A study of local effect and global effect on the microthermal bio-flows by molecular dynamics

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Abstract

This study develops a hybrid numerical scheme based on a molecular dynamics (MD) algorithm and the GROMACS protein data bank to analyze the thermal bio-flow of alanine molecules in a microchannel. The numerical results show that the velocity profiles in the microchannel are highly dependent on both global effects, i.e. the effective channel width and local effects, i.e. the thermal boundary conditions. Specifically, the magnitude of the fluctuations observed in the velocity profiles increase as the channel width decreases or as the thermal boundary temperature increases. The results presented in this study provide useful information regarding suitable microchannel widths and operational temperatures for bio-chip devices and contribute a further understanding of basic human thermal bio-flow phenomena, particularly, regarding the correlation between the rate of local metabolism, burn and frostbite events, respectively.

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1. Introduction

In constructing a thermal bio-flow model to analyze heat and mass transfer phenomena, a key requirement is to establish the correlation between the flow fields established in body fluids and the thermal gradient at fluid’s contact boundary. The flow field of the body fluid on the bio-chip and the local metabolism, burn and frostbite will be disclosed as the thermal bio-flow model can be detected. Researchers have employed a variety of bio-heat models to investigate heat transfer phenomena in bio-tissue, including the Pennes equation, Keller and Seiler’s analytical method, molecular dynamics (MD) simulations and so forth [1–3]. In general, researchers have considered both micro- and nano-scale thermal flow problems. For example, Niu et al. [4] studied the microthermal flow problem using the thermal lattice Boltzmann model and found that the numerical results were consistent with those obtained under conventional velocity slip and temperature jump boundary conditions. Han [5] investigated the problem of thermophoresis in liquids using a MD approach and showed that the nature of the phenomena induced during thermophoresis is determined principally by the characteristic size of the system involved. Khare et al. [6] employed MD simulations to examine the heat and momentum transfer at a solid–liquid interface characterized by laminar shear flow conditions.

MD simulations are characterized by a fine temporal resolution and therefore, make possible an accurate modeling of the rapid variations inherent in natural molecular systems. Furthermore, the elevation of the protein’s force field is the key process in MD. Therefore, MD simulation is one of the most promising methods for acquiring the basic phenomena in the protein system. These phenomena are of great interest to bio-chemical researchers attempting to compile a complete understanding of the roles played by various protein materials in common biomedical problems. Therefore, the protein data banks, which play the important role in the calculation of the molecular dynamics, have been studied in most of the recent papers. Increasingly, these data banks have been used as the basis for MD studies aimed at exploring the basic properties and phenomena of bio-molecules.

For example, El-Bastawissy et al. [7] have studied the protein material at normal and elevated temperature in MD. Suenaga [8] investigated a small-sized protein folding with implicit solvent. The comparison of sampling efficiency between the molecular dynamics and the Monte Carlo method in protein is investigated
The velocities and positions of the alanine molecules are computed using the leap-frog method [13,14] (i.e. a modified Verlet algorithm), while the effect of the thermal boundary conditions on the protein molecules are modeled using the Andersen thermodbath method [15]. The instantaneous velocities of the alanine molecules adhering to the microchannel wall are corrected at each time step in order to maintain the wall temperature at the required value, i.e.

\[ T_a = \frac{1}{3N} \left( \sum_i v_i^2 \right), \quad v_i^{\text{new}} = v_i \sqrt{\frac{T_s}{T_a}} \]  

where \( N \) is the number of molecules in the specified region, \( T_a \) the instantaneous temperature of the specified region following all of the colliding processes at each time step, \( T_s \) the initial temperature of the specified region, \( v_i \) the velocity of the \( i \)th molecule following all of the colliding processes at each time step and \( v_i^{\text{new}} \) is the corrected molecular velocity of the \( i \)th molecule.

The simulations commence by performing an equibration process in which Eq. (1) is used to adjust the velocities of the molecules when the system is maintained to be in a particular temperature. From basic statistical thermodynamic principles, it is known that the initial velocities of the molecules in an equilibrium system are distributed in accordance with a Maxwell–Boltzmann velocity distribution provided that the temperature of the isolated system is constant. In addition, in a Maxwell–Boltzmann velocity distribution with a system temperature of \( T \), the probability of the \( i \)th molecule having a velocity value between \( v \) and \( v + dv \) is given by

\[ p(v) \, dv = \sqrt{\frac{m}{2\pi k_B T}} \exp \left( -\frac{m}{2k_B T} v^2 \right) \, dv \]  

In addition, the net momentum of the system must be equal to zero in order to guarantee that the system will not move due to an external force. The conservation conditions for the momentum are described as below.

\[ v_i^{\text{new}} = v_i - \frac{1}{N} \sum_{i=1}^{N} p_i \]  

where \( p_i \) is the momentum of the \( i \)th molecule. As well, the heat current \( J [16] \) is

\[ J = \frac{1}{2} \left( \sum_{i=1}^{N} m v_i^2 \bar{v}_i + \sum_{i=1}^{N} \sum_{j \neq i}^{N} \left( \phi(r_{ij}) \bar{v}_i - w(r_{ij}) \frac{\bar{v}_i - \bar{v}_j}{r_{ij}} - \frac{\bar{v}_j}{r_{ij}} \right) \right) \]  

where \( \phi(r_{ij}) \) is the potential between molecule \( i \) and \( j \). Additionally, \( w(r_{ij}) \) is the pair virial function and defines as

\[ w(r_{ij}) = \frac{\partial \phi(r_{ij})}{\partial r_{ij}} \]  

The objective of the current flow problem is to establish the gross fluid motion rather than the instantaneous velocity. The average dimensionless velocity \( v_{i,k,z} \) of the gross fluid motion by Yamashita et al. [9]. In addition, the development of softcore potential functions for overcoming steric barriers is reported by Hornak and Simmerling [10]. As well, Komeiji et al. [11] studied the protein simulation by parallel molecular dynamics.

Zal and Gascoigne [12] use the live FRET imaging to reveal early protein–protein interactions. Despite the contributions of the studies above, a review of the literature reveals that the micro-scale thermal bio-flow problem has received comparatively little attention. Accordingly, the current study combines the GROMACS protein data bank with the liquid–solid interface on the velocity profiles of the alanine molecules. The results of the simulations are intended to provide a further understanding of basic human thermal bio-flow phenomena and to provide useful information regarding a suitable design and operational parameters for bio-chip microchannels.

In this present study, MD is used to calculate the micro-scale bio-flow problem, the reason is that the ratio of the microchannel diameter and the bio-molecule diameter is similar as the ratio of the nano-channel diameter and the water molecule diameter.

The remainder of this paper is organized as follows. Section 2 presents a high-level overview of the current simulation procedure and introduces the relevant mathematical formulations. Section 3 describes the detailed steps involved in the simulation procedure and presents the relevant simulation parameters. Section 4 presents and discusses the numerical results obtained for the velocity flow fields under various effective microchannel width and thermal boundary conditions. Finally, Section 5 summarizes the overall contributions and findings of the study.

2. Mathematical model

As discussed above, the simulations conducted in this study consider the thermal bio-flow of alanine (NHC\(_2\)H\(_4\)CO) molecules in a microchannel under various microchannel width and thermal boundary conditions. Fig. 1 presents a schematic illustration of the simulation system. The simulations are performed using a hybrid iterative scheme comprising a MD algorithm and the GROMACS protein data bank.

The current study focusses on the respective effects of the effective diameter and the bio-molecule diameter is similar as the ratio of the microchannel width and thermal boundary conditions. Finally, Section 5 presents and discusses the numerical results obtained for the velocity flow fields under various effective microchannel width and thermal boundary conditions.

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is shown as follows [17]:

\[ v_{i,k,z} = \left( \frac{x(i, k) - x(i, k - Z)}{Z \Delta t}, \frac{y(i, k) - y(i, k - Z)}{Z \Delta t} \right) \]

where \((x(i, k), y(i, k))\) is the position of the molecule \(i\) at time \(t_k = k \Delta t\) and \((x(i, k - Z), y(i, k - Z))\) represents the position of the molecule \(i\) at time \(t_{k-Z} = (k-Z) \Delta t\).

### 3. Simulation details

The present simulations consider a total of 15 different models, corresponding to three different channel widths and five different thermal boundary conditions, respectively. The effective channel width \((D^*\) \) is defined in dimensionless form as the effective channel width \((D)\) divided by the molecular diameter \((\sigma)\) and has values of 10, 50 and 100, respectively, in the current simulations, corresponding to a total of \(N = 500, 12,500\) and 50,000 alanine molecules in the fluid. The alanine molecules have a diameter of approximately 100 nm and thus, the global density \((\rho)\) is approximately 100 N/m² in each case. The thermal boundary is specified as a fixed temperature conditions at the microchannel boundary surface \((T^w)\) are assigned values of \(-10, -5, 0, 5\) and 10 K, respectively, where \(T^w\) is the wall temperature \((T_w)\) minus the fluid temperature \((T_f)\). The thermal boundary condition is imposed at the position at which the alanine molecules are absorbed intact on the wall [18]. Furthermore, periodic boundary conditions (PBCs) are imposed in the \(x\)-direction.

In the simulations, the GROMACS protein data bank is used to model the complicated potential interactions between two alanine macromolecules [19]. Basically, the position, velocity and acceleration of each alanine molecule are computed using the GROMACS modeling package and are then exported to the MD simulations, corresponding to a total \(N = 500\) and 50,000 alanine molecules in the fluid. The alanine molecules are absorbed intact on the wall [18]. Further- more, periodic boundary conditions (PBCs) are imposed in the \(x\)-direction.

In the simulations, the GROMACS protein data bank is used to model the complicated potential interactions between two alanine macromolecules [19]. Basically, the position, velocity and acceleration of each alanine molecule are computed using the GROMACS modeling package and are then exported to the MD simulations, which then computes the new position and velocity of each molecule using the leap-frog algorithm. In this study, the driven acceleration \((\dot{a}_D)\) is specified as 0.3 nm/ps. In general, the accuracy of the results obtained from MD simulations is dependent on the truncation distance applied when modeling the interactions between two molecules. In accordance with the recommendations of Allen and Tildesley [20], the current study adopts a truncation distance of \(r_c = 0.2\), where \(l\) is the length of the model, to ensure that the effects of long-range interactions are reflected in the simulation results.

The simulations commence by performing an equilibration process in which the velocities of the molecules are adjusted such that they conform to a Maxwell velocity distribution, i.e. a similar period of equilibration with the external field switched on. The total number of time steps in the simulations (excluding those of the equilibration process) is specified as \(2.5 \times 10^7\), with each time step having a duration of 0.1 fs. The realistic CPU time is about 40 h in the case of \(N = 500\) on the Intel Pentium D 945 3.4 G, 1 G RAM, Linux system. According to Schlick et al. [21], the general criterion for the time interval to ensure stability when using the leap-frog method is \(\Delta t = \Gamma / \pi \tau\) for a harmonic oscillator of period \(\Gamma\). The time step in the current simulations, i.e. 0.1 fs, is much less than that of 6.4 fs for H–O–H bending and 3.1 fs for O–H stretching, respectively, and is therefore, sufficiently small to ensure numerical stability. The initial temperature and pressure of the simulation system are specified as \(T = 309\) K and \(P = 1\) atm, respectively. The parameter values applied in the current simulations are summarized in Table 1.

**Table 1**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wall temperature (K)</td>
<td>319, 314, 309, 304, 299</td>
</tr>
<tr>
<td>Initial system temperature (K)</td>
<td>309</td>
</tr>
<tr>
<td>Pressure (atm)</td>
<td>1</td>
</tr>
<tr>
<td>Effective channel width</td>
<td>10, 50, 100</td>
</tr>
<tr>
<td>Chemical formula</td>
<td>NHC2H4CO</td>
</tr>
<tr>
<td>Sample molecule</td>
<td>Standard alanine macromolecule</td>
</tr>
<tr>
<td>Protein data bank</td>
<td>GROMACS</td>
</tr>
<tr>
<td>Simulation duration</td>
<td>0.1 ms (= 2.5 \times 10^7) runs</td>
</tr>
<tr>
<td>Time step</td>
<td>(\Delta t = 0.1) fs</td>
</tr>
</tbody>
</table>

Fig. 2 presents a flow chart showing the various procedures involved in the iterative GROMACS/MD simulations. Briefly, the major steps can be summarized as follows:

**Step 1.** The GROMACS protein data bank is used to build the initial model; the sample molecule is alanine.
macromolecule. The initial position of each molecule is assigned to construct a regular triangular grid in the plane. With initialization accomplished, the run itself can begin. Over a period of time steps, the system relaxes from the assigned initial conditions and approaches equilibrium. The equilibrium process is from Steps 2–5.

3.1. Equilibrium process

Step 2. The acceleration between two alanine molecules, \( \ddot{a}_i \), is computed by GROMACS and is used to represent the interaction between two molecules.

Step 3. At each time step, GROMACS exports an output file to the MD simulation algorithm indicating the position, velocity and acceleration of each alanine molecule. This file is taken as a new initial input file by the MD algorithm and is used to compute the updated position and velocity of each molecule using the leap-frog algorithm.

Step 4. The velocity of each molecule is adjusted using Eq. (1) in order to maintain the simulation system at the desired temperature.

Step 5. If the velocity distribution satisfies the Maxwell velocity distribution then the equilibration process is terminated, otherwise the computations return to Step 2.

3.2. Start simulation

Step 6. Step 2 is repeated to obtain the acceleration of each alanine molecule.

Step 7. Step 3 is repeated to obtain the new position and velocity of each molecule on the external force switches on.

Step 8. At each time step, the thermobath model is applied to correct the position and velocity of each molecule in accordance with the imposed thermal boundary conditions.

Step 9. To ensure momentum conservation within the system and to maintain the wall temperature at the required value, the velocity of each molecule is further corrected using Eqs. (1) and (3).

Step 10. The GROMACS/MD simulation process is terminated if the specified number of simulation time steps has been performed; else the simulation process returns to Step 6.

4. Results and discussions

To demonstrate the advantage of the proposed method for the estimation of the velocity profiles of the thermal bio-flow in the microchannel from the global effect and local effect on the results of the molecular dynamics simulations are investigated. The behavior of the thermal bio-flow of the alanine is shown. In the present study, 15 kinds of cases (i.e. three kinds of effect channel widths and five kinds of thermal boundary) are applied on the channel.

Fig. 3. Simulated flow velocity profiles for various wall temperatures \( T^\ast \) at \( D^\ast = 10 \).

To illustrate the effects of various thermal boundary conditions \( (T^\ast = 10, 5, 0, −5 \) and \( −10 \) K), Fig. 3 presents the normalized fitting velocity profiles in microchannel at \( D^\ast = 10 \), separately. The normalized velocity profile is the velocity divided by the average velocity. It is observed that each velocity profile has three distinct peaks, located at \( y/D = −0.5, 0.0 \) and \( 0.5 \), respectively. These velocity fluctuations are the result of a non-uniform density distribution of the alanine molecules in the microchannel. The magnitude of the velocity fluctuations reduces as the boundary temperature, \( T^\ast \) decreases. This result is reasonable since the velocity of the molecules increases as the quantity of heat flux supplied to the channel increases. Finally, it is clear that the current molecular-scale velocity profiles are markedly different from the quadratic profile characterizing macro-scale flows.

It is also interesting to investigate the effect of the effective channel width on the estimated results. Therefore, this study will further test the effect of the effective channel width, the various channel widths are adopted to estimate the velocity profiles of the thermal bio-flow. The normalized velocity profiles in microchannel with various \( D^\ast \) in Fig. 4 are derived at \( T^\ast = 10 \) K. As expected, the estimation of the velocity profile is still deviated from the classical result. In general, it is seen that the magnitude of the velocity fluctuations decreases as the effective microchannel width increases. This observation is consistent with previous findings of the current group that the velocity fluctuations of water in nano-scale channels increase in magnitude as the channel width reduces \([18]\). It is also seen that the current molecular-scale velocity profiles deviate more significantly from the classical profile as the effective channel width reduces. The results also show that the number of peaks in the velocity profiles reduces as the effective microchannel width increases, which implies that the density distribution of the alanine molecules in the microchannel becomes more uniform as the channel width increases.

Fig. 5 presents the variation of the spatial-average energy of the dimensionless velocity fluctuations \( ((v − \bar{v})/\bar{v})^2 \) as a
Fig. 4. Simulated flow velocity profiles for various effective channel widths $D^*$ at $T^* = 10K$.

function of the effective microchannel width and thermal boundary conditions, respectively. It is clear that the value of $((v - \bar{v})/\bar{v})^2$ reduces as $T^*$ reduces. Additionally, for an effective microchannel width of $D^* < 50$, the fluctuation velocity increases significantly as $D^*$ reduces, which implies that for $D^* > 50$, the bio-flow is stabilized by a global effect. However, for $D^* < 50$, the flow field depends on both the channel width (i.e. a global effect) and the thermal boundary conditions (i.e. a local effect). Specifically, for narrower microchannels, the velocity fluctuations become stronger as $D^*$ reduces or $T^*$ increases.

Overall, the results presented in Figs. 3–5 show that the magnitude of the velocity profile fluctuations increases as the channel width decreases or the thermal boundary temperature increases. Under such conditions, the flow field is clearly not stable, and hence, molecules carried in the fluid are less readily deposited on the microchannel walls. Accordingly, it can be inferred that the rate of deposition of molecules in bio-chip devices can be enhanced by specifying a wider channel width and a lower operating temperature. In the context of the human body, the present qualitative results offer a preliminary explanation for the reduced local metabolic rate observed in patients suffering from frostbite and the higher metabolic rate found in those suffering from burns. These results can be applied in the design of bio-chip’s channel and the building of the fundamental phenomena of the burn or frostbite.

5. Conclusion

This study has developed a hybrid computational scheme comprising an MD simulation algorithm and the GROMACS protein data bank to investigate the thermal bio-flow of alanine molecules in a microchannel. The MD simulations are based on the leap-frog algorithm and apply the Andersen thermostat to model the effect of the thermal boundary conditions on the protein molecules. The simulations have focused specifically on the respective effects of the microchannel width and the thermal boundary at the solid–fluid interface on the velocity profiles within the microchannel. In general, the simulation results have shown that the current molecular-scale velocity profiles differ markedly from that observed in classic macro-scale flows. Specifically, the current velocity profiles are characterized by fluctuations whose magnitudes reduce with an increasing microchannel width or a decreasing temperature at the solid–fluid boundary. The results have also shown that the number of peaks in the velocity profiles reduces as the microchannel width increases, which implies that a more uniform density distribution of the alanine molecules is achieved in broader microchannels. The results presented in this study for the flow of alanine molecules in a microchannel are consistent with those reported by the current group in a previous study for the flow of water in nano-scale channels.

Overall, the current results have demonstrated the feasibility of the hybrid GROMACS/MD simulation scheme for investigating thermal bio-flows in a microchannel. The current results have clarified the influence of global and local effects on thermal bio-flows and provide useful information regarding suitable configuration and operational parameters for bio-chip devices. Furthermore, the qualitative results have provided a feasible explanation for the reduced metabolic rate observed in patients suffering from frostbite, and the higher rate of metabolism found in those suffering from burns. In a future study, the current group intends to perform a more precise quantitative analysis of thermal bio-flows in order to obtain a greater understanding of the effect of thermal bio-flow phenomena on the rate of local metabolism.

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