

Static charges cannot drive a continuous flow of water molecules through a carbon nanotube

To the Editor — The need to simulate physical systems over longer and longer time periods is motivating the use of computational approximations and ‘short cuts’ that can lead to artefacts. Gong *et al.* report molecular dynamics (MD) simulations in which charge-induced ordering of water leads to spontaneous and continuous unidirectional flow through a carbon nanotube that connects two reservoirs¹ (inset to Fig. 1). The simulations were performed with the Gromacs package². They attribute this observation to a stationary asymmetric charge distribution along the nanotube created by three discrete electric charges. This charge distribution was chosen to mimic the electric field inside an aquaporin protein³. They propose this phenomenon as a basis for the design of new molecular pumps^{1,4}. Clearly the energy needed to drive this flow must come from somewhere, and Gong *et al.* argue that it comes from the constraints imposed on the charges. Here, based on simulations with Gromacs, we argue that the flow observed by Gong *et al.* is an artefact caused by the incorrect use of charge groups in their MD simulations. We have also uncovered problems with the use of thermostatting and neighbour lists (NLs) in the simulations.

Charge groups are commonly used to speed up MD simulations of systems that contain explicit electric charges. The basic idea is that a selected number of charges from different atoms in a molecule can be combined into a charge group. Although the interactions between the individual charges belonging to different groups are computed, the locations of charge groups are defined by the averages of their coordinates (see ref. 2 for a detailed account). Gong *et al.* treated the water molecules in their simulations individually, but the three charges along the nanotube were included in the same charge group. (We have examined their initial settings.) When we repeated the simulation without charge groups, the flow was not observed (Fig. 1).

We will explore the role of charge groups in more detail below, but first we will look at the use of thermostatting and NLs in simulations. To investigate the results

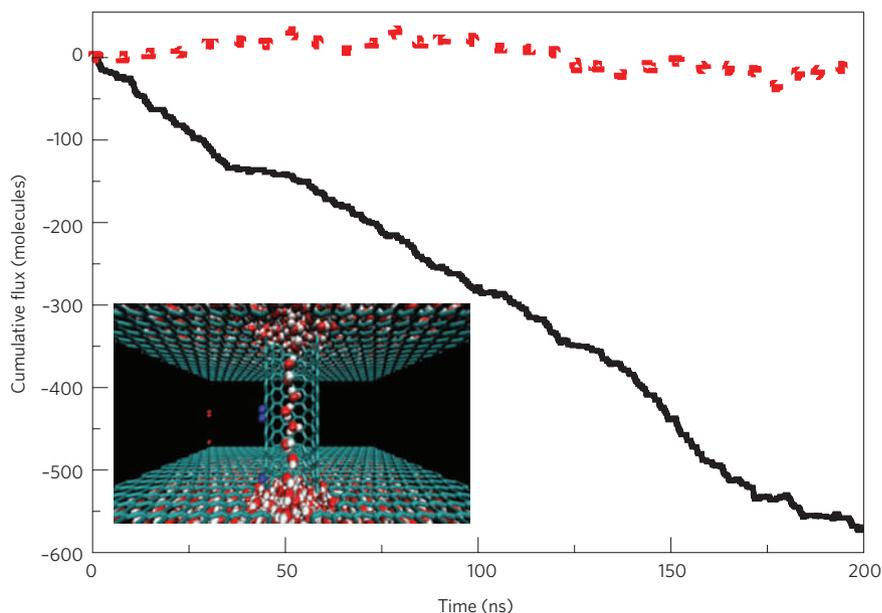


Figure 1 | Cumulative flux of water molecules as a function of time for two different MD simulations of the system shown in the inset. The inset shows a carbon nanotube connecting two reservoirs of water molecules (shown in red and white) with three static charges (blue spheres) placed beside the nanotube. Based on MD simulations with the Gromacs package, in which the three charges are treated as a single charge group, Gong *et al.*¹ reported a flow of water molecules from the top reservoir to the bottom reservoir (black line). However, when we repeated this simulation, treating the three charges separately, there was no flow (red line), which suggests that the flow is an artefact caused by the three charges being treated as a single charge group¹. We used 5,992 TIP3P water molecules in the simulation and the nanotube was 2.3 nm long. The charges were placed 0.37 nm, 1.09 nm and 1.21 nm from the bottom of the nanotube, and the charges were +e, +e/2 and +e/2 respectively, where -e is the charge on the electron.

reported by Gong *et al.*, we started with their initial settings with the charge-group error corrected, and then changed a number of parameters (NLs, thermostats, truncation distance and barostats) in subsequent runs (Fig. 2).

When applied with care, NLs reduce the CPU time needed for a given simulation without tampering with the dynamics. Two cutoff lengths, r_1 and r_2 ($r_1 < r_2$), are used with the NLs: interactions are computed only for $r < r_1$. r_2 defines the range within which the NL of a nearby particle is constructed. To work properly one has to have $r_1 < r_2$ and to update the NLs frequently enough

(determined by a preliminary control simulation). When we used the same NL settings as Gong *et al.* ($r_1 = r_2$, with the NLs being updated after every ten time steps; these are the default settings in Gromacs), we also observed a continuous flow of water molecules through the nanotube (solid black line in Fig. 2). We then repeated the simulations, updating the NLs after every time step (which should result in a more accurate simulation), and noticed that the flow was weaker (dashed red line).

Next, we examined the effect of the thermostat used in the simulations, comparing the Berendsen thermostat⁵ used

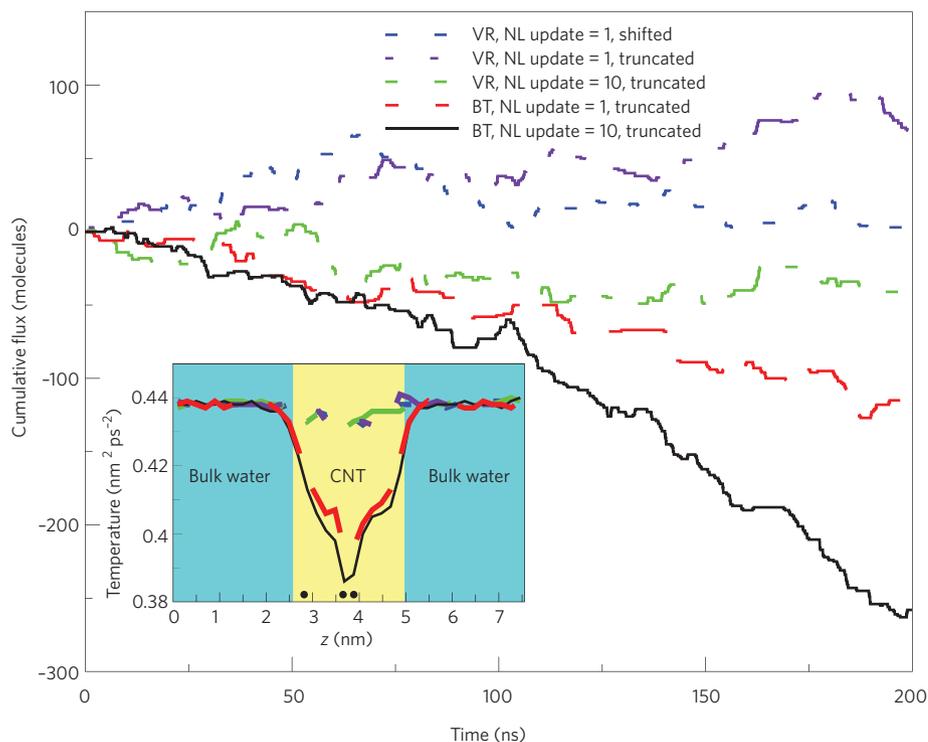


Figure 2 | Cumulative flux of water molecules as a function of time for five different MD simulations of the system shown in the inset to Fig. 1. The five different lines are explained in the main text. The inset shows how the temperature of the water molecules varies with position for these five simulations. The quantity plotted as temperature on the y axis is actually $\langle v^2(z) \rangle - \langle v(z) \rangle^2$ where v is the velocity of the molecules, z is position and $\langle \rangle$ denotes an average. The black dots indicate the positions of the charges, which were placed 0.17 nm (+e), 1.08 nm (+e/2) and 1.22 nm (+e/2) from the bottom of the nanotube. VR = velocity-rescaling thermostat; NL = neighbour list; BT = Berendsen thermostat; CNT = carbon nanotube. 'Shifted' indicates that the short-range Lennard-Jones interaction potential was shifted and 'truncated' means truncation at the cutoff distance. The scales in Figs 1 and 2 are different because all the simulations in Fig. 2 were done with correct charge groups.

by Gong *et al.* with the velocity-rescaling thermostat of Bussi *et al.*⁶. Although the Berendsen thermostat is unable to produce the thermodynamic fluctuations of the canonical ensemble⁷, it has been widely used in MD simulations because non-physical phenomena are only rarely observed as a result of this artefact. When we repeated the simulations with the velocity-rescaling thermostat and the NLs being updated after every ten time steps, the long-time average of the cumulative flux approached zero (dashed green line) unlike in the previous two cases. The same occurred when we repeated the simulations with the velocity-rescaling thermostat and the NLs being updated after every time step (dashed purple line). We also explored the effect of shifting the short-range Lennard-Jones interaction because it was recently reported that “erroneous force truncation can give rise to spurious flow effects for static electric fields” for MD simulations of water in nanochannels⁸. When we repeated the simulations with the

velocity-rescaling thermostat, the NLs being updated after every time step and a shifted Lennard-Jones interaction potential, we did not observe any net flow (dotted blue line). Performing the simulations in constant volume (that is, without a barostat) did not influence the flow.

Further analysis showed that the flow observed in these simulations is related to a variation in the temperature along the nanotube. The typical setting in Gromacs (Berendsen thermostat, NLs being updated every ten steps) led to a clear dip in the local temperature in the nanotube (inset to Fig. 2; solid black line). Updating the NLs after every time step slightly reduced the depth of the dip, and replacing the Berendsen thermostat with the velocity-rescaling thermostat resulted in little or no measurable variation in the temperature along the nanotube. This finding is consistent with simulations that found that although the Berendsen thermostat works quite well for bulk systems, it leads

to a decrease in the internal temperature of individual particles and small clusters⁹.

It has also been shown that maintaining a temperature gradient between the ends of the nanotube is enough to drive a flow¹⁰, although this would suggest that the temperature variation associated with the typical setting in Gromacs would result in water molecules flowing from both ends of the nanotube towards the centre, and hence there would be no net flow. However, when a temperature gradient (an artificial one in this case) is coupled to an appropriate asymmetric charge distribution, the resulting asymmetric potential will lead to a unidirectional flow¹¹. The temperature gradient produced in simulations with the most commonly used setting in Gromacs would therefore be enough to create a flow. Furthermore, when the NLs are updated after every time step and the Berendsen thermostat is replaced with the velocity-rescaling thermostat, this temperature gradient disappears.

Returning to the issue of charge groups, we note that the length of the nanotube in these simulations is 2.3 nm, and that the electric charges are placed 0.37 nm, 1.09 nm and 1.21 nm from the bottom of the nanotube, so the charge group is 0.9 nm (the average of these three distances) from the bottom. As the NL and the real-space coulomb cutoff¹² is 1.0 nm, water molecules moving from the top of the tube travel 0.4 nm (from the top) into the nanotube without having any real-space interaction with any of the charges. Then, once they have travelled more than 0.4 nm into the nanotube, the water molecules experience real-space interactions with all three charges. This creates a very strong flow that overrides the effect of any thermostat. However, when the three charges are treated separately the flow disappears (and the CPU time needed for the simulations increases). We note that charge groups are very useful when applied correctly and can significantly reduce the CPU time needed for simulations².

While revising this correspondence we became aware that Zuo *et al.* had also reached the conclusion that “asymmetrically positioned charges cannot generate robust unidirectional water flow” in nanotubes¹³ based on simulations with the NAMD2 package¹⁴. We have not had the chance to examine their initial configuration, but because NAMD2 does not use charge groups in the same way that Gromacs does¹⁴, the charge-group artefact as described above was not present in the simulations of Zuo *et al.* They also used the Langevin thermostat instead of the Berendsen thermostat. Although the Langevin thermostat does not conserve momentum, it is local and thus

circumvents the build-up of the artificial temperature gradient.

Simulations are an invaluable tool but a small number of errors have been discovered in 'accepted' protocols, including random-number generation¹⁵, protein-structure prediction¹⁶ and the treatment of electrostatic interactions¹⁷. The errors discovered influenced hundreds of studies, which then had to be redone or re-evaluated. However, the ultimate result has been increased reliability and accuracy in numerical simulations. □

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Jirasak Wong-ekkabut^{1,2†}, Markus S. Miettinen^{3†}, Cristiano Dias⁴ and Mikko Karttunen^{1*}

¹Department of Applied Mathematics, The University of Western Ontario, 1151 Richmond St. N., London, Ontario N6A 5B7, Canada, ²Department of

Physics, Faculty of Science, Kasetsart University, 50 Phahon Yothin Rd, Chatuchak, Bangkok 10900, Thailand,

³Department of Biochemistry, Institute of Biochemistry and Biology, University of Potsdam, Karl-Liebknecht-Str. 24–25, 14476 Potsdam-Golm, Germany,

⁴Department of Biochemistry, University of Toronto, Toronto, Ontario M5S 1A8, Canada. [†]These authors contributed equally to this work.

*e-mail: mkarttu@uwo.ca

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