Scaling behaviour for the water transport in nanoconfined geometries

Eliodoro Chiavazzo1,*, Matteo Fasano1,2,3,*, Pietro Asinari1 & Paolo Decuzzi2,3,4

The transport of water in nanoconfined geometries is different from bulk phase and has tremendous implications in nanotechnology and biotechnology. Here molecular dynamics is used to compute the self-diffusion coefficient $D$ of water within nanopores, around nanoparticles, carbon nanotubes and proteins. For almost 60 different cases, $D$ is found to scale linearly with the sole parameter $\theta$ as $D(\theta) = D_B[1 + (D_C/D_B - 1)\theta]$, with $D_B$ and $D_C$ the bulk and totally confined diffusion of water, respectively. The parameter $\theta$ is primarily influenced by geometry and represents the ratio between the confined and total water volumes. The $D(\theta)$ relationship is interpreted within the thermodynamics of supercooled water. As an example, such relationship is shown to accurately predict the relaxometric response of contrast agents for magnetic resonance imaging. The $D(\theta)$ relationship can help in interpreting the transport of water molecules under nanoconfined conditions and tailoring nanostructures with precise modulation of water mobility.
Despite its fundamental importance in science and technology, the physical and transport properties of water are far from being completely understood. The self-diffusion of water molecules $D$ in proximity of solid surfaces, at the interface between immiscible liquids, and in confined geometries, such as nanotubes and nanopores, is a very different process as compared to the bulk phase\textsuperscript{2–4}. The thermal agitation of the water molecules in the bulk liquid is only dictated by the local temperature and pressure conditions, and molecular diffusion follows the Einstein relation\textsuperscript{5}. Differently, under confined conditions, the mobility of water molecules is perturbed by the presence of additional interaction forces arising at the water/solid interfaces, mainly van der Waals and Coulomb interactions. These additional forces usually reduce the local molecular diffusion\textsuperscript{6,7}. Even if considerable work has been done in recent years, both experimentally and theoretically, to understand and characterize the perturbed behaviour of the water molecules in confined geometries, there is still no complete comprehension of the process and often the published results are contradictory\textsuperscript{8}.

Controlling the mobility of water molecules is of relevance to several scientific disciplines and has implications in multiple technological applications. For instance, water adsorption/desorption in nanoporous materials, such as zeolites, has potential in long-term thermal storage and energy engineering\textsuperscript{9,10}, filters with nanopores and nanochannels are increasingly explored for their large surface area and higher efficiency\textsuperscript{11,12}; in heat transfer processes, nanofluids are under investigation because of their peculiar thermal properties\textsuperscript{13,14}; in micro/nanotechnology processes, controlling the deposition and surface diffusion of water molecules is critical for precise manufacturing\textsuperscript{15,16}; in biology, the mechanisms regulating the transport of single water molecules through cell membrane channels (aquaporins) and the multi-scale water compartmentalization in tissues are still elusive\textsuperscript{17–20}. Also, proteins tend to modify their structure and function according to the surrounding aqueous environment\textsuperscript{21,22}.

Certainly, nanomedicine is one of the fields where several exciting discoveries and technological applications can be directly related to the anomalous behaviour of water in confined geometries. A few examples are the enhancement in longitudinal relaxivity associated with the entrapment of $\text{Gd}^{3+}$-ion complexes in mesoporous structures\textsuperscript{23,24}; the dynamics of water molecules in nanotubes and nanochannels for controlled drug delivery\textsuperscript{25,26}; and the design of hydrogel-based nano/microparticles\textsuperscript{27,28}. In particular, the dynamics of water molecules is essential in magnetic resonance imaging (MRI), in that contrast enhancement is influenced by the local diffusion of water molecules\textsuperscript{29,30}. It is known that for paramagnetic metal complexes, such as $\text{Gd}^{3+}$ ions, the Solomon–Bloembergen–Morgan theory\textsuperscript{31} would predict a change in longitudinal relaxivity $r_1$ of the complex following a variation in the relative translational diffusion time ($\tau_D$) of the water molecules surrounding the complex, and in the residence lifetime ($\tau_M$) of the water molecules bound to the complex. Similarly, for magnetic nanoparticles (NPs), such as the iron oxide NPs, an increase in $\tau_D$ (that is, decrease in $D$) would enhance the transversal relaxivity $r_2$ (ref. 32). Hence, the modulation and precise control of the diffusion of the water molecules in the vicinity of an MRI contrast agent plays an important role in imaging performance. This concept has been already successfully proved by experiments\textsuperscript{23}, but a clear rationale (and a computationally efficient tool) for optimally designing such agents is still missing.

In this work, the self-diffusion coefficient $D$ of water molecules is investigated through molecular dynamics (MD) simulations under five different isothermal configurations, namely, within silica ($\text{SiO}_2$) nanopores, around spherical hydroxylated NPs, within $\text{SiO}_2$ nanopores filled by NPs, around single-wall carbon nanotubes (CNTs) and proteins. The coefficient $D$ has been estimated for almost 60 cases by varying the size of the NPs and nanopores, the electrostatic surface charges and level of hydrophobicity, as well as the type of protein. The self-diffusion coefficient $D$ for all different configurations has been found to scale with a single non-dimensional parameter $\beta$, incorporating both geometrical and physicochemical information, following the relationship $D(\beta) = D_0[1 + (\Delta D / D_0 - 1)/\beta]$. The $D(\beta)$ scaling is modulated by the coefficients $D_0$ and $\Delta D$, which represent the bulk and totally confined diffusion of water, respectively. This $D(\beta)$ law has been applied to estimate the enhancement in MRI contrast in magnetic nanoconstructs obtained by geometrically confining super-paramagnetic iron oxide NPs (SPIONs) into silicon mesoporous matrices. It has been confirmed that the transversal relaxivity of SPIONs can be significantly augmented by modulating the diffusion of water molecules. This law would help in explaining and rationalizing previous experimental evidences\textsuperscript{23}, and represent a ready-to-use tool for the rational design of nanoconstructs based on the nanoscale confinement of water molecules.

**Results**

**Computing the diffusion of nanoconfined water molecules.** MD simulations were used to compute the self-diffusion coefficient $D$ of water molecules confined under different configurations. These are shown in Fig. 1 and include the case of water molecules (blue dots) moving (a) around spherical hydroxylated nanoparticles (NPs) (grey dots); (b) within a hydrated nanopore (grey dots); (c) around hydroxylated NPs (red dots) adsorbed on the surface of a hydrated nanopore (grey dots); (d) around and within single-walled carbon nanotubes (CNTs); (e,f) around proteins. The NPs are made out of magnetite ($\text{Fe}_3\text{O}_4$) crystals (red and cyan dots), with $\text{OH}^–$ functional groups on their surface, or $\text{SiO}_2$ crystals (grey dots), with silanol $\text{SiOH}$ functional groups on the surface. The nanopores are made out of $\text{SiO}_2$ only.

To investigate the influence of geometry and material properties, the self-diffusion coefficient $D$ of the water molecules was computed for 58 different cases. In particular, these cases were different in terms of NP diameter, being 1.3, 2.0 or 5.2 nm; nanopore diameter, with values 2.0, 4.1, 8.1 and 11.0 nm; number of NPs adsorbed on the nanopore wall, varying from 0 to 66 NPs per pore; CNT armchair chirality, namely, (5,5), (10,10), (20,20) and (30,30); and type of proteins, including molecules with a spherical (for example, ubiquitin) and elongated (for example, $\text{Ca}^{2+}$-$\text{ATPase}$) shapes; of small (for example, 562 atoms of $\text{B1-immunoglobulin-binding domain}$) and large (for example, 9667 atoms of $\text{Ca}^{2+}$-$\text{ATPase}$) sizes; and exhibiting a catalytic (for example, glucokinase), hormonal (for example, leptin) and transport (for example, myoglobin) function. As per the material properties, two types of interactions were considered in the MD simulations: bonded interactions and non-bonded interactions between the water molecules and the solid surfaces, described via van der Waals and Coulomb potentials. In the $\text{SiO}_2$ structures and spherical NPs, the bonded interactions are modelled by means of harmonic terms. For the NPs, the strength $\varepsilon$ of the Lennard–Jones potential was varied from 2.49 to 24.94 kJ mol\textsuperscript{-1} and the partial electrostatic charges of atoms were set to either the nominal value or zero for NPs and nanopores. For simulations with CNTs, the non-bonded interactions between CNTs and water molecules were modelled by the Lennard–Jones potential, with neutral carbon atoms and $\sigma_{CC} = 0.36\text{ nm}$, $\varepsilon_{CC} = 0.29$ kJ mol\textsuperscript{-1} (ref. 33). Finally for the proteins, all bonded and
non-bonded interactions were modelled using the GROMOS96 43a2 force field34, which has been widely used for studying similar applications35,36. Finally, various hydration levels were considered providing an overall water density ranging from 715 to 941 kg m\(^{-3}\). Note that for these density values, there is no heterogenous wetting and consequently no anomalous behaviour related to low water-filling regimes37.

All computed values of the self-diffusion coefficient \(D\) are reported in the Supplementary Tables 1–11 and Supplementary Note 1. In general, it is observed that the coefficient \(D\) decreases compared with the bulk value, \(2.60 \pm 0.10 \times 10^{-9} \text{ m}^2\text{s}^{-1}\) at 300 K (ref. 37), as the ratio between the total area of the solid–liquid interface and the total volume occupied by the water (\(V_s\)) increases. More specifically, for a SiO\(_2\) nanopore, \(D\) is reduced from \(2.50 \pm 0.09 \times 10^{-9} \text{ m}^2\text{s}^{-1}\) to \(0.82 \pm 0.22 \times 10^{-9} \text{ m}^2\text{s}^{-1}\) as the pore diameter decreases from 11.0 to 2.0 nm. Moreover, \(D\) is inversely proportional to the NP concentration and diameter. For a 5.2-nm SiO\(_2\) NP, \(D\) decreases from the almost unconfined value of \(2.12 \pm 0.04 \times 10^{-9} \text{ m}^2\text{s}^{-1}\) following a 36% increase in NP concentration. Indeed, the increase in NP concentration is associated with a decrease in separation distance between adjacent NPs and, consequently, a decrease in the volume available to water molecules. Consistently, \(D\) reduces as the concentration of Fe\(_3\)O\(_4\) NP increases within a nanopore: \(D\) is \(2.20 \pm 0.10 \times 10^{-9} \text{ m}^2\text{s}^{-1}\) in an 8.1-nm SiO\(_2\) nanopore; however, if 2 Fe\(_3\)O\(_4\) NPs, of 2.0 nm in diameter, are adsorbed on the nanopore surface, \(D\) decreases to \(2.07 \pm 0.14 \times 10^{-9} \text{ m}^2\text{s}^{-1}\) and it drops to \(0.44 \pm 0.05 \times 10^{-9} \text{ m}^2\text{s}^{-1}\) (\(~80%\) decrease), if 16 Fe\(_3\)O\(_4\) NPs, of 2.0 nm in diameter, are added in the nanopore. In addition, for 16 Fe\(_3\)O\(_4\) NPs adsorbed on the wall of an 8.1-nm nanopore, \(D\) is \(1.46 \pm 0.09 \times 10^{-9} \text{ m}^2\text{s}^{-1}\) for 1.3 nm NPs and becomes \(0.44 \pm 0.05 \times 10^{-9} \text{ m}^2\text{s}^{-1}\) (\(~70%\) decrease) for 2.0 nm NPs. A similar trend is observed for the CNTs and proteins by reducing the size of the water box. More specifically, around the (5,5) chirality CNT with a length of 5 nm, the water diffusivity \(D\) decreases from the bulk value (box of 316 nm\(^3\)) to \(1.22 \pm 0.12 \times 10^{-9} \text{ m}^2\text{s}^{-1}\) (box of 21 nm\(^3\)). Similarly, around the B1-immunoglobulin-binding domain, the diffusivity \(D\) decreases from \(2.41 \pm 0.04 \times 10^{-9} \text{ m}^2\text{s}^{-1}\) (box of 348 nm\(^3\)) to \(0.87 \pm 0.10 \times 10^{-9} \text{ m}^2\text{s}^{-1}\) (box of 23 nm\(^3\)). As expected, the above data qualitatively demonstrate that the self-diffusion coefficient \(D\) of water is strongly correlated to the ratio between the interface surface and the total water volume: the larger this ratio the smaller the water mobility. However, the possible contribution of other parameters should also be assessed.

To this end, sensitivity analyses were performed to elucidate the effect of the Lennard–Jones potential strength \(\varepsilon\) and Coulomb interactions on \(D\). Larger values of the parameter \(\varepsilon\) are associated with lower mobility of the water molecules. As an example, let us consider the case of eight Fe\(_3\)O\(_4\) NPs (2.0 nm diameter) adsorbed on the walls of an 8.1-nm diameter SiO\(_2\) nanopore. A one order of magnitude decrease of \(\varepsilon\) of Fe\(_3\)O\(_4\) atoms only carries a 10% increase of \(D\); for \(\varepsilon = 24.94 \text{ kJ mol}^{-1}\) \(D\) is equal to \(1.33 \pm 0.13 \times 10^{-9} \text{ m}^2\text{s}^{-1}\), whereas \(D\) increases to \(1.47 \pm 0.11 \times 10^{-9} \text{ m}^2\text{s}^{-1}\) for \(\varepsilon = 2.49 \text{ kJ mol}^{-1}\). Moreover, \(D\) increases as the surface electrostatic charges decrease. For neutral Fe\(_3\)O\(_4\) NPs, \(D\) grows to \(1.64 \pm 0.04 \times 10^{-9} \text{ m}^2\text{s}^{-1}\) and, if both the NPs and nanopore wall are electrically neutral, \(D\) takes the value of \(1.69 \pm 0.20 \times 10^{-9} \text{ m}^2\text{s}^{-1}\) (\(~30%\) increase as compared with the example above). Although the water molecule confinement is affected by the strength of the interaction potentials (van der Waals and Coulomb), geometrical parameters show a greater influence on the coefficient \(D\). The reason is that all considered surfaces have effective wall potentials that are strong enough to induce a significant reduction of the water mobility in a region close to the wall. On the other hand, as clarified below, the volume of the low mobility region only slightly depends on the wall potential strength, namely, the minimum of the potential well generated by the wall.

![Figure 1](https://example.com/figure1.png)

**Figure 1 | Selected configurations.** (a) SiO\(_2\) particle in water, diameter \(\phi = 5.2\) nm (blue dots: water molecules; grey dots: SiO\(_2\) atoms); (b) SiO\(_2\) nanopore filled by water, diameter \(\Phi = 8.1\) nm; (c) sixteen Fe\(_3\)O\(_4\) NPs within a SiO\(_2\) nanopore filled by water, \(\phi = 2.0\) nm and \(\Phi = 8.1\) nm (red and cyan dots: Fe\(_3\)O\(_4\) atoms); (d) single-walled CNT with chirality (5,5); (e) green fluorescence protein; (f) leptin protein (the standard ribbon visualization of secondary structures has been used for proteins). In d-f water molecules have been removed for clarity. Almost 60 different cases have been analysed by varying the size and surface properties of the NPs, nanopores and nanotubes as well as the type of protein.
Finally, the self-diffusion coefficient \( D \) did not change significantly with the level of hydration in the considered range, in accordance with previous studies.\(^7\) Considering again the representative case of eight Fe\(_3\)O\(_4\) NPs, of 2.0 nm in diameter, adsorbed on the wall of an 8.1-nm SiO\(_2\) nanopore, \( D \) ranges from \( 1.30 \pm 0.11 \times 10^{-9} \) to \( 1.40 \pm 0.07 \times 10^{-9} \) m\(^2\) s\(^{-1}\) (<10% variation) as the water density increases from 700 to 930 kg m\(^{-3}\).

**Characteristic length of confinement.** In the bulk fluid, the water molecules fluctuate with a kinetic energy proportional to \( k_T T \), where \( k_B \) is the Boltzmann constant \((1.38 \times 10^{-23} \text{ J K}^{-1})\) and \( T \) is the temperature. As opposed to molecules in the bulk, those in a close proximity of solid surfaces are subjected to additional van der Waals \((U_{vdw})\) and Coulomb \((U_c)\) interactions interfering with their state of agitation. This induces a layering of water molecules with reduced mobility near the solid surface (see Supplementary Figs 1–3 and Supplementary Discussion), as already pointed out in other works. A characteristic length \( \delta_i \) can be introduced to quantify the thickness of such confined water layer.

Referring to the popular notion of solvent accessible surfaces (SAS)\(^{40–42}\), the quantities \( S_{\text{tot}} \) and \( S_{\text{loc}} \) can be introduced as the total and specific (per atom) SAS areas, respectively. For an arbitrary atom \( i \) of the solid structure, a number \( N_n \) of nearest neighbours (including the atom \( i \) itself) can be identified within a fixed cutoff radius (Fig. 2a,b). The corresponding effective potential energy \( U_{\text{eff}} \) on the water molecules, due to both van der Waals \((U_{vdw})\) and Coulomb \((U_c)\) interactions, can be computed as:

\[
U_{\text{eff}}(n) = U_{vdw}(n) + \langle U_c \rangle(n),
\]

along the \( n \) direction, orthogonally to the SAS and passing through the centre of the atom \( i \) (Fig. 2b). For the 12-6 Lennard–Jones potential, it follows that \( U_{vdw}(n) = \sum_{k=1}^{N_n} 4\varepsilon_{ij} \left( \frac{r_k}{\sigma_k} \right)^{12} - \left( \frac{r_k}{\sigma_k} \right)^6 \), with \( \varepsilon_{ij}, \sigma_k \) and \( r_k \) denoting the depth of the potential well, the distance at which such potential becomes zero and the Euclidean distance between the generic line point with coordinate \( n \) and the centre of \( k \)th nearest neighbour, respectively. For the Coulomb interactions, the average potential energy at a fixed temperature \( T \) between the \( N_n \) atoms and the water dipoles is \( \langle U_c \rangle(n) = -E \mu_w \Gamma(E \mu_w/k_BT) \), where \( E \), \( \mu_w \), \( k_B \) and \( \Gamma \) denote the electrical field strength, water dipole moment \((7.50 \times 10^{-30} \text{ C m})\) for the SPC/E model), the Boltzmann constant and the Langevin function \( \Gamma(x) = \coth(x) - 1/x \). The strength of the electrical field \( E \) can be readily computed following the law of electrostatics (see Methods). Knowing the effective potential \( U_{\text{eff}}(n) \) for the atom \( i \), a corresponding characteristic length \( \delta_i \) can be estimated within which the water molecules have reduced mobility. This length \( \delta_i \) is given by \( \delta_i = n_{i,2} - n_{i,1} \) where

---

**Figure 2 | The characteristic length of confinement \( \delta_i \).** (a) A local characteristic length \( \delta_i \) can be defined at any atom \( i \) (with non-vanishing SAS). (b) The contribution to the total potential energy of neighbors along a direction orthogonal to the SAS (line \( l \) with local coordinate \( n \)) is computed. (c) The thermal energy level provides a criterion to (locally) define the characteristic length \( \delta_i \), which typically varies along the whole SAS. (d) A characteristic length of confinement \( \delta_i \) for the whole structure can be defined by a weighted average of all \( \delta_i \). (e) The length of confinement is reported for a SiO\(_2\) nanopore (\( \delta_i \approx 0.33 \text{ nm} \)) and for a Fe\(_3\)O\(_4\) NP (\( \delta_i \approx 0.50 \text{ nm} \)). For SiO\(_2\), only the first water layer (with distance \( r_{w,1} \) from the pore axis) is located within the volume of influence. For Fe\(_3\)O\(_4\), both the first and the second water layers (with distances \( r_{w,1} \) and \( r_{w,2} \) from the particle centre, respectively) are found within the volume of influence (more cases are reported in the Supplementary Figs 1 and 2).
and $n_{1,2}$ are the two zeros of the equation $U_{\text{eff}}(n) + k_B T/4 = 0$ (Fig. 2c). Therefore, based on the definition of $\delta$, all the water molecules located within such a distance are significantly affected by the van der Walls and Coulomb interactions, whereas all the water molecules beyond the characteristic length $\delta$ can escape the potential well generated by the solid wall. Here $k_B T/4$ is half the kinetic energy per independent degree of freedom according to the equipartition of energy (see Methods). By proper averaging over the surface, the mean characteristic length $\delta$ of the overall solid surface (Fig. 2d) can be derived as

$$\delta = \frac{\sum_{i=1}^{N} \delta_i S_{\text{loc},i}}{S_{\text{tot}}}, \quad (2)$$

with $S_{\text{loc},i}$ and $N$ being the specific (per atom) SAS for the atom $i$ and the total number of atoms, respectively. Note that the above formulation is general and applies to hydrophilic and hydrophobic surfaces, regardless of their electrostatic surface charge. Also, the characteristic length $\delta$ can be conveniently computed based on the geometry of the problem, Lennard–Jones force field parameters and the partial electrostatic charges using the script provided in the Supplementary Software 1.

In Fig. 2e, the water density profile within (a) a SiO$_2$ nanopore and (b) around a single Fe$_3$O$_4$ NP is shown, where peaks denote the typical water layers nearby a solid wall at the nanoscale$^{2,39}$. It is noteworthy that despite the great difference in the potential strength between SiO$_2$ and Fe$_3$O$_4$ ($\min(U_{\text{eff},2})/\min(U_{\text{eff},1}) \approx 2.7$), the corresponding difference in terms of characteristic lengths is much more moderate ($\delta_2/\delta_1 \approx 1.5$). From the density profiles, Fe$_3$O$_4$ clearly induces a stronger perturbation in the nearby water molecules' distribution. However, except for a first thin water layer strongly adsorbed to the NP surface (and accounted by $\delta_2 > \delta_1$), the amplitude of these perturbations rapidly decays further away and becomes comparable in the remaining confined volume for both cases. Although, there is a significant difference in the potential minimum between green fluorescence protein and (5,5) chirality CNT ($\min(U_{\text{eff},2})/\min(U_{\text{eff},1}) \approx 1.5$), the difference between the two characteristic lengths is negligible. The above observations suggest that geometrical parameters could more significantly affect $D$ as compared to energetic parameters.

**Scaling law.** Since water mobility is impaired mostly in a thin layer next to the liquid–solid interface with thickness $\delta$, it is reasonable to assume that the observed variation in the self-diffusion coefficient $D$ is mainly associated with the altered mobility of the water molecules within such a layer and the corresponding volume (volume of influence—Fig. 2d). In addition, it has been already observed that the self-diffusion coefficient $D$ reduces as the ratio between the total interfacial area and the total volume occupied by water increases. On the basis of such an evidence, a scaling parameter $\theta$ can be introduced as the ratio between the total water volume of influence ($V_{\text{in}}$) and the total volume accessible to the water molecules ($V_w$); thus,

$$\theta = \frac{V_{\text{in}}}{V_w} \approx \frac{\sum_{p} S_{\text{tot}}^{(p)} \delta^{(p)}}{V_w}. \quad (3)$$

This parameter $\theta$ varies from 0 (bulk water case) to 1 (totally confined water). The volume of influence ($V_{\text{in}}$) is the volume of water that feels the van der Walls and Coulomb interactions and is therefore influenced by the presence of solid walls. This volume is readily given by $V_{\text{in}} = \sum_{p} S_{\text{tot}}^{(p)} \delta^{(p)}$, where $S_{\text{tot}}^{(p)}$ and $\delta^{(p)}$ represent the total SAS and characteristic length of the $p$th particle, respectively. As detailed in the Methods, possible overlap of the volumes of influence due to several particles/pores (for example, several NPs loaded within a SiO$_2$ nanopore) can be easily taken into account by the continuum percolation theory (CPT), and a more accurate estimate of $V_{\text{in}}$ may include the effect of particle curvature.

Assuming $\theta$ as the sole, independent variable for $D$, all computed values relax within a narrow band around a linear curve (Fig. 3) that can be readily described by the relationship

$$D(\theta) = D_0 \left\{ 1 + \left[ \frac{D_C}{D_0} - 1 \right] \theta \right\}, \quad (4)$$

where $D_0$ is the self-diffusion coefficient of bulk water, while $D_C$ the self-diffusion coefficient of totally confined water. Remarkably, Fig. 3 presents data from 58 different cases analysed in this work as well as data available in the published literature. Here despite the variety of the considered configurations, particles and sources of the results, a simple law is found to be sufficiently accurate to describe the phenomenon under study, thus confirming that $\theta$ is indeed an important controlling parameter under very diverse conditions and geometrical configurations. To have a more explicit formulation of equation (4), details about the evaluation of $D_C$ are provided in the section below.

**Thermodynamic insights.** Nanoconfined water shares some features with supercooled ordinary water in that it may not crystallize on cooling below the melting temperature of $T_M \approx 273.15$ K (refs 1,43). Within the thin $\delta$ layer of water molecules next to a solid surface, the thermodynamic state depends on the characteristic confinement length scale$^{44}$. In particular, the specific heat capacity $c_p$ of nanoconfined water has been experimentally measured in narrow SiO$_2$ nanopenes and its variation with the temperature $T$ is plotted in Fig. 4a for a pore diameter of 1.7 nm (ref. 45). Using these experimental data, the energy variation associated with the transition from bulk water to the nanoscale can be determined ($\Delta U \approx 20$ mJ m$^{-2}$) and is therefore influenced by the presence of solid walls. This volume is readily given by $V_{\text{in}} = \sum_{p} S_{\text{tot}}^{(p)} \delta^{(p)}$, where $S_{\text{tot}}^{(p)}$ and $\delta^{(p)}$ represent the total SAS and characteristic length of the $p$th particle, respectively. As detailed in the Methods, possible overlap of the volumes of influence due to several particles/pores (for example, several NPs loaded within a SiO$_2$ nanopore) can be easily taken into account by the continuum percolation theory (CPT), and a more accurate estimate of $V_{\text{in}}$ may include the effect of particle curvature.

Assuming $\theta$ as the sole, independent variable for $D$, all computed values relax within a narrow band around a linear curve (Fig. 3) that can be readily described by the relationship

$$D(\theta) = D_0 \left\{ 1 + \left[ \frac{D_C}{D_0} - 1 \right] \theta \right\}, \quad (4)$$

where $D_0$ is the self-diffusion coefficient of bulk water, while $D_C$ the self-diffusion coefficient of totally confined water. Remarkably, Fig. 3 presents data from 58 different cases analysed in this work as well as data available in the published literature. Here despite the variety of the considered configurations, particles and sources of the results, a simple law is found to be sufficiently accurate to describe the phenomenon under study, thus confirming that $\theta$ is indeed an important controlling parameter under very diverse conditions and geometrical configurations. To have a more explicit formulation of equation (4), details about the evaluation of $D_C$ are provided in the section below.

**Thermodynamic insights.** Nanoconfined water shares some features with supercooled ordinary water in that it may not crystallize on cooling below the melting temperature of $T_M \approx 273.15$ K (refs 1,43). Within the thin $\delta$ layer of water molecules next to a solid surface, the thermodynamic state depends on the characteristic confinement length scale$^{44}$. In particular, the specific heat capacity $c_p$ of nanoconfined water has been experimentally measured in narrow SiO$_2$ nanopenes and its variation with the temperature $T$ is plotted in Fig. 4a for a pore diameter of 1.7 nm (ref. 45). Using these experimental data, the energy variation associated with the transition from bulk water to the nanoscale can be determined ($\Delta U \approx 20$ mJ m$^{-2}$). 

![Figure 3](image-url) **Figure 3 | Scaling behaviour of the water diffusion coefficient $D$.** The self-diffusion coefficient of water $D$ has been calculated for over 60 different cases including spherical NPs in water, water within nanopenes with and without spherical NPs, proteins and CNTs in water. Fifty-eight cases are the results of MD simulations performed in this work, under isothermal conditions. Results from the literature are also provided, for which the scaling variable $\theta$ was computed as from the Supplementary Discussion. The solid and the dashed lines represent equation (4) for $D_C = 0$ and $D_C = 0.39 \times 10^{-6}$ m$^2$ s$^{-1}$, respectively. Equation (4) accurately recovers simulation and literature results with high coefficient of determination ($R^2 > 0.90$). The uncertainties on the value of $D$ (vertical bars) refer to the fitting of the mean square displacement, whereas the uncertainties on the value of $\theta$ (horizontal bars) refer to the estimate of the total volume accessible to water molecules $V_w$ (see Methods).
to confined water can be readily computed as
\[ \Delta h = -\int_{T}^{\infty} c_0 dT = f(T), \]
with \( f(T_0) = 0 \) at the bulk water temperature \( T_0 = 300 \) K. From this, the inverse function \( T = f^{-1}(\Delta h) \) can be derived as plotted in Fig. 4b. The energy variation associated with water nanoconfinement can also be written as \( \Delta h = h_C - h_B \leq 0 \), where \( h_B \) and \( h_C \) are the energy of bulk and confined water, respectively. Since the confined region is typically limited to 1–2 layers of water molecules (for all the considered structures, \( \delta < 0.6 \) nm), it can be assumed that \( h \approx -\varepsilon \), which is the minimum of the effective potential \( (U_{\text{eff}}) \) generated by the solid surface. The function \( f^{-1} \) can be used to compute the supercooled temperature of nanoconfined water corresponding to the energy variation \( -\varepsilon \), that is, to say \( T = f^{-1}(-\varepsilon) \). In the work by Chen et al., the diffusion coefficient of water molecules under strong nanoconfinement (that is, within SiO2 pores with diameter of 1.4–1.8 nm) is reported as a function of the temperature. From the latter experimental data, the diffusion coefficient of totally confined water \( D_C \) can be readily expressed in the form \( D_C = D_B g(T) \) (Fig. 4c). Therefore, by combining the two sets of experimental data and knowing the value of \( \varepsilon \), the diffusion coefficient of totally confined water \( D_C \) can be computed as \( D_C/D_B = g(T)/g'(f^{-1}(-\varepsilon)) = g'/g(-\varepsilon) \). The ratio \( D_C/D_B \) is plotted in Fig. 4d for the different 58 cases analysed here. For the iron oxide NPs and CNTs, which are characterized by a fairly strong effective potential (large \( \varepsilon \)), \( D_C \approx 0 \). As the strength of the effective potential reduces, the value for the diffusion coefficient of totally confined water increases. However, even for the SiO2 NPs and nanoropes, and for the proteins that are characterized by lower \( \varepsilon \), in our computations \( D_C \) is at most 15% of \( D_B \). We stress that the function \( g(\Delta h) \) is a property of water, and here we have chosen to estimate it on the basis of measurements in SiO2 nanoropes only, because such experiments are among the very few that are well documented in literature.

In general, the volume of water can be partitioned into bulk (B) and confined (C). Invoking the mixing rule, the average diffusivity \( D \) of the system can be presented as
\[ D = \left( 1 - \frac{N_C}{N_B + N_C} \right) D_B + \frac{N_C}{N_B + N_C} D_C, \]
where \( N_C \) and \( N_B \) are the number of water molecules in the confined and bulk regions, respectively. Considering that \( N_C = \rho_C V_C/m_w \), with \( \rho_C \) being the water (mean) density in the adsorbed region and \( m_w \) being the mass of one water molecule, it follows:
\[ D(\theta) = D_B \left( 1 + \frac{D_C}{D_B} \right) - \frac{\rho_C \theta}{\rho_C \theta + \rho_B (1 - \theta) \left( \frac{D_C}{D_B} \right) + 1 - \theta \right). \]

This implies that the average diffusivity \( D \) depends in general on a geometrical parameter \( \theta \) and an energetic parameter \( \varepsilon \). However, the following approximation \( \rho_C \varepsilon / (\rho_C \varepsilon + \rho_B (1 - \theta)) \approx \theta \) can be safely made for the full range of \( \theta \) (see Supplementary Fig. 4 and Supplementary Discussion). Therefore, equation (6) degenerates into equation (4) demonstrating that the diffusion of nanoconfined water can be interpreted invoking the thermodynamics of supercooled water. Moreover, based on the above discussion on \( D_C \) (see Fig. 4d), for a large variety of nanoconfined systems, the simplifying assumption \( D_C/D_B \approx 0 \) can be safely made. In such cases, the much simpler law \( D(\theta) = D_B (1 - \theta) \) is readily derived showing the direct linear dependence of the water diffusion coefficient on the sole scaling parameter \( \theta \). Note that no empirical factor is needed to derive \( D(\theta) \), with the latter law matching the values of the 58 MD simulations as well as 13 further configurations from the literature with a quite good coefficient of determination \( (R^2 = 0.95, \text{solid line in Fig. 3}) \). The dashed line in Fig. 3 represents, instead, equation (4) with \( D_C/D_B = 0.15 \), corresponding to the largest value of \( D_C \) only observed in a few simulated cases (Fig. 4d).

**Discussion**

It has been shown that the relaxometric properties of contrast agents for MR imaging can be enhanced by proper modulation of the water molecule dynamics \(^{26}\). Recently, Decuzzi and collaborators\(^{23,24}\) have shown that the geometrical confinement of Gd\(^{3+}\)-based MRI contrast agents and SPIOs within mesoporous structures can increase by several folds the longitudinal and transversal relaxivities, respectively, of the original agents. Here it is shown that the scaling law \( D(\theta) \) can
be effectively used to predict the enhancement in transversal relaxivity exhibited by SPIOs confined in mesoporous silicon structures. Referring to Fig. 5a, discoidal mesoporous silicon particles (SiMPs) of 1,000 nm in diameter and with an average pore size of 40 nm are synthesized by a combination of optical lithographic techniques and electrochemical etching. These particles are exposed to a concentrated solution of SPIOs, which are loaded within the pores by capillary suction and form clusters of controlled size. As schematically shown in Fig. 5c, the SPIOs are distributed more or less uniformly within the pores and across the porous matrix of the silicon particles. The black and red spots, respectively, in the TEM and EDX images identify the SPIO clusters within the mesoporous silicon matrix. In these experiments, commercially available SPIOs (Sigma-Aldrich) are considered, coated with a thin layer of polyethylene glycol to facilitate their dispersion in water, and presenting an average core diameter of 5.13 ± 1.07 nm, as derived by TEM analysis. In bulk water the transversal relaxivity of the unconfined SPIOs has been measured to be \( r_2 = 107 \pm 24 \text{ mM}^{-1} \text{s}^{-1} \), whereas on geometrical confinement within the SiMPs, the relaxivity rises up to \( r_2 = 270 \pm 73 \text{ mM}^{-1} \text{s}^{-1} \).

From the theory on the MR relaxation of iron oxide NPs, the transversal relaxivity \( r_2 \) of the SPIOs dispersed in an aqueous solution can be estimated as \[^{29,32,47}\]

\[
r_2 = \left( \frac{1}{T_2} - \frac{1}{T_{2,w}} \right) \times \frac{1}{M_{Fe}} \times \frac{v}{D},
\]

where \( T_2 \) and \( T_{2,w} \) are the transversal relaxation times for the solution with contrast agents and bulk water (\( = 2,800 \text{ ms} \)), respectively; \( M_{Fe} \) is the iron concentration (mM) in the solution; \( v \) is the volume fraction of the SPIOs; and \( D \) is the diffusion of the water molecules surrounding the SPIOs. Details on equation (7) are provided in the Supplementary Discussion.

For a fixed iron concentration \( M_{Fe} \), the solution, the enhancement in transversal relaxivity is directly related to the ratio \( E_{n} = (v/D)/(v_{2g}/D_{2w}) \), where the quantity \( v/D \) has to be estimated for confined SPIOs and \( v_{2g}/D_{2w} \) for the free SPIOs dispersed in bulk water. Since the distribution of the SPIOs within the SiMP is not uniform, the diffusion coefficient \( D \) and the local SPIO volume fraction \( v \) are expected to vary within the porous matrix. The local enhancement in relaxivity \( E_{n} \) is plotted in Fig. 5d. Areas are shown with mild and high enhancement, up to 20-fold, corresponding to different levels of SPIO loading and clustering, and therefore different levels of water confinement. By integrating over the whole silicon particle, an average relaxivity enhancement \( E_{n} \) can be computed as being \( \sim 2.7 \), which is in excellent agreement with the experimental value of \( \sim 2.52 \) (see Methods for details). Note that the proposed law can be used in several other fields to analyse different cases of water confinement.

In summary, it has been shown that the self-diffusion coefficient of nanoconfined water can be described by a unique dimensionless parameter \( \theta \), representing the ratio between the confined and total water volumes. The coefficient \( D \) scales linearly with \( \theta \) and can be readily estimated, knowing the bulk \( D_{20} \) and totally confined \( D_{2c} \) diffusion of water. This has been validated on the basis of almost 60 different cases and 5 different geometrical configurations, including the analysis of the water molecule dynamics within nanopores and CNTs, around NPs and proteins. The coefficient of diffusion for confined \( D_{2c} \) water is quantified on the basis of the thermodynamics of supercooled water. As an example, the scaling relation has been shown to accurately predict the enhancement in magnetic resonance relaxivity of iron oxide NPs confined into mesoporous silicon structures.

The proposed approach may be used to interpret experimental data collected in different scientific disciplines on the dynamics of water molecules under confined conditions and to rationally design nanostructures for modulating the diffusion of water. This is of relevance in nanomedicine, nanotechnology as well as in more traditional engineering fields such as heat transport, fluid dynamics and energy storage.

**Methods**

**MD simulations.** Atomic coordinates of FeO\(_4\) crystals are generated from FeO\(_4\) crystals\(^{36}\), whereas SiO\(_2\) crystals are considered in the case of nanopores and SiO\(_2\) NPs (Supplementary Figs 5–8)\(^{37}\). Crystal structures of proteins are taken from the Protein Data Bank (http://www.rcsb.org; Supplementary Figs 9 and 10). CNTs are generated by means of the Vjual Molecular Dynamics software (Supplementary Fig. 11)\(^{38}\). The SPC/E model\(^{39}\) is used for water molecules, which is known to accurately predict some of the properties of water relevant for this study at room temperature\(^{37}\). However, it is also worth noticing that the SPC/E model does not accurately predict some other properties of water. For instance, shear viscosity or thermal conductivity were found to be off by more than 50% at room temperature\(^{37}\). Bonded interactions of SiO\(_2\) and FeO\(_4\) are treated by means of harmonic stretching and angle potentials\(^{31}\). Van der Waals interactions are
modelled by a 12-6 Lennard–Jones potential; partial charge interactions between solid surfaces and water are modelled by a Coulomb potential (Supplementary Tables S1.4 and S1.5). Non-zero partial charges are only assigned to atoms on the surface of nanopore or NP, which belong to silanol and FeOH groups, whereas all other atoms (bulk of SiO₂ and Fe₂O₃) are considered as neutral. Simulations are carried out with a leap-frog algorithm (time step: Δτ = 0.5 fs), and periodic boundary conditions are applied along the three Cartesian directions. After equilibration of Np nanoparticles or nanotube setups, the two subsystems (solid crystals and water) are initialized at 300 K (Maxwellian distribution of velocities) and fully coupled to a Nosé–Hoover thermostat⁵⁷,⁵⁸ (at 300 K and time constant τ = 0.2 ps) for 50 ps, until the energies of the system relax to a steady state. During the latter preliminary calculation, one thermostat for each subsystem is adopted. Afterwards, Nosé–Hoover thermostats (at 300 K) are maintained attached to solid crystals only, whereas the simulation is continued up to 2 ns. In the case of the proteins, the MD protocol is slightly changed to improve the solvation and ions are added when needed for achieving the neutrality of the system, which is then equilibrated in two steps: 100 ps in canonical ensemble (fixed number N of particles, volume V and temperature T - NVT) at 300 K (initialization with Maxwellian distribution of velocities, Berendsen thermostats separately attached to proteins and water, τ = 0.1 ps; Parrinello–Rahman pressostat⁶⁰ applied to the whole system, τ = 2 ps). During the equilibration, all bonds in the proteins are kept rigid using the LINCOS (Linear Constraint Solver) algorithm⁵¹. Finally, a Nosé–Hoover thermostat (300 K, τ = 0.2 ps) is attached to protein’s atoms and the simulation is continued for 1 ns.

To illustrate the above issue is encountered in the scaling parameter for water self-diffusion coefficient are reported in Supplementary Discussion and Supplementary Figs 31 and 32. In equation (3) (the particle curvature is neglected; thus, this is accurate in the limit δ⁰ ≪ δ⁰, with δ⁰ being a representative radius of curvature of the particle. If the latter approximation is not properly fulfilled, a more accurate estimation of the numerator at the right-hand side of equation (3) can be easily adopted (see also a few examples in the Supplementary Discussion).

Clearly, in cases of strong confinement (and high values of θ) with the presence of several particles (for example, the reported studies where a number of spherical NPs are loaded within cylindrical nanoropes), a partial overlap of the volumes of influence becomes more and more probable. However, we notice that volumes of influence due to different particles are not additive. As a result, the quantity θ computed by equation (3) is only apparent, with the effective fraction of the volume of influence being smaller than θ. The above issue is encountered in the framework of CPT. To this respect, a classical result of CPT, under the assumption of randomly placed volumes suggests that, to properly recover the effective fraction, the apparent volume fraction should be corrected as: 1 − exp − θ. Hence, we suggest that the above correction applies in the presence of overlap of volumes of influence (for example, several particles within the computational box).

The volume \( V_{\text{C}} \) for fully hydrated simple geometries, \( V_{\text{C}} \) can be computed by considering the nominal size of a particle/pore (see the discussion below about relaxation enhancement). However, in general, the volume \( V_{\text{C}} \) in equation (3) can be defined as:

\[
V_{\text{C}} = V_{\text{pore}} + V_{\text{surf}}.
\]

In equation (3) the particle curvature is neglected; thus, this is accurate in the limit \( \delta^0 \ll \delta^0 \), with \( \delta^0 \) being a representative radius of curvature of the particle. If the latter approximation is not properly fulfilled, a more accurate estimation of the numerator at the right-hand side of equation (3) can be easily adopted (see also a few examples in the Supplementary Discussion).

Clearly, in cases of strong confinement (and high values of θ) with the presence of several particles (for example, the reported studies where a number of spherical NPs are loaded within cylindrical nanoropes), a partial overlap of the volumes of influence becomes more and more probable. However, we notice that volumes of influence due to different particles are not additive. As a result, the quantity θ computed by equation (3) is only apparent, with the effective fraction of the volume of influence being smaller than θ. The above issue is encountered in the framework of CPT. To this respect, a classical result of CPT, under the assumption of randomly placed volumes suggests that, to properly recover the effective fraction, the apparent volume fraction should be corrected as: 1 − exp − θ. Hence, we suggest that the above correction applies in the presence of overlap of volumes of influence (for example, several particles within the computational box).
Characterization of nanoconstructs and NPs. Details on the fabrication and characterization of the discoidal SiMPs and the SPIOs are provided in the Supplementary Methods and Supplementary Figs 33 and 34, together with the protocols for the loading of SPIOs into SiMPs.

Relaxivity measurements. In vitro relaxation times were measured in a Bruker Minispec (mq 60) bench-top relaxometer operating at 60 MHz and 37 °C. The transverse ($T_2$) relaxation times were measured using the Carr–Purcell–Meiboom–Gill sequence.

Analysis of relaxivity enhancement. The function $f_{\text{SPIO}}(X,Y)$ of the two spatial coordinates $X$ and $Y$ is built from the EDX image for iron (Fig. 5c) and denotes the position of the centre of a generic pixel. Let $N_{\text{SPIO}}$ be the average number of SPIOs within a single SiMP. Hence, a surface density function at a pixel scale for the SPIOs can be written as

$$\rho_{\text{SPIO}} = \frac{\int_{A_{\text{pore}}} f_{\text{SPIO}}(X,Y)dXdY}{A_{\text{pore}}},$$

where $A_{\text{pore}}$ and $A_{\text{real}}$ are the surface area of a single pixel and the surface area of a SiMP, respectively. The function $\rho_{\text{SPIO}}$ has been reported in the (left) bottom part of Supplementary Fig. 35. The total number of SPIOs within the SiMP pores is computed as $N_{\text{SPIO}} = \sum f_{\text{SPIO}}(X,Y)$. Hence, the water volume near the SPIOs (for the latter pore) $V_{\text{w}}$ can be estimated as $V_{\text{w}} = A_{\text{pore}} c_{\text{fill}} - V_{\text{SiMP}} N_{\text{SPIO}}$, where $V_{\text{SiMP}}$ is the SiMP height, while $0 \leq c_{\text{fill}} \leq 1$ indicates the fraction of the SiMP pore that has been effectively occupied by SPIOs. Clearly, for homogeneously distributed SPIOs within the pore, $c_{\text{fill}} = 1$. For the considered representative pore, an estimate of the average scaling parameter $\theta$ can be obtained as: $\theta = 1 - \exp(-\theta')$ with

$$\theta' = \sum_{A_{\text{pore}}} \frac{N_{\text{SPIO}} \cdot \delta_{\text{SPIO}} + \tilde{D} \cdot \bar{B} \cdot \bar{d}_{\text{SIO}}}{V_{\text{w}}},$$

where $\tilde{D}$ is the average diameter of the pores. Finally, a map of the scaling parameter $\theta = \theta(X,Y)$ is derived by the map $\rho_{\text{SPIO}}$ as $\theta(X,Y) = C \rho_{\text{SPIO}}(X,Y)$, where the constant $C$ is determined by imposing

$$\frac{1}{A_{\text{pore}}} \int_0 A_{\text{pore}} \theta(X,Y)dXdY = \theta,$$

hence

$$C = \frac{\theta_A}{\int_0 A_{\text{pore}} \rho_{\text{SPIO}}(X,Y)dXdY}.$$

On the estimate of the scaling parameter map $\theta = \theta(X,Y)$, the computation of the corresponding map for the diffusion coefficient $D = D(X,Y)$ is straightforwardly achieved by adopting the law suggested in this work.

The above procedure is slightly sensitive to the choice of the representative pore. However, from our computations no significant changes in the final result (map of $\theta = \theta(X,Y)$) were experienced by making difference choices. In Supplementary Fig. 36, we report both the map of the scaling parameter $\theta = \theta(X,Y)$ and the corresponding $D = D(X,Y)$ at different pore filling.

Let us consider two contrast agents with the same iron molality $M_{\text{Fe}}$. Let the first one be based on SPIOs homogeneously dispersed in bulk water, while the second one adopts the same SPIOs (nanocoated) within SiMPs. Given the definition of $r_3$ (Supplementary equation (9)), we can define a relaxivity enhancement as follows:

$$E_n = \frac{r_3}{(r_2)_1} = \frac{\tau_2}{M_{\text{Fe}}} \left( \frac{1}{\tau_y} - \frac{1}{\tau_x} \right)_{21},$$

Since $1/T_2 \gg 1/T_{\text{M}_n}$.

Finally, using the outer sphere theory (see Supplementary Discussion), the enhancement can be recast as

$$E_n \approx \frac{1}{\tau_x} - \frac{1}{\tau_y} = \frac{1}{\tau_x} \left( \frac{D_1}{D_1 + v_1} \frac{V_{\text{SPIO}}}{V_{\text{w}}} \frac{v_1}{D_1 + v_1} \right).$$

Consistently with the above procedure, we aim at estimating the map $E_n(X,Y)$:

$$E_n \approx \frac{D_1}{v_1} \frac{v_1}{D_1 + v_1} \frac{V_{\text{SPIO}}}{V_{\text{w}}},$$

and

$$E_n = \frac{N_{\text{SPIO}} \cdot \rho_{\text{SPIO}}(X,Y) dXdY}{A_{\text{real}}},$$

In Fig. 5d we report the function $E_n(X,Y)$ corresponding to the SiMP particle of Fig. 5c. Finally, the average enhancement due to the entire SiMP can be estimated as

$$E_n = \frac{\int_{A_{\text{real}}} E_n(X,Y) dXdY}{A_{\text{real}}},$$

where $f_{\text{SPIO}}(X,Y)$ is the following distribution function

$$f_{\text{SPIO}}(X,Y) = \frac{\rho_{\text{SPIO}}(X,Y)}{A_{\text{real}}} dXdY.$$
27. Key, J. ARTICLE NATURE COMMUNICATIONS | DOI: 10.1038/ncomms4565

41. Lee, B. & Richards, F. M. The interpretation of protein structures: estimation of

40. Eisenhaber, F., Lijnzaad, P., Argos, P., Sander, C. & Scharf, M. The double cubic

14. Murshed, S., Leong, K. & Yang, C. Thermophysical and electrokinetic

30. Caravan, P. Strategies for increasing the sensitivity of gadolinium based MRI

34. Schuler, L. D., Daura, X. & van Gunsteren, W. F. An improved GROMOS96

37. van der Spoel, D., van Maaren, P. J. & Berendsen, H. J. A systematic study of

17. Tait, M. J., Saadoun, S., Bell, B. A. & Papadopoulos, M. C. Water movements in

15. Gates, B. D. ARTICLE NATURE COMMUNICATIONS | DOI: 10.1038/ncomms4565

28. Briones, O., Wolf, H., Wiseman, J. C., Trusko, G. I., Schuerch, T. & Goetz, A. A.

16, 171–176 (2004).

17. Tait, M. J., Saadoun, S., Bell, B. A. & Papadopoulos, M. C. Water movements in

16, 171–176 (2004).

17. Tait, M. J., Saadoun, S., Bell, B. A. & Papadopoulos, M. C. Water movements in

16, 171–176 (2004).

17. Tait, M. J., Saadoun, S., Bell, B. A. & Papadopoulos, M. C. Water movements in

16, 171–176 (2004).

17. Tait, M. J., Saadoun, S., Bell, B. A. & Papadopoulos, M. C. Water movements in

16, 171–176 (2004).

17. Tait, M. J., Saadoun, S., Bell, B. A. & Papadopoulos, M. C. Water movements in

16, 171–176 (2004).

17. Tait, M. J., Saadoun, S., Bell, B. A. & Papadopoulos, M. C. Water movements in

16, 171–176 (2004).

17. Tait, M. J., Saadoun, S., Bell, B. A. & Papadopoulos, M. C. Water movements in

16, 171–176 (2004).

17. Tait, M. J., Saadoun, S., Bell, B. A. & Papadopoulos, M. C. Water movements in

16, 171–176 (2004).
Author contributions
E.C. and M.F. designed the computational plans. M.F. performed all the MD simulations. P.A. and E.C. conceived the idea of the suggested scaling. P.D. conceived the idea of the study, and with P.A. designed and coordinated the project. All the authors interpreted and discussed the computational and experimental results and wrote the manuscript.

Additional information
Supplementary Information accompanies this paper at http://www.nature.com/naturecommunications

Competing financial interests: The authors declare no competing financial interests.

Reprints and permission information is available online at http://npg.nature.com/reprintsandpermissions/

How to cite this article: Chiavazzo, E. et al. Scaling behaviour for the water transport in nanoconfined geometries. Nat. Commun. 5:3565 doi: 10.1038/ncomms4565 (2014).

This work is licensed under a Creative Commons Attribution 3.0 Unported License. The images or other third party material in this article are included in the article’s Creative Commons license, unless indicated otherwise in the credit line; if the material is not included under the Creative Commons license, users will need to obtain permission from the license holder to reproduce the material.
To view a copy of this license, visit http://creativecommons.org/licenses/by/3.0/