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Lubrication at physiological pressures by poly(zwitterionic) brushes.

Meng Chen^{a,1}, Wuge H. Briscoe^{a,2}, Steven P. Armes^b and Jacob Klein^{a,c}

^a – Physical and Theoretical Chemistry Laboratory, University of Oxford, Oxford OX1 3QZ, UK

^b – Department of Chemistry, University of Sheffield, Sheffield S3 7HF, UK

^c - Weizmann Institute, Rehovot 76100, Israel

¹ – Present address: Procter & Gamble (Beijing) Technical Centre, Floor 5-8 Tongfang Building, 18 Shuangqing Road, Haidian District, Beijing 100084, P.R.China

² – Present address: School of Chemistry, University of Bristol, Bristol BS8 1TS, U.K.

Abstract: The very low sliding friction at natural synovial joints, with friction coefficients $\mu < 0.002$ at pressures up to 5 MPa or more, has not to date been attained in any man-made joints or between model surfaces in aqueous environments. We find that surfaces bearing grafted-from polyelectrolytic brushes in water can have μ values down to 0.0004 at pressures up to 7.5 MPa. This extreme lubrication is attributed primarily to the strong hydration of the phosphocholine-like monomers comprising the robustly-attached brushes, and may have relevance to a wide range of man-made aqueous lubrication situations.

Rubbing of opposing bones during the articulation of mammalian joints is mediated by layers of articular cartilage coating their surfaces, which provide uniquely efficient lubrication as they slide past each other (1, 2). The associated very low friction at the high pressures of human joints such as hips or knees, with friction coefficients $\mu < 0.002$, has not to date been emulated in man-made systems. Model studies (3-7) between smooth sliding surfaces bearing neutral or charged polymer brushes demonstrated sliding friction coefficients as low as $\mu < 0.001$, values lower than with any other boundary lubricant system. As noted(8, 9), in earlier studies with polymer brushes(3-6) the friction increases sharply at mean pressures $P > \text{ca. } 0.3 \text{ MPa}$, which is far below the pressures, of 5 MPa or more, where low friction persists in nature. In the present work we sought to overcome the limitations of these earlier studies(3-6). We use polymer brushes, which make good boundary lubricants as they do not bridge the intersurface gap, that are strongly attached to each surface to resist being sheared off; and that are highly hydrated, to utilize the very efficient lubrication by hydration sheaths observed earlier(10, 11).

Brushes of the polymer poly[2- (methacryloyloxy)ethyl phosphorylcholine], pMPC, were grown from the surfaces of macroinitiator-coated mica sheets pre-mounted onto cylindrical lenses for surface force balance (SFB) measurements(12-section A, 13). Following calibration in dry air, control measurements of the normal forces $F_n(D)$ and shear forces $F_s(D, v_s)$ between the macroinitiator-coated mica surfaces were carried out(12-section B, 14) as a function of their absolute separation D and their sliding velocity v_s . Measurements were carried out both in polymer-free water, and following incubation in a 0.3% w/v pMPC homopolymer solution in order to compare with the subsequent pMPC brush profiles. These controls, shown in fig. 1, reveal the high friction associated with the macroinitiator alone (figs. 1B and 1C), prior to growing of the polymer layers. They also show, importantly, that the pMPC homopolymer does not adsorb onto the macroinitiator-bearing mica (fig. 1A), confirming that surface growth of the polymer results in true brush formation. Following the grafting-from growth of the polymer brushes, $F_n(D)$ and $F_s(D, v_s)$ profiles between the brush layers were carried out in water and in aqueous NaNO_3 solutions up to physiological salt concentrations.

Figure 2 shows typical normal-force vs. surface separation profiles between pMPC brush-bearing mica surfaces in the standard crossed cylinder SFB configuration, in pure water and at salt concentrations ca. 0.01M and 0.1M NaNO₃ (the pMPC brush and monomer structure is inset to fig. 2A). Some contraction of the pMPC brushes is seen in the salt solutions relative to pure water. The highest normal loads F_n applied are some 2 or more orders of magnitude higher than in earlier brush studies(4, 5) using the SFB. This leads to substantial flattening at the contact region, as indicated in the photo of the interference fringes, fig. 2B (and schematically in fig. 2C), from which the contact area A between the surfaces is measured directly (the mean pressures P across the flattened contact area are given by $P = F_n/A$). Comparison with the control profiles from fig. 1A in the absence of polymer (dotted and broken curves in fig. 2A) reveals the extension of the unperturbed brushes from the macroinitiator layer, while fits to the force profiles provide more detailed information on the brush characteristics(12-section C, 13). We note the similarity of the profiles both on approach and separation of the surfaces (characteristic of brush interactions), and particularly their insensitivity to repeated shear up to the highest compressions, revealing the robustness of the layers to friction and shear-off(15).

Characteristic traces of shear-(or frictional-)force F_s vs. time as two pMPC brushes slide past each other under different loads/compression-ratios (corresponding to different surface separations) and different salt concentrations, taken directly from the SFB, are shown in fig. 3. Traces both at low compressions (higher D values, fig. 3 left) and high compressions (lower D values, fig. 3 right) show that the shear forces remain very weak - within the noise level of the SFB - up to mean contact pressures of ca. 2 – 2.5 MPa, and then increase measurably with load up to the largest loads applied. Such traces are characteristic of all pMPC brushes and salt concentrations studied; the fact that the traces are unchanged in time indicates that there is no detectable wear of the layers over the range of parameters studied. Shear force results are summarized in fig. 4 and in Table 1. These show that the friction coefficient μ – taken as the slope of the F_s vs F_n plot - is in the range of values $\mu \approx (1.5 \pm 1) \cdot 10^{-3}$ up to the highest mean contact pressures applied, $P \approx 7.5$ MPa (75 atmospheres). The values of μ , though remaining very low, are seen to increase slightly within this range as the salt concentration increases. The

variation of the shear or friction force with sliding velocity v_s is shown in fig. 4b, revealing a weak $F_s(v_s)$ dependence over 3 orders of magnitude in v_s .

Our findings show that brushes of pMPC, a polyzwitterion whose monomers carry the phosphorylcholine group (as in naturally-occurring phospholipid headgroups), can reduce friction to levels previously seen only in natural joints (μ of order 0.001 at pressures of 5 MPa or more). Earlier studies(4, 5) between polymer-brush-coated surfaces showed similarly low friction coefficients, but only at very much lower pressures. At higher pressures, the coefficient of friction became large, either due to entanglement or vitrification of the brushes(4), or as a result of the increasing frictional shear at these pressures removing the relatively-weakly-attached charged brushes from the surface(5). What is the mechanism underlying the strikingly low friction in the present study?

Earlier studies with charged brushes attributed comparably low friction coefficients (at much lower pressures) to a combination of factors. At low to moderate pressures, interpenetration (and therefore entanglement) of the opposing brushes was suppressed by configurational entropy effects(4, 6, 16). At the higher compressions of the present study, such interpenetration during the sliding is attributed instead to a self-regulation mechanism within the interfacial region (6, 17). According to this, the mutual interpenetration zone of the sliding brushes, where the viscous dissipation leading to frictional drag occurs, has a thickness δ . This thickness varies so that the relaxation rate of the polymer moieties within it equals the shear-rate within the zone, that is, $(1/\tau(\delta)) \approx (v_s/\delta)$. Such self-regulation can readily be seen to lead to a weak dependence of friction on sliding velocity v_s , which is in line with the observed data at high loads, fig. 4B, and a similar variation has been seen earlier for friction between sliding, highly compressed brushes(17). Qualitatively, this occurs because at higher sliding velocities the extent of brush interpenetration decreases, so that the overall frictional drag varies more weakly with increasing v_s than if the interpenetration zone remained at constant thickness(6, 17). At elevated pressures lubrication by charged brushes was previously attributed(5) to counterion osmotic pressure, together with the lubricating action of hydration layers surrounding the charged monomers. In the present study, the overall-neutral zwitterionic chains have no

counterions associated with them so that osmotic pressure due to trapped counterions cannot be playing a role. The effect of any counterions associated with the residual charge of the underlying macroinitiator-coated mica is negligible. The primary mechanism underlying the low friction observed must therefore be attributed almost exclusively to the high level of hydration of the zwitterionic phosphorylcholine (PC) groups on the monomers. These are known to bind around 15 – 25 or more water molecules per monomer (depending on the method of measurement(18-23)). Similar strongly-bound hydration layers about such phosphorylcholine-coated biomaterials are also responsible for repelling proteins from their surfaces(22, 24).

Water molecules in hydration layers have been shown to act as very efficient lubricants in the case of hydrated ions trapped between charged surfaces(10). This results from their being tenaciously attached, on a time-average, to the enclosed ionic charges, so that the resistance to dehydration leads to their ability to support a large pressure. At the same time, the hydration-water molecules are able to rapidly exchange with other hydration or free water molecules(10, 25), and so to behave fluidly when sheared at rates lower than these exchange (relaxation) rates. This, we believe, is also the origin of the low friction in the present system. Together with the stronger attachment of the grafted-from chains, it ensures the robust nature of the brushes when compared with the polyelectrolyte chains that were sheared off(15). We attribute the ability of the hydration shells about the MPC monomers to lubricate at much higher mean pressures, relative to those at which previously-studied polyelectrolyte brushes were removed by friction, to the higher and more tenacious hydration(18-21, 23) of their phosphorylcholine groups. The slight increase in the friction coefficient with increasing salt concentration, Table 1, may be attributed to some salting-out of the pMPC monomers at the higher salt concentration, as observed in other PC systems(26), leading to reduced hydration of the monomers and thus to less efficient lubrication. Such an effect would also explain the small contraction of the brush height at the higher salt concentrations, seen in Fig. 2.

It is appropriate to note the large reduction in wear of polymer/metal hip implants recently achieved(27) by growing a pMPC layer from the polyethylene acetabular surface. The

corresponding friction coefficient, $\mu \sim 0.1$, was not especially low. It is likely that this value of μ is dominated by a small number of high-friction asperity contacts between the sliding surfaces, which are far rougher than the mica substrate in our experiments, or by bridging of the pMPC chains between the acetabular surface and the metal countersurface to which they may adsorb. This would result in higher friction relative to the values we measure between two pMPC brushes. A comparably high friction coefficient, ~ 0.1 , was also measured(28) in a recent pin-on-disk tribological study between pMPC-coated surfaces under water.

Finally, in view of their similarly low friction at comparably high pressures, it is of interest to consider the relevance of our study to mechanisms of lubrication between articular cartilage surfaces. Biological lubrication at such synovial joints, despite many decades of study, is not yet well understood at the molecular level (29-31). Recent models have focused on the role of pressurized interstitial water(31) and of macromolecules at the outer cartilage surface(30). Our system of synthetic polyzwitterionic brushes polymerized from molecularly smooth mica surfaces does not have a clear analog at the cartilage surface, at which macromolecular components of the cartilage and the synovial fluid surrounding it are likely to be present (including proteins, hyaluronic acid, proteoglycans, glycoproteins and lipidic molecules(30)). The detailed role of these in the lubrication process, as well as of the cartilage substrate itself, has yet to be clarified. Moreover, cartilage is softer and much rougher than mica, though at these high pressures it may deform affinely (30): experiments on similarly soft and roughened brush-coated surfaces could potentially provide insight into the mechanisms operative in cartilage-cartilage friction. We note here the very efficient lubrication afforded by the highly-hydrated, phosphorylcholine-like monomers on our pMPC chains. The structure of these is similar to that of lipid headgroups, which provides some context for the recent, if controversial suggestion that lipid multilayers may have a role in mediating synovial lubrication(29), particularly in view of recent findings on the mechanism of boundary lubrication under water(11). Finally, although our polyzwitterionic brushes have no direct analogue at cartilage surfaces, our results underline the possible importance at such surfaces of highly hydrated macromolecules in both chondroprotective and lubrication roles.

In summary, we have shown that brushes of a biocompatible polyelectrolyte, pMPC, are capable of providing extremely efficient lubrication in aqueous media, with coefficients of friction $\mu \approx 0.001$ at mean pressures up to 7.5 MPa, comparable to values in human synovial joints. We attribute the low friction at the high pressure primarily to the lubricating action of tenaciously-attached but labile water molecules about the strongly hydrated MPC monomers. Our results may have relevance for boundary lubrication in man-made systems in aqueous or physiological media, as in biomedical devices where friction and wear is often an issue.

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15. This robustness is consistent with the nature of the pMPC brushes attachment to the mica and the shear forces applied. For an area per macroinitiator $A_m \approx 16 \text{ nm}^2$ (13) and a mean pressure P , the shear force $F_{s(m)}$ acting on a single macroinitiator molecule through the chains growing from it is given by $F_{s(m)} = \mu P A_m$. Since the chains are attached covalently to the initiation sites, any detachment due to shear is

expected to commence at the weaker bonds attaching the macroinitiator to the mica. These bonds (on average ca. 18 such bonds per macroinitiator) each have a net adhesion energy $\epsilon_1 \approx k_B T$ arising from replacement of counterions at the negatively-charged mica surface by the positively-charged quaternary $-N^+(CH_3)_3$ groups on the macroinitiator. In the worst-case scenario, all the shear force $F_{s(m)}$ on the macroinitiator during sliding will act on one of the quaternary groups at the surface, and this may initiate ‘un-zipping’ of the macroinitiator from the mica. Putting $\mu = 0.001$ and $P = 7.5$ MPa, gives $F_{s(m)} = 1.2 \times 10^{-13}$ N. This is smaller than the force $f_1 \approx \epsilon_1 / \delta$ needed to detach a single $-N^+(CH_3)_3$ group from the mica, where δ is of order 1 Å or less. Putting $\delta = 1$ Å gives $f_1 \approx 4 \times 10^{-11}$ N. Thus the friction force on a macroinitiator at the highest pressures we apply is too weak (by a factor of order 100 or more) to detach even a single bond anchoring the macroinitiator to the mica surface, consistent with our observations of the robustness of the pMPC layer to shear under all conditions in our study.

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33. We thank A.L. Lewis (Biocompatibles Ltd.) for kind donation of the MPC monomer, X.Y. Chen for synthesis of the macroinitiator, I.E. Dunlop, S. Perkin and W. Feng for help and advice, and P. Pincus for a discussion. SPA is the recipient of a Royal Society Research Merit Award. WHB thanks the TTRF for support. This work was supported by the EPSRC, the Petroleum Research Fund (grant 45694-AC7), the Charles McCutchen Foundation and the Minerva Foundation at the Weizmann Institute.

Table 1: Friction coefficient between pMPC-brush-coated mica surfaces sliding past each other at mean pressures P (in the range 2 – 7.5 MPa) at different salt concentrations

Aqueous solution	$\mu = (\partial F_s / \partial F_n)_{P = 2 - 7.5 \text{ MPa}}$
Pure water ^a	0.00043±0.0001
0.01M NaNO ₃	0.001±0.0004
0.1M NaNO ₃	0.0026 ^{+0.0005} _{-0.001}

^a – see (12-section B, 14).

Figure Captions

Figure 1: Control measurements of normal force (F_n) vs surface separation (D) profiles (panel A) and of friction force (F_s) (panels B and C) between bare mica and between macroinitiator-coated mica surfaces across water and across pMPC homopolymer solution. A: \blacktriangle - forces between bare mica in pure water on approach (normalized as $F_n(D)/R$ where $R \approx 1$ cm is the mean surface curvature radius); dashed line is a fit to the Derjaguin-Landau-Verwey-Overbeek theory based on numerical solution of the nonlinear Poisson-Boltzmann equation(32) for a 1:1 electrolyte concentration $c = 5 \times 10^{-5}$ M, with constant surface potential $\psi_0 = -80$ mV, and Hamaker constant $A = 2 \times 10^{-20}$ J. \bullet , \circ - $F_n(D)$ profiles between macroinitiator-coated (20 min incubation) mica in pure water on approach and separation respectively. \blacklozenge , \blacklozenge - profiles between macroinitiator-coated mica following 13 hr incubation in 0.3 % w/v pMPC homopolymer ($M_w = 22,000$, $M_w/M_n = 1.3$) in aqueous solution on approach and separation respectively. The solid line is a guide to the eye. The cartoons illustrate schematically the configurations corresponding to the 3 control measurements, with short black chains representing the macroinitiator, and the longer random-coil chains (red online) the pMPC homopolymer in solution. B: A summary of friction force F_s vs. load, extracted from traces as in panel 1C, between macroinitiator coated surfaces in water (\triangle) and in 0.3% w/v MPC homopolymer solution (\blacktriangle), where the solid line corresponds to friction coefficient $\mu = 0.33$. C: Typical F_s vs. time traces between two macroinitiator-coated mica surfaces in water at different surface separations D , in response to lateral applied motion of top mica surface (upper zig-zag trace).

Figure 2: Normal interactions between pMPC-brush-coated mica surfaces across water and across aqueous salt solutions (normalized as above). A, normal force profiles: \bullet , \circ - water (no added salt); \blacktriangle , \triangle - 8.7 mM NaNO_3 ; \blacklozenge , \blacklozenge - 88.6 mM NaNO_3 . Closed and open symbols are for compression and decompression respectively. The pMPC layers are 2-1.5 brushes(12-section C). Prior to solvation the brushes were characterized(12-section A, 13) using X-ray photoelectron spectroscopy, multiple-beam interference, X-ray reflectometry and AFM, which revealed a uniform, smooth layer (r.m.s. roughness 0.4 nm), while from a fit to the

data (solid curves, see (*I2-section C*)) we estimate mean interanchor spacings $s = 3.5 \pm 1$ nm and unperturbed brush-heights $L = 37 \pm 5$, 28 ± 5 and 25 ± 5 nm for the solvated brushes at respective increasing salt concentrations. The brush-chain polydispersity is estimated at ca. 1.2 (*I2-section A, I3*). The pMPC brush-like configuration and its monomer structure are also shown. The dashed and dotted lines summarize the brush-free controls between bare and between macroinitiator-coated mica respectively from fig. 1A. B: FECO interference fringes revealing the flattening of the mica surfaces at a high load, indicated by arrow in A. C: the schematic configuration corresponding to B (with contact area $A \equiv \pi r^2$).

Figure 3: Typical shear force (F_s) vs. time traces between pMPC-coated mica surfaces taken directly from the SFB. L.H. column is for 20-1.5 brushes in pure water and R.H. column is for 2-1.5 brushes in ca. 0.1M salt solution (*I2-section C*). The top trace A in each column is the lateral motion applied to the top surface, while traces B – E are the corresponding shear forces transmitted between the surfaces at the compression ratios β ($2L/D$) shown. Trace F in the L.H. column is a frequency (ω) analysis of trace E, where the magnitude of $F_s(\omega)$ at the drive frequency (arrow) is used to reveal the onset of frictional force above any systematic signal (*5, I0*) at large D.

Figure 4: Variation of friction F_s with load F_n and with sliding velocity v_s between pMPC-brush-coated surfaces. A) Main: Variation of F_s with F_n for both 20-1.5 (●, ○) and 2-1.5 (▲) brushes across water; within the scatter there is little systematic difference between these two brushes. Note double logarithmic scale; the solid curve corresponds to a friction coefficient $\mu = 0.00043$. Inset: the same data on a linear scale; the solid line for $F_n > 1.5$ mN corresponds to the same friction coefficient as in the main plot. The sharply-rising dotted line is the friction between macroinitiator-coated surfaces with no pMPC brushes (based on inset to figure 1). The arrows indicate the maximal loads applied in the polyelectrolyte brush friction study (*5*). B) Typical variation of F_s with v_s at different compressions and salt concentrations. In ca. 10 mM NaNO_3 : ▲, △ - $D = 13 \pm 0.3$ nm, on approach and on separation of surfaces respectively. In ca. 100 mM NaNO_3 : ● - $D = 13.3 \pm 0.3$ nm in approach run; ◆, ◇ - $D = 10.2 \pm 0.3$ nm, on approach and on separation of surfaces respectively; ⊗ : $D = 8.5 \pm 0.3$ nm, in separation run.

There is little variation between data sets whether on approach or on separation of surfaces, and whether in ca. 10 mM or 100 mM salt.

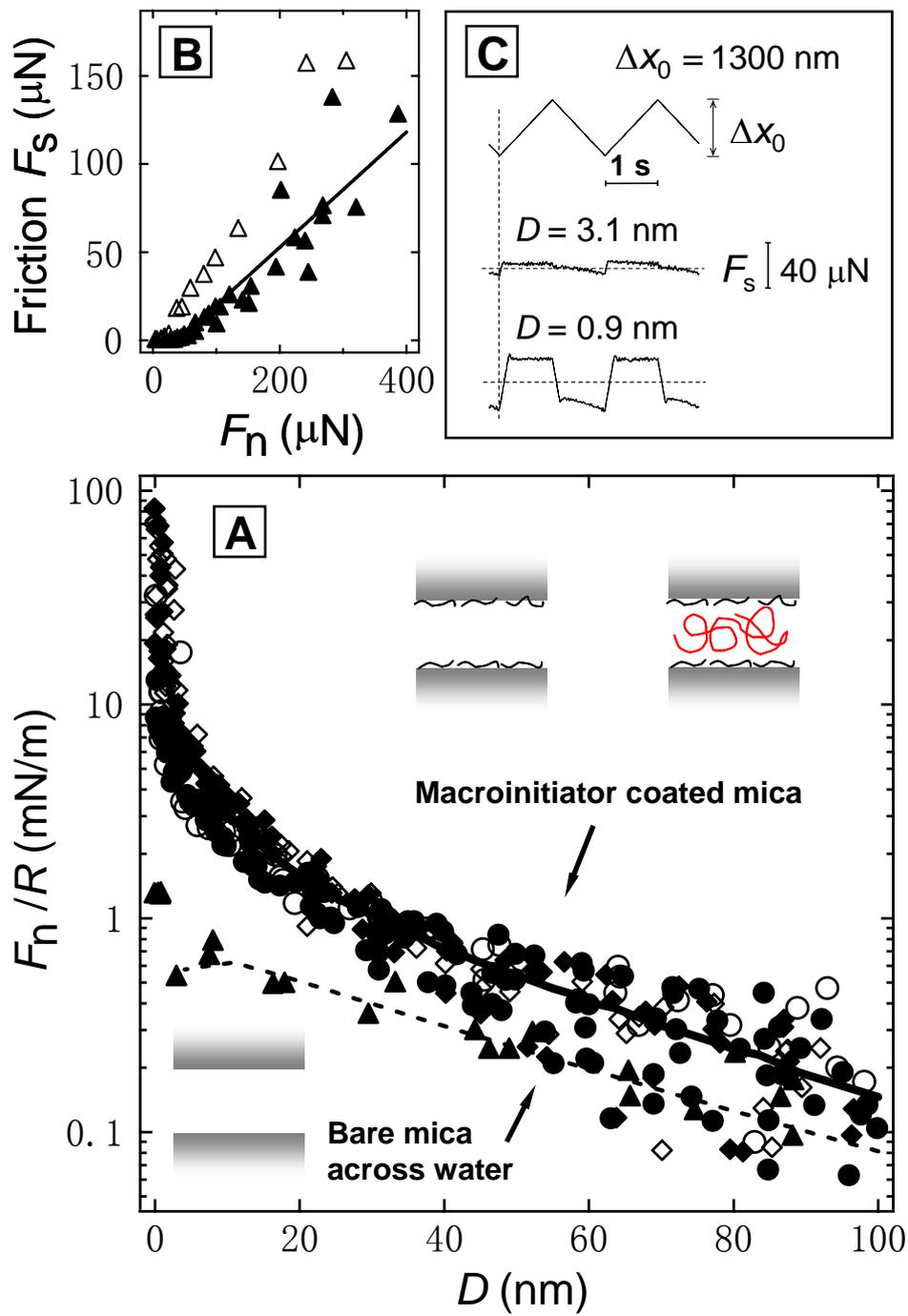


Figure 1

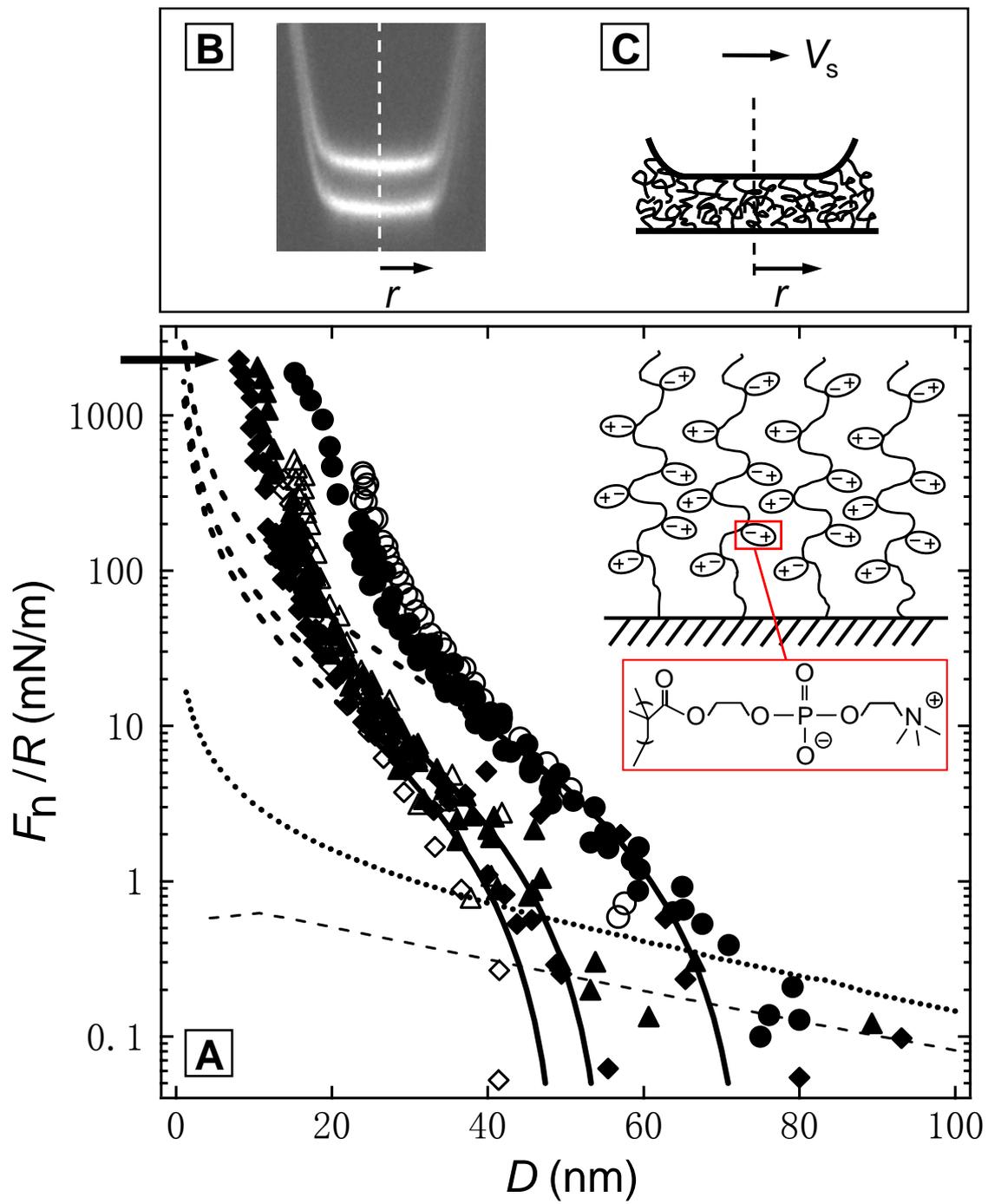


Figure 2

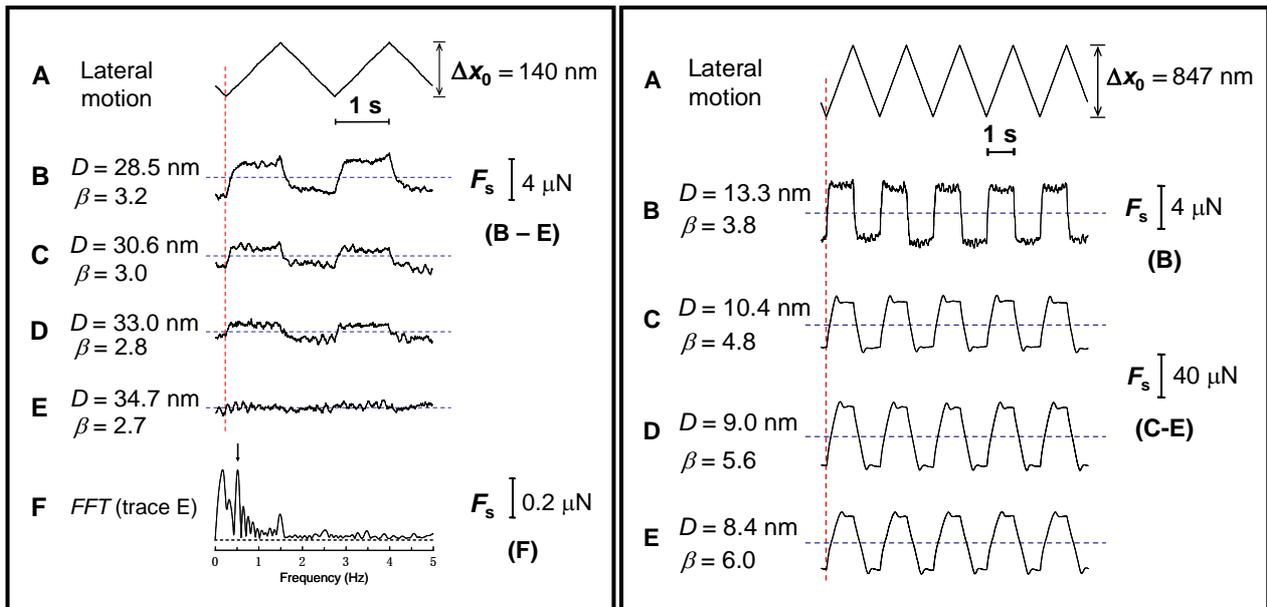


Figure 3

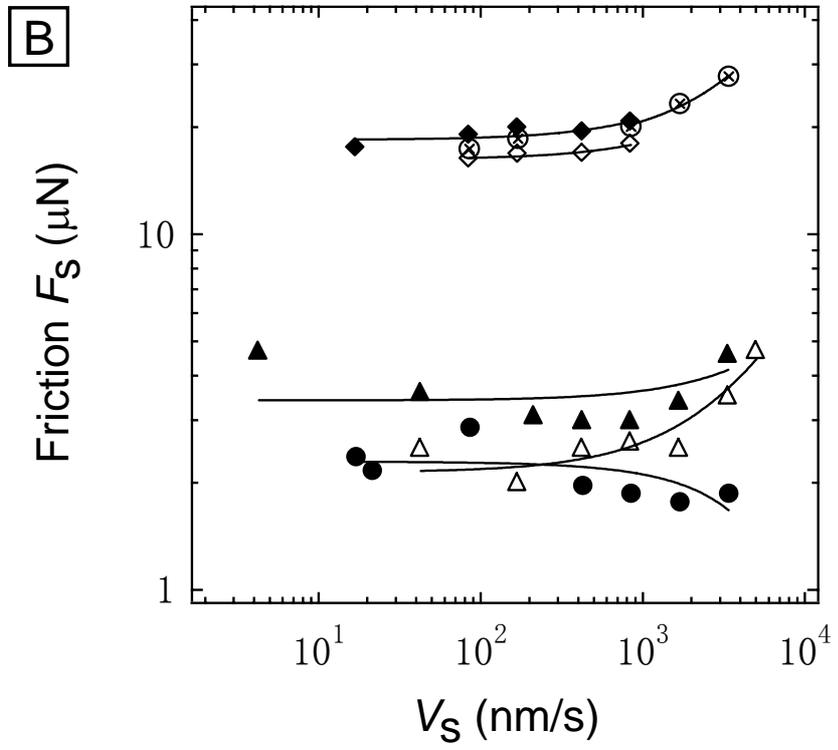
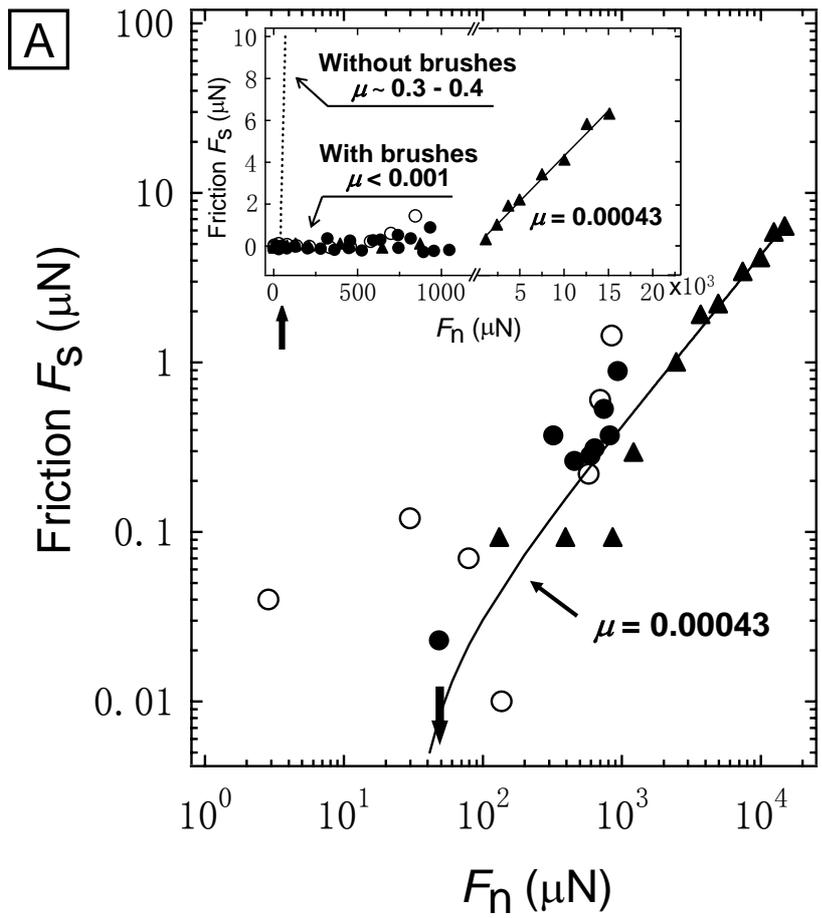


Figure 4