used to simulate the protein molecules in an aqueous solution of sodium chloride. First, one GNNQQNY molecule was put into the left entrance of the channel, followed by water molecules and ions. The initial speeds were generated under Maxwell-Boltzmann distribution at 300K. Energy minimization was done after 400 steps by the steepest descent method. Then molecular hot bath was carried out based on Berendsen methods after 200 steps without external voltage until the system reached balance. 400 ps molecular simulation was performed with external electric field along the *x* axis.

As time step was set to be 2.0 fs, the simulation steps were up to 300,000. The Newton motion equation was solved with leap-frog algorithm [16,17]. The results were tracked every 100 steps. A series of such simulations was carried out varying the channel height, number of positive and negative ions and external electric field strength. Table 1 lists the simulation parameters.

## RESULTS AND DISCUSSION

Fig.2 shows the key frames of the transport movement of protein biomolecules. The protein molecule moved to the right according to the direction of the external electric field. Since the room was enlarged, the protein molecule turned over to a large extent. In the whole process, the positive $Na^+$ ions were mainly concentrated in the central channel while the negative $Cl^-$ ions were mainly located near the wall.

Root-mean-square deviations (RMSD) [14] were here used to measure the oscillating amplitude of the molecules. Larger RMSD value means more dramatic changes of molecular position and better transport of protein molecules in the simulation process. Fig.3 shows the RMSD analysis results in No.1 ~ No.3 simulation systems listed in Table 1.

With the decrease in channel height, the RMSD value changed drastically till 100 ps ～ 150 ps reaching a dynamic balance. This is because the EDL's effect was stronger with the decreasing and resulted in greater influence on the ions' movements. Under the drive of electric field generated by EDL, the chloride ions moved directionally. The protein molecules, which were negatively charged after absorbing electrons in the solution, were excluded at a certain distance from the chloride ions and then moved to the same direction as the chloride ions.

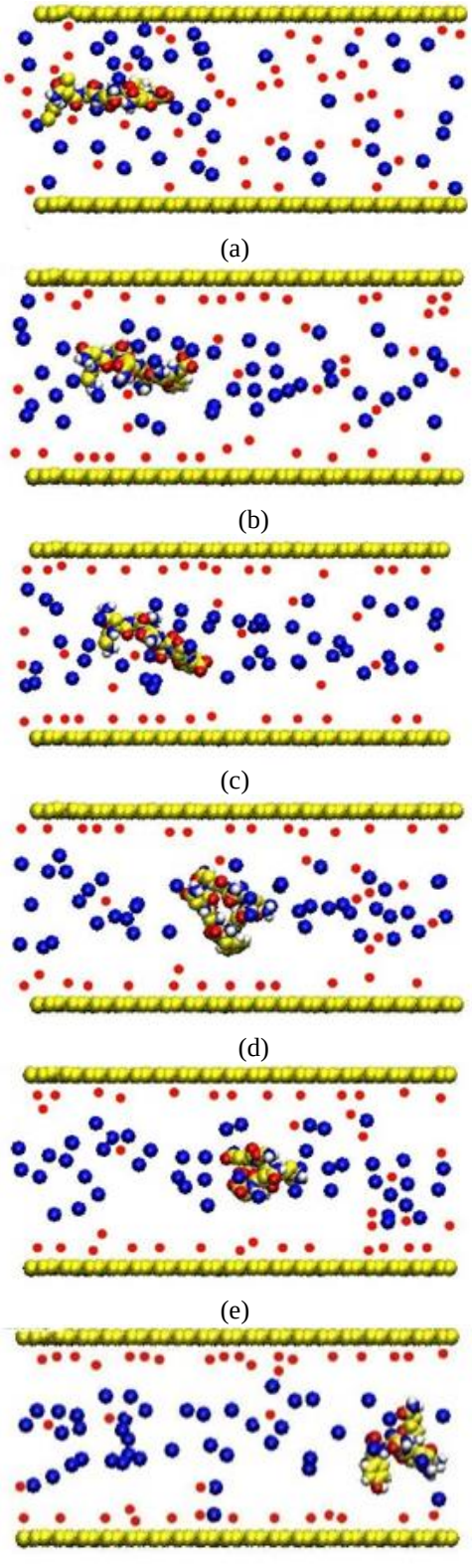


**Fig.2.** Simulation movement snaps of a biomolecular transport process (a) 1st step; (b) 4000th step; (c) 25000th step; (d) 100000th step; (e) 150000th step; (f) 200000th step.

**Table 1.** List of the simulation parameters

| Simulation system | No.1 | No.2 | No.3 | No.4 | No.5 | No.6 | No.7 |
|---|---|---|---|---|---|---|---|
| Channel height (nm) | 3.1 | 3.4 | 2.7 | 3.1 | 3.1 | 3.1 | 3.1 |
| Number of $Na^+$ ions (per unit) | 50 | 50 | 50 | 20 | 70 | 50 | 50 |
| Number of $Cl^-$ ions (per unit) | 50 | 50 | 50 | 20 | 70 | 50 | 50 |
| External electric field strength (V/nm) | 1 | 1 | 1 | 1 | 1 | 0.5 | 2 |

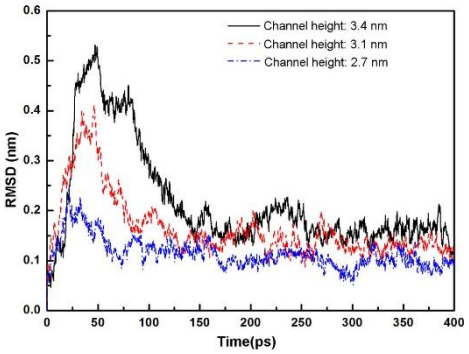


**Fig.3.** Oscillating amplitude of protein molecules at different channel heights

On the contrary, the stretch room of the protein became larger with the increase in channel height. RMSD value changed drastically at the very beginning. However, the movements tended to be weaker and the passage time turned shorter because of the conjunct action of surrounded ions, water molecules and the channel wall.

The density distribution of ions and water molecules along the height direction is given in Fig.4. The curve of water molecule distribution has two peaks nearby the wall. The chloride ions were attracted by the wall charge and gathered near the wall. There were few chloride ions but a large number of sodium ions around the protein molecules. However, the sodium ions were neither concentrated on the protein molecules nor absorbed by them. They just moved regularly and induced the movements of protein molecules. The width of EDL decreased with the increase in channel height because the motive force exerted on the protein molecules from the ions was weakened.

Fig.5 shows the comparisons of the oscillating status under different ion concentrations in No.1, No.4 and No.5 simulation systems. The ion concentration greatly influenced the RMSD value of protein molecules. When the number of ions increased to 70 per unit, the RSMD value strongly changed and hardly got up to a balance in a quite long time of 400 ps. When the ion's number decreased to 50 per unit, the balance time could be about 200 ps. When the ion's number further decreased to 20 per unit, the balance time correspondingly decreased to 100 ps. With the help of the viewer toolbox, it could be observed that the protein molecules obviously interacted with ions and moved rapidly through the channel at a high concentration, and *vice versa*.

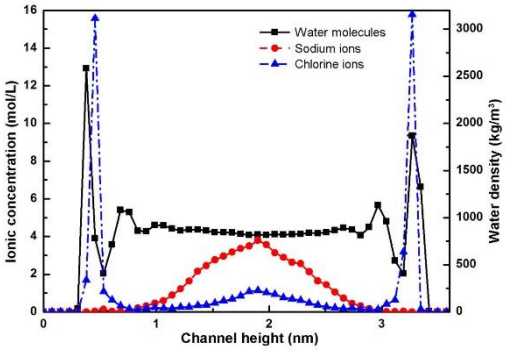


**Fig.4.** Density distribution of molecules and ions along the y axis at a channel height of 3.4 nm

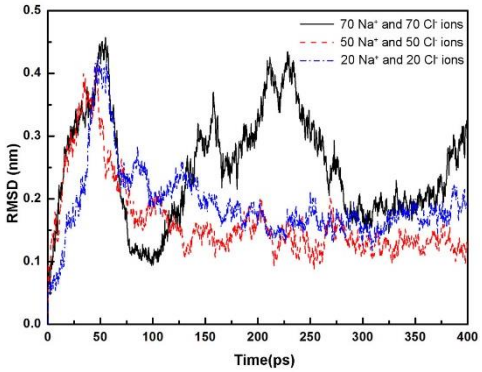


**Fig.5.** Oscillating amplitude of protein molecules at different concentrations

Fig.6 shows the density distribution of water molecules and ions in simulation system No.5. The water molecules and the negative ions mainly gathered on the two sides near the channel wall and displayed two peaks.

But the positive ions looked quite different. Many sodium ions concentrated in the center of the channel. With the increase of ionic concentrations, the central ionic concentration also increased, which favored the movement of protein molecules. Meanwhile, the layered concentration phenomenon of molecules and ions nearby the channel wall aggravated with the average ionic density. The RMSD comparison of different electric field strength in simulation systems No.1, No.6 and No.7 is shown in Fig.7.

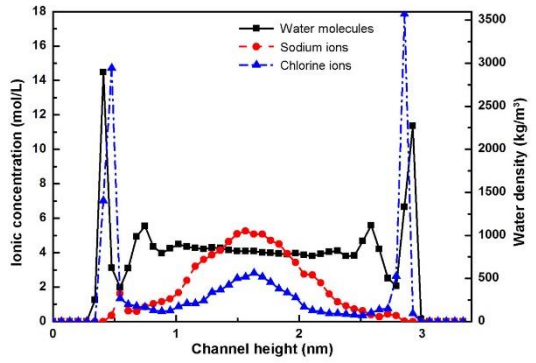


**Fig.6.** Density distribution of molecules and ions at 70 $Na^+$ ions and 70 $Cl^-$ ions per unit

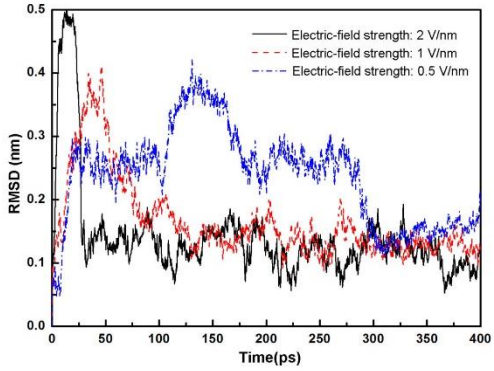


**Fig.7.** RMSD values of protein molecules at different electric field strength

When electric field of 2 V/nm strength was exerted along the *x* direction, the RMSD value strongly oscillated and then quickly relaxed, which showed that the conformations of the protein molecules were easy to get to balance. However, with the decrease of exerted voltage, the RMSD value still oscillated but the amplitude weakened. Meanwhile, the balance time was extended with reduced electric field strength. The proteins moved so rapidly that those of them with no charge on the side chain could not force the whole peptide chain to interact with ions. Although the far side chain had the trend to move to the wall, it could not approach the wall surface due to steric hindrance. The stronger the electric field force, the faster moved the ions, hence the more quickly the protein molecules passed thought the channel. Large initial RSMD value and reduced balance time helped the transport of protein molecules.

Fig.8 shows the density distribution of water molecules and ions under electric field in system No.7. The water molecules distribution was almost unchanged at different electric field strengths. With the increase in electric field strength, the negative ions concentrated in the two sides while the positive ions moved to the centre of the channel.

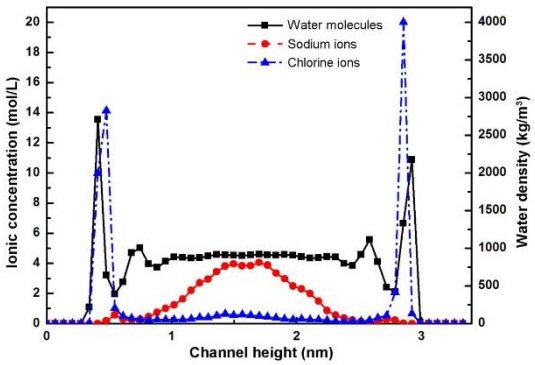


**Fig.8.** Density distribution of molecules and ions at electric field strength of 2 V/nm

The chloride ions moved quickly and came close to the wall surface while the sodium ions moved along the electric field direction in the central channel with a high flow rate. That is because the electroosmotic flow formed in the channel was strengthened by the strong electric field. The accelerated flow carried over more ions around the protein molecules and weakened the interaction between the ions and protein molecules. So the electric field force was prior to the LJ impact and the Coulomb force at strong electric field.

## CONCLUSIONS

The transport process of biomolecules and ions in nanoscale channels was investigated using seven groups of parameters. Based on the simulated results, several conclusions could be drawn, as follows:

(1) The channel height greatly influenced the transport of proteins. With the decrease in channel height, the EDL effect became more obvious, so the moving proteins received more repulsive force from the counter chloride ions. As the transport direction of protein molecules was the same as that of the counter ions, the transport became more difficult, and *vice versa*.

(2) The ionic concentration also influenced the transport of protein molecules. At higher ionic concentration, the interaction between ions and protein molecules became stronger, which forced the protein molecules to move more rapidly and pass through the channel more quickly, and *vice versa*. Meanwhile, the layered concentration phenomenon of molecules and ions nearby the channel wall aggravated with the average ionic density.

(3) The electric field strength played an important role on the transport of protein molecules. The protein molecules passed more easily and more quickly with the increase in electric field strength because the flow velocity turned higher and the electric field force prevailed over other forces such as LJ impact and Coulomb force.

***Acknowledgements:*** *This work has been jointly supported by National Natural Science Foundation of China (51376039), Doctoral Fund of Ministry of Education of China (20120042110031) and the Fundamental Research Funds for the Central Universities of China (N120403006).*

REFERENCES

1. T. Yamamoto, T. Fujii. *Nanotechnology*, **21**, 395502(2010).
2. S. L. Levy, H. G. Craighead. *Chem. Soc. Rev*., **39**, 1133(2010).
3. S. M. Stavis, J. Geist, M. Gaitan, L. E. Locascio, E. A. Strychalski. *Lab Chip*, **12**, 1174 (2012).
4. C.H. Duan, W. Wang, Q. Xie. *Biomicrofluidics*. **7**, 026501 (2013).
5. M. Napoli, J. C. T. Eijkel, S. Pennathur., *Lab chip*, **10**, 957 (2010).
6. R. Qiao, N. R. Aluru, *J. Chem. Phys*., **118**, 4692 (2003).
7. R. Qiao, N. R. Aluru, *Phys. Rev. Lett.*, **92(19)**, 1 (2004).
8. R. Karnik, R. Fan, M. Yue, D. Li, P. Yang, A. Majumdar, *NanoLett.*, **5**, 943(2005).
9. R. Karnik, K. Castelino, *Appl. Phys. Lett*., **88**, 123 (2006).
10. K. Liu, D.C.Ba, X.G.Gu, G.Y.Du, Z.Lin, X. H. Liu, Z. X. Wang, S.W.Xiao. *Appl. Surf. Sci*., **258**, 2157 (2012).
11. D.V.D. Spoel, E. Lindahl, B. Hess, G. Groenhof, A.E. Mark, H. J. C. Berendsen. *J. Comput. Chem.*, **26,** 1701 (2005).
12. B. Hess, C. Kutzner, D. Spoel, E. Lindahl, *J. Chem. Theory and Comput***., 4**, 435 (2008).
13. W. D. Cornell, P. Cieplak, C.I. Bayly, I. R. Gould, K. M. Merz, D. M. Ferguson, D. C. Spellmeyer, T. Fox, J. W. Caldwell, P. A. Kollman. *J. Am. Chem. Soc*, **117**, 5179 (1995).
14. B. R. Rooks, R. E. Bruccoleri, B. D. Olafson, D. J. States, S. Swaminathan, M. Karplus. *Journal of Comput. Chem*., **4**, 187(1983).
15. I. D. Kuntz, J. M. Blaney, S. J. Oatley, R. Langridge, T. E. Ferrin. *J. Mol. Biol.*, **161**, 269 (1982).
16. W. L. Jorgensen, J. Chandrasekhar, J. D. Madura, R. W. Impey, M. L. Klein. *J. Chem. Phys.*, **79**, 926 (1983).
17. H. J. C. Berendsen, J. R. Grigera, T. P. Straatsma. *J. of Chem. Phys*., **91**, 6269 (1987).

# ЧИСЛЕНО СИМУЛИРАНЕ НА ТРАНСПОРТНИ ПРОЦЕСИ НА БИОМОЛЕКУЛИ И ЙОНИ НА МОЛЕКУЛЯРНО РАВНИЩЕ В УСПОРЕДНИ КАНАЛИ С НАНОРАЗМЕРИ СЪС СТЕНИ ОТ ВЪГЛЕРОД

К. Лю[1*], Й. Ч. Нинг[1], Д. Ч. Ба[1 *], С. У. Ксиао[2], Кс. Л. Жанг[3], Д. Ю. Уанг, Г. Ю. Ду[1], Я. Ш. Ба[1]

[1]*Училище по механо-инженерство и автоматизация, Североизточен университет, Шенянг, Китай*
[2]*Институт по физика на високите енергии, Китайска академия на науките, Бейджин, Китай*
[3]*Столична компания по космическо машиностроене, Бейжин, Китай*

Постъпила на 4 април, 2015 г.

(Резюме)

Манипулирането на био-молекули в канали с нано-размери е твърде интересно и предизвикателно. Едно от пред-условията е да се разберат транспортните процеси на биомолекули и йони в нано-размерни канали. В настоящата работа е извършено числено моделиране на молекулно ниво. Въведен е модел на полипептида GNNQQNY като молекула на протеин за изследване на поведението му спрямо движещи фактори като височина на каналите, концентрацията му и интензитета на електрично поле. Резултатите от симулирането са обсъдени и анализирани чрез сравнение на разпределението на молекулите, амплитудите на движението на протеиновите молекули и потенциалната енергия. Намаляването на височината на каналите влияе значително на движението на молекулите главно чрез ефекта на двойния електричен слой (EDL).Повишаването на йонната концентрация спомага за преминаването на протеиновите молекули, докато слоистото концентриране на молекулите и йоните в близост до стените на каналите се влошава със средната йонна плътност. Силата на електричното поле също е ефективно средство за контролиране на преминаването на протеиновите молекули. Резултатите са полезни за разбирането на преноса на био-молекули в нано-флуидни канали.