

Tribology in biology

I. C. Gebeshuber*^{1,2,3}, M. Drack⁴ and M. Scherge⁵

Man has conducted research in the field of tribology for several thousands of years. Nature has been producing lubricants and adhesives for millions of years. Biotribologists gather information about biological surfaces in relative motion, their friction, adhesion, lubrication and wear, and apply this knowledge to technological innovation as well as to the development of environmentally sound products. Ongoing miniaturisation of technological devices such as hard disk drives and biosensors increases the necessity for the fundamental understanding of tribological phenomena at the micro- and nanometre scale. Biological systems excel also at this scale and might serve as templates for developing the next generation of tools based on nano- and microscale technologies. Examples of systems with optimised biotribological properties are: articular cartilage, a bioactive surface which has a friction coefficient of only 0.001; adaptive adhesion of white blood cells rolling along the layer of cells that lines blood vessels in response to inflammatory signals; and diatoms, micrometre sized glass making organisms that have rigid parts in relative motion. These and other systems have great potential to serve as model systems also for innovations in micro- and nanotechnology.

Keywords: Biotribology, Joint lubrication, Adaptive adhesion of white blood cells, Diatom tribology, Low friction coefficient, Switchable adhesives

Introduction

All organisms face tribological problems. Surfaces in relative motion occur, e.g. in joints, in the blinking with the eye, in the foetus moving in the mothers womb. Systems with reduced friction such as joints and articular cartilage (AC) as well as systems with increased friction, such as bird feather interlocking devices and friction in fish spines, have evolved.¹ Furthermore, systems with increased adhesion (such as sticking in tree frogs and adhesion in bats) as well as antiadhesives mechanisms are found in nature. The frictional devices of insects (attachment pads, like in flies or geckos) have gained very much attention.

During the long evolution of biological systems, the environment and the continuous improvements due to the struggle for existence between and among species, strong selective mechanisms resulted in extinction of many species that were not among the best adapted.

Materials found in nature combine many inspiring properties such as sophistication, miniaturisation, hierarchical organisations, hybridation, resistance and

adaptability. The hydrodynamic, aerodynamic, wetting and adhesive properties of natural materials are remarkable. Elucidating the basic components and building principles selected by evolution allows for the development of more reliable, efficient and environment respecting materials.²

The results of evolution often converge on limited constituents or principles. For example, the same material component will be found just slightly but effectively varied to obey different functions in the same organism (e.g. collagen occurs in bones, skin, tendons and the cornea).² One smart feature of natural materials concerns their beautiful organisation in which structure and function are optimised at different length scales.

Ongoing miniaturisation of technological devices such as hard disk drives and biosensors increases the necessity for the fundamental understanding of tribological phenomena also at the micro- and nanometre scale.³⁻⁵ In micro- and nanotribology, at least one of the two interacting surfaces in relative motion has relatively small mass, and the interaction occurs mainly under lightly loaded conditions. In this situation negligible wear occurs and the surface properties dominate the tribological performance.⁶

Biological systems excel also at this scale and might serve as templates for developing the next generation of tools based on nano- and micrometre scale technologies.¹

The objective of this manuscript is to discuss biological examples that show features that might be of high interest to tribologists and stimulate further research and novel technological developments.

¹Institut für Allgemeine Physik, Vienna University of Technology, Wiedner Hauptstraße 8-10/134, 1040 Wien, Austria

²TU BIONIK Center of Excellence for Biomimetics, Getreidemarkt 9/166, 1060 Wien, Austria

³AC²T Austrian Center of Competence for Tribology, Viktor Kaplan-Straße 2, 2700 Wiener Neustadt, Austria

⁴Department of Theoretical Biology, University of Vienna, Althanstraße 14, 1090 Wien, Austria

⁵Fraunhofer IWM Freiburg, Micro- and Nanotribology, Wöhlerstraße 11, 79108 Freiburg, Germany

*Corresponding author, email gebeshuber@iap.tuwien.ac.at

Three key examples for biological model systems of possible interest to tribologists

This section focuses on three biological examples with amazing tribological properties. In joints, several problems have to be solved: bone is hard, muscles, nerves and tendons are soft – yet they are connected and move relatively to each other. Friction and wear should be small. Practically all the coefficients of sliding friction for diverse dry or lubricated systems fall within a relatively narrow range of 0.1 to 1. In some cases, the coefficient of friction may be less than 0.1 and as low as 0.01 or 0.001. In other cases, e.g. very clean unlubricated metals in vacuum, friction coefficients may exceed one. Articular cartilage, the bioactive surface on synovial joints (like the hip, the knee, the elbow, the fingers, the shoulder or the ankle) has a very small friction coefficient. Some groups report friction coefficients for normal synovial joints as low as 0.001 and some report slightly higher values. Such low friction coefficients are still to be reached with man made systems.

The second example deals with adhesion of white blood cells in the blood vessels. White blood cells serve as the immune police of the body. They flow in the blood stream and have to be stopped at the site of an inflammation. An exquisite arrangement of different, switchable adhesives enables control of inflammation in our bodies.

Diatoms are the third example of organisms that are relevant to tribology. These algae are just a couple of micrometres large, have surfaces in relative motion and have evolved self-healing adhesives, nanostructured glass surfaces, interconnected junctions and rubber band like behaviour pointing toward elaborated lubrication.

These and other systems comprise great potential to serve as model systems for innovations in technology, and indeed, some first devices based on bio-inspired materials are already available.⁷

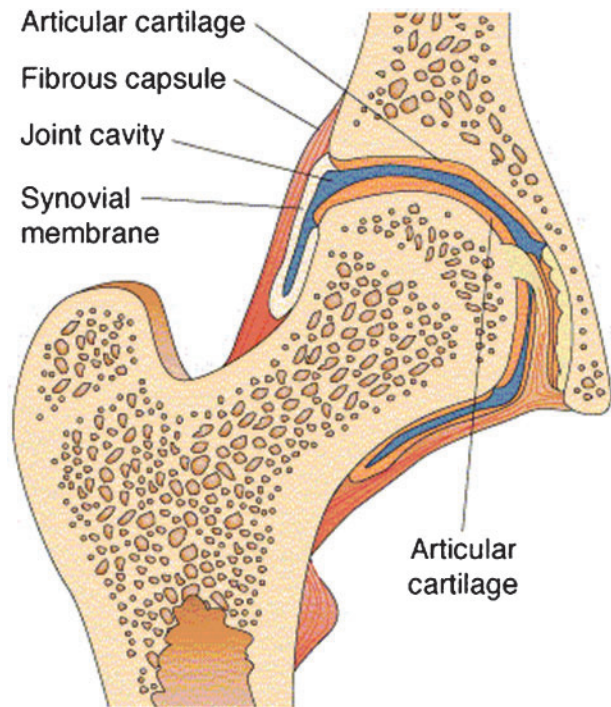
Articular cartilage – low friction coefficient in natural joints

In nature exceptional designs for interfacing soft and hard materials with capabilities well beyond present day technologies have developed. A major challenge is to extract design lessons from nature especially for the interface of soft (organic) and hard material that are mechanically, chemically and electrically compatible.

Articular cartilage is the cartilage that lines bones in joints (Fig. 1). Articular cartilage is a functionally gradient material (FGM). In FGMs a continuous spatial change in composition or microstructure gives rise to position dependent physical and mechanical properties that can extend over microscopic or macroscopic distances.⁸

Articular cartilage exhibits gradients in collagen/proteoglycan (mortar-like substances made from protein and sugar) concentrations and in collagen fibre orientation. Often FGMs are used to provide an interfacial transition between dissimilar materials or to provide multiple functions.

Bone is a remarkably tough bio-nanocomposite material of brittle hydroxyapatite crystals and a soft organic matrix (mainly collagen). Such as in abalone nacre, a molecular mechanistic origin for that remarkable toughness has just recently been shown with atomic



1 Synovial joint as exemplified by hip joint (Lippincott Williams and Wilkins, instructor's resource CD-ROM to accompany Porth's *Pathophysiology: concepts of altered health states*, 7th edn)

force microscopy investigations performed by the Hansma group at UCSB. In short, such tough bionanocomposites contain 'hidden length' tied up with renewable 'sacrificial bonds'. The energy to break a polymer designed in this way can be hundreds or even thousands of times greater than the energy to break a covalent bond because the polymer must be stretched further every time a sacrificial bond breaks and releases more hidden length. This finding suggests that the sacrificial bonds (calcium ion dependent cross-links) found within or between collagen molecules may be partially responsible for the toughness of bone.⁹ The fact that sacrificial bonds and hidden length dissipate energy as mineralised fibrils separate during bone fracture might be the key to the remarkable mechanical properties of bone¹⁰ and should also be taken into account for engineering tough new materials.

Articular cartilage is the bearing surface with low friction and wear in freely moving synovial joints that permits smooth motion between adjoining bony segments.¹¹ Because of its compliance, AC helps to distribute the loads between opposing bones in a synovial joint. Hip, knee, elbow, fingers, shoulder and ankle are examples of synovial joints (Fig. 1).¹² Synovial joints are complex, sophisticated systems not yet fully understood. The loads are surprisingly high and the relative motion is complex.

The entire joint is enclosed in a fibrous tissue capsule, the inner surface of which is lined with the synovial membrane that secretes a fluid known as synovial fluid. Synovial fluid is essentially a dialysate of blood plasma with added hyaluronic acid. In a common joint less than 1 mL synovial fluid is present.

Synovial fluid is a thick, stringy fluid. With its egg-like consistency (the term synovial stems from Latin for 'egg'

and was introduced by Paracelsus) synovial fluid reduces friction between the AC in joints to lubricate and cushion them during movement. During natural joint movements, shear rates of up to 10^4 s^{-1} occur, and huge amounts of energy have to be absorbed by the synovial fluid.¹³ Synovial fluid also contains a substance called lubricin that is secreted by synovial cells. Lubricin^{14,15} or hydrophobic lubricants (phospholipids carried by lubricin)¹⁶ or related glycol proteins such as superficial zone protein, e.g. Ref. 17, are responsible for the boundary lubrication, which reduces friction between opposing surfaces of cartilage.

Already in 1987, Schurz and Ribitsch showed that in case of diseased synoviae all rheological parameters (e.g. shear viscosity, apparent normal viscosity, apparent shear modulus, zero shear viscosity, shear modulus, critical shear rate) deteriorate.¹⁸

Wear occurs in healthy and in arthritic joints (see e.g. Refs. 19 and 20). Wear particle shape can be used as an indicator of the joint condition (see e.g. Ref. 21). In particular, the fractal dimension of the particle boundary was shown to correlate directly with the degree of osteoarthritis (degenerative joint disease).²¹

Articular cartilage is a nanocomposite material. About 70 to 85% of its weight is water. About 30% of the dry weight is composed of high molecular weight proteoglycans and 60 to 70% of the dry weight is made up of a network of collagen, a fibrous protein with huge tensile strength.

The collagen structure changes from the articular surface to the bone: layers, leaves, linked bundles and networks of fibrils.

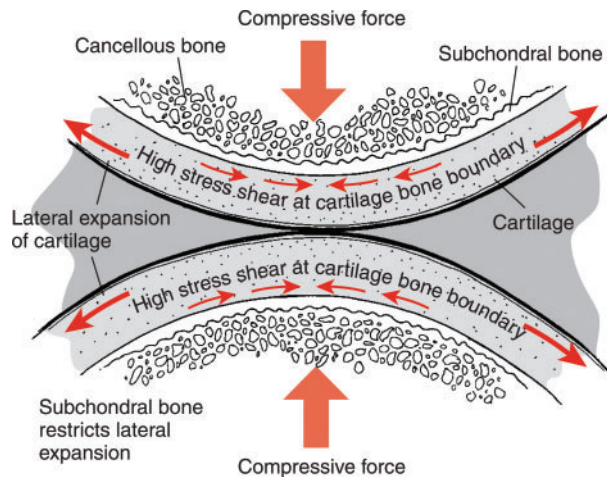
An amorphous layer that does not appear to contain any fibres is found on the articular surface. The mechanical behaviour of AC is determined by the interaction of its predominant components: collagen, proteoglycans and interstitial fluid.

Mechanical behaviour of AC

In solution the proteoglycan molecule occupies a large volume. In the cartilage matrix, the volume occupied by proteoglycan aggregates is limited by the entangling collagen framework. The swelling of the aggregated molecule against the collagen framework is an essential element in the mechanical response of cartilage. When aggregated cartilage is compressed, its compressive stiffness increases and is very effective in resisting compressive loads.

The mechanical response of cartilage is also strongly tied to the flow of fluid through the tissue. Cartilage behaves like a sponge, albeit one that does not allow fluid to flow through it easily.

Under impact loads (see Fig. 2), cartilage behaves as a single phase, incompressible, elastic solid, that is, its Poisson's ratio is 0.5;¹¹ there simply is not time for the fluid to flow relative to the solid matrix under rapidly applied loads. The Poisson's ratio is a measure of the tendency of a material to get thinner in the other two directions when it is stretched in one direction. It is defined as the ratio of the strain in the direction of the applied load to the strain normal to the load. For a perfectly incompressible material, the Poisson's ratio would be exactly 0.5. Most practical engineering materials have a Poisson's ratio between 0.0 and 0.5. Cork is close to 0.0 (this makes cork function well as a bottle stopper, since an axially loaded cork will not swell



2 Under impulsive compressive loads, cartilage experiences relatively large lateral displacement due to its high Poisson's ratio: this expansion is restrained by much stiffer subchondral bone, causing high shear stress at cartilage bone interface; from Ref. 11, Lippincott Williams and Wilkins, 2003

laterally to resist bottle insertion), most metals are between 0.25 to 0.35, and rubber is almost 0.5. Theoretical materials with a Poisson's ratio of exactly 0.5 are truly incompressible, since the sum of all their strains leads to a zero volume change.

Material properties of AC

The Young's modulus of cartilage is in the range of 0.45 to 0.80 MPa.¹¹ For comparison, the Young's modulus of steel is 210 GPa and for many woods is about 10 GPa parallel to the grain. These numbers show that cartilage has a much lower stiffness (modulus) than most engineering materials.

The permeability of cartilage is typically in the range of 10^{-15} to $10^{-16} \text{ m}^4 \text{ Ns}^{-1}$.

Permeability is not constant through the tissue. The permeability of AC is highest near the joint surface (making fluid flow relatively easy) and lowest in the deep zone (making fluid flow relatively difficult).²²⁻²⁴ Permeability also varies with deformation of the tissue. As cartilage is compressed, its permeability decreases.^{25,26}

Under increasing load, fluid flow will decrease because of the decrease in permeability that accompanies compression.

This variable permeability has clinical relevance: deformation dependent permeability may be a valuable mechanism for maintaining load sharing between the solid and fluid phases of cartilage. If the fluid flowed easily out of the tissue, then the solid matrix would bear the full contact stress, and under this increased stress, it might be more prone to failure.

The fact that cartilage is a mixture of a solid and fluid leads to the whole tissue behaving as a compressible material, although its components are incompressible.

The relative influence of the collagen network and proteoglycans on the tensile behaviour of cartilage depends on the rate of loading.²⁷ When pulled at a slow rate, the collagen network alone is responsible for the tensile strength and stiffness of cartilage. At high rates of loading, interaction of the collagen and proteoglycans is responsible for the tensile behaviour; proteoglycans

restrain the rotation of the collagen fibres when the tissue is loaded rapidly.

Mechanical failures of cartilage

Repeated tensile loading (fatigue) lowers the tensile strength of cartilage as it does in many other materials.^{28–30}

Repeated compressive loads applied to the cartilage surface *in situ* also cause a decrease in tensile strength, if a sufficient number of load cycles are applied.³¹

Joint lubrication

Normal synovial joints operate with an amazingly low coefficient of friction. Some groups report friction coefficients as low as 0.001,^{32–34} generally slightly higher values (between 0.002 and 0.006) appear in the literature (e.g. Refs. 35 and 36). Values of up to 0.02 are reported for the friction coefficient in synovial joints. One reason for the huge variation in the hip joint friction coefficient might be its distinct temperature dependence (S. Chizhik, personal communication). Whatever the exact value, such low friction coefficients are still to be reached with man made systems. For comparison, Teflon sliding on Teflon (or Teflon sliding on steel) has a coefficient of friction of about 0.04;³⁷ this is an order of magnitude higher than that for synovial joints.

In biological systems especially, however, friction and wear are not simply related phenomena;^{19,20} low friction systems do not necessarily result in low levels of wear. Since worn material can be replaced (regrown) by many biological systems, low friction is in many cases more preferable than low wear.

Identifying the mechanisms responsible for the low friction in synovial joints has been an area of ongoing research for decades. Furey lists more than 30 theories that have been proposed to explain the mechanisms of joint lubrication.³⁸ And even if similar theories are grouped together, still over a dozen very different theories remain. These have included a wide range of lubrication concepts, e.g. hydrodynamic, hydrostatic, elasto-hydrodynamic, squeeze film, boundary, mixed regime, weeping, osmotic, synovial mucin gel, boosted, lipid, electrostatic, porous layers and special forms of boundary lubrication (e.g. lubricating glycoproteins, structuring of boundary water, see e.g. Ref. 38 for a review on joint lubrication).

Stachowiak and co-workers report sliding experiments of cartilage surfaces against stainless steel plates under dry conditions and with irrigation by synovial fluid or saline solution.³⁹ These experiments support the concept of a low friction, wear resistant surface layer. The smooth articulating surface allows movements with as little friction as possible. Friction and wear of the cartilage were initially low in these experiments but increased in severity as a superficial lubricating layer was progressively removed by wear. Irrigation of the cartilage by synovial fluid reduced friction to very low levels, but saline solution had no lubricating effect. It has been concluded that the outer surface of cartilage is covered by a substance capable of providing lubrication for limited periods when synovial fluid is unable to prevent contact between opposing cartilage surfaces.

Both fluid film and boundary lubrication mechanisms have been investigated. For a fluid film to lubricate moving surfaces effectively, it must be thicker than the roughness of the opposing surfaces. The thickness of the

film depends on the viscosity of the fluid, the shape of the gap between the parts, and their relative velocity, as well as the stiffness of the surfaces. A low coefficient of friction can also be achieved without a fluid film through the mechanism known as boundary lubrication. Sir William Bate Hardy at Cambridge introduced the term boundary lubrication in 1922.⁴⁰ In boundary lubrication the lubricant film is too thin to provide total surface separation. This may be due to excessive loading, low speeds or a change in the fluid's characteristics. In such a case, contact between surface asperities occurs. Friction reduction and wear protection is then provided via chemical compounds rather than through properties of the lubricating fluid. In the case of boundary lubrication, molecules adhered to the surfaces are sheared rather than a fluid film.

It now appears that a combination of boundary lubrication (at low loads) and fluid film lubrication (at high loads) is responsible for the low friction in synovial joints.^{41–43}

This conclusion is based on several important observations. First, at low loads, synovial fluid is a better lubricant than buffer solution, but synovial fluid's lubricating ability does not depend on its viscosity. Digesting synovial fluid with hyaluronidase, which greatly reduces its viscosity, has no effect on friction. This shows that a fluid film is not the predominant lubrication mechanism, since viscosity is needed to generate a fluid film. In contrast, digesting the protein components in synovial fluid (which does not change its viscosity) causes the coefficient of friction to increase. This result suggests that boundary lubrication contributes to the overall lubrication of synovial joints. A glycoprotein that is effective as a boundary lubricant has been isolated from synovial fluid.⁴⁴ Newer evidence suggests that phospholipids may be important boundary lubricant molecules for AC.^{45–50}

Hyaluronan molecules and phospholipids are both present in the joint cavity. Pasquali-Ronchetti and co-workers report interactions of these two substances forming huge perforated membrane-like structures and 12 nm-thick 'cylinders' (rollers) with a tendency to aggregate. They suggest they may also do so *in vivo* within the joint cavity, where both chemical species are present, giving rise to complexes that might exhibit peculiar lubricating and protective properties. It is also proposed that such interactions may not be as efficient in arthritic joints, where hyaluronan is degraded to less effective low molecular weight fragments.⁴⁸

Atomic force microscopy studies of hyaluronic acid deposited on mica and graphite show that this substance forms networks in which molecules run parallel for hundreds of nanometres. The interchain and intrachain interactions of hyaluronic acid molecules in solution give rise to flat sheets and tubular structures that separate and rejoin into similar neighbouring aggregates.⁵⁰ Such layers and sheets might be used as lubricants.

Surface active phospholipid is capable of remarkable antiwear action comparable to the best commercially available lubricants and reducing friction to values anticipated from lamellated solid lubricants such as graphite or MoS₂. For more information on solid lubricants, see Ref. 51.

Hills proposes hydrophobic oligolamellar lining as a possible ubiquitous physiological barrier, also in joints.^{52,16} Evidence comes from electron microscopy, epifluorescence microscopy and simple tests of hydrophobicity.⁴⁵ Essentially the same lubrication system is in his view present in many sites in the body where tissues slide over each other with such ease. The graphite-like (dry) lubrication by adsorbed SAPL is an excellent lubrication system in the human lung (Fig. 3).^{53,54} On the articular surface SAPL should act as graphite-like back-up boundary lubricant wherever the fluid film fails to support the load: in this case, joints are lubricated by shearing between surface lamellae of phospholipid just as occurs in graphite when writing with a pencil.

In his view, lubricin and hyaluronic acid have 'carrier' functions for the highly insoluble SAPL, while hyaluronic acid has good wetting properties needed to promote hydrodynamic lubrication of a very hydrophobic articular surface by an aqueous fluid wherever the load permits.

At high loads, the coefficient of friction with synovial fluid increases, but there is no difference in friction between buffer and synovial fluid. This suggests that the boundary mechanism is less effective at high loads and that a fluid film is augmenting the lubrication process. Numerous mechanisms for developing this film have been postulated.^{33,55-60} If cartilage is treated as a rigid material, it is not possible to generate a fluid film of sufficient thickness to separate the cartilage surface roughness. Treating the cartilage as a deformable material leads to a greater film thickness. This is known as *elastohydrodynamic lubrication*: the pressure in the fluid film causes the surfaces to deform. However, as the surfaces deform, the roughness on the surface also deforms and becomes smaller. Models, which include deformation of the cartilage and its surface roughness, have shown that a sufficiently thick film can be developed.⁵⁶

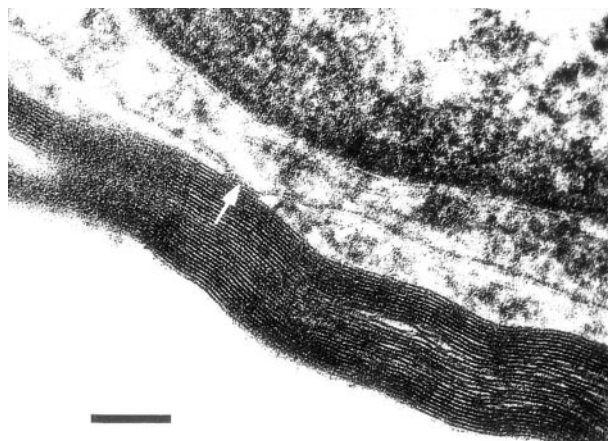
Deformation also causes fluid flow across the cartilage surface, which modifies the film thickness (*microelastohydrodynamic lubrication*), although there is some question as to the practical importance of flow across the surface.^{56,61,62}

In summary, AC provides an efficient load bearing surface for synovial joints that is capable of functioning for the lifetime of an individual. The mechanical behaviour of this tissue depends on the interaction of its fluid and solid components.

In 1743, Sir William Hunter read to a meeting of the Royal Society 'Of the structure and diseases of articulating cartilages'.⁶³ Since then, a great deal of research has been carried out on this subject. And yet, the mechanisms involved are still unknown. Further investigation of the complex field of joint lubrication will improve our understanding of this amazing system, help to develop effective pharmaceuticals for people suffering from arthritis and provide innovative ideas for new materials and technologies.

Switchable adhesives – leukocyte rolling

The understanding of adhesives on the molecular level is important for engineering tailored man made adhesives. Depending on the application, either increased adhesion or effective antiadhesive mechanisms are necessary. Nanorobots floating in the blood stream, acting as micro surgeons, should for example not aggregate, and



3 Electron micrograph of human lung showing layers of SAPL directly adsorbed to alveolar epithelium which is also typical for other sliding surfaces *in vivo*: interlamellar spacing is about 4.5 nm; scale bar 100 nm; from Ref. 54, American Physiological Society, 1999

therefore exhibit strong non-adhesive properties regarding the environment (see e.g. Ref. 64). On the other hand, in implants, good adhesive interaction of the implant surface with the surrounding tissue is a necessity. Furthermore, the implants should not cause immune reactions via small wear particles (see e.g. Ref. 65).

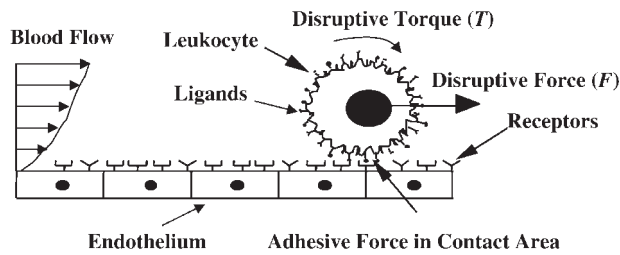
The interaction of leukocytes (also known as white blood cells or immune cells) with blood vessels shows very interesting adaptive adhesion features and might serve as template for switchable man-made adhesives.

Physiologically, leukocytes help to defend the body against infectious disease and foreign materials as part of the immune system. There are normally between 4×10^9 and 11×10^9 white blood cells in a litre of healthy adult blood. The size of a leukocyte is about 10 to 20 μm . Leukocytes are capable of active amoeboid motion, a property that allows their migration from the blood stream into the tissue.⁶⁶

Leukocytes in the blood circulation may arrest at a particular site as a result of interaction with the layer of cells that lines the blood vessel walls (the endothelium) or the subendothelial matrix.⁶⁷

Traditionally, the endothelium is thought to be specialised to resist adhesive interactions with other cells. However, such interactions do occur during certain important biological events such as at the surface of activated endothelial cells during leukocyte migration through the blood vessel to the site of inflammation. A special issue of Cells Tissues Organs contains reviews on these interactions.⁶⁸

Leukocyte adhesion to the endothelium plays a central role in inflammation. Adhesion molecules on the leukocytes and the endothelium regulate cell interactions in inflammation. The adhesion of leukocytes is mediated by adhesion molecules and also by the force environment present in the blood vessel (Fig. 4, from Ref. 69). The specific molecular mechanisms of adhesion often vary with the local wall shear stress.^{70,71} Shear stress is a measure of the force required to produce a certain rate of flow of a viscous liquid and is proportional to the product of shear rate and blood viscosity. Physiologic levels of venous and arterial shear stresses range between 0.1–0.5 Pa and 0.6–4 Pa respectively.



4 Leukocyte adhesion to endothelium involves competition between adhesive and disruptive forces: flow of blood exerts disruptive force on leukocyte in direction of flow as well as torque (which is also disruptive); adhesive force at interface (i.e. contact area) between leukocyte and endothelium counters disruptive force; source of adhesive force is non-covalent bonds that form between complementary moieties on surface of leukocyte (ligands) and surface of endothelium (receptors); From Ref. 69, International Union of Physiological Science/American Physiological Society, 2003

Initially, the leukocytes move freely along with the blood stream. Leukocyte adaptive adhesion involves a cascade of adhesive events⁷² commonly referred to as initial tethering, rolling adhesion (an adhesive modality that enables surveillance for signs of inflammation), firm adhesion, and escape from blood vessels into tissue (Fig. 5, from Ref. 73). After initial tethering, leukocytes may detach back into the free stream or begin to roll in the direction of the blood flow.⁶⁹ Their rolling velocity is typically 10 to 100 times lower than a non-adherent leukocyte moving next to the vessel wall.

The rolling velocity is not constant, the cells tend to speed up and slow down as they roll along the endothelium.

At some point, the leukocyte may become 'activated', i.e. adheres firmly to the endothelium, and might migrate through the blood vessel to the site of the inflammation.

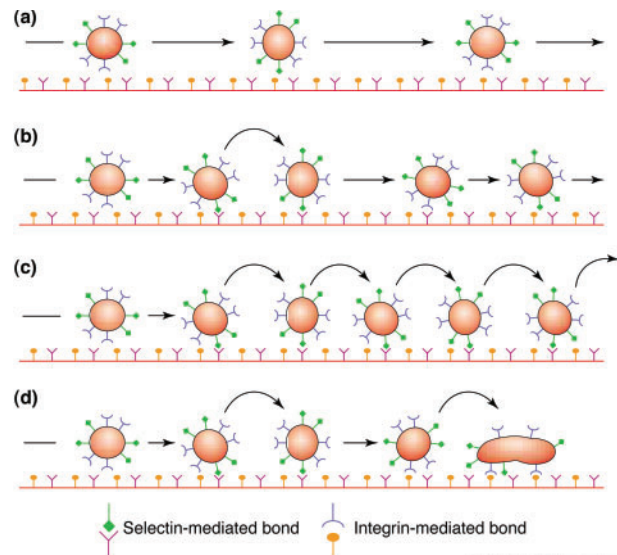
Lawrence and co-workers examined leukocyte adhesion to certain endothelial cells under well-defined flow conditions *in vitro*.^{71,74,75}

The initial flow studies were followed by many further studies both *in vitro*^{76–80} and *in vivo*^{81–84} which clearly distinguish separate mechanisms for initial adhesion/rolling and firm adhesion/leukocyte migration.

Research has further shown that in a variety of systems, selectin/carbohydrate interactions are primarily responsible for initial adhesion and rolling, and firm adhesion and leukocyte migration are mediated primarily by integrin/peptide interactions (at the site of inflammation).⁸⁵

Integrins are the most sophisticated adhesion molecules known. In less than a second, signals from other receptors are transmitted to integrin extracellular domains, which undergo conformational movements (change in their molecular arrangement) that enable ligand binding (i.e. the adhesives switches from non-adhesive to adhesive). These unique switchable adhesives rapidly stabilise contacts between leukocytes in the bloodstream and endothelium at sites of inflammation.⁸⁶

Characterisation of the molecular and cellular properties that enable such a transient form of adhesion (which would be of interest for many technological applications such as grippers) under the high forces experienced by cells



5 a no adhesion (cells contact surface but do not bind; cells always move at or near bulk fluid velocity V_H), b transient adhesion mediated by selectins (cells bind very briefly and slow below bulk fluid velocity; cells rapidly lose contact with surface and achieve bulk fluid velocity; cells move at $V < 0.5V_H$), c rolling adhesion mediated by selectins (cells bind and translate along surface at reduced velocity; cells move at $V < 0.5V_H$) and d firm adhesion mediated by integrins (cells bind strongly to surface and move at very slow rate): green, selectin; red, selectin ligand; blue, integrin receptor; orange, integrin ligand; from Ref. 73, Elsevier Science Ltd, 2001

in blood vessels is investigated by a multitude of groups, experimentally as well as in theory (e.g. Refs. 86–91).

In inflammation, firm adhesion can be mediated by *activated* integrins once the leukocytes have been slowed by selectin mediated rolling.^{75,83} Integrins can also mediate firm adhesion when activated^{92,93} and may, through conformational changes, mediate both 'firm' and 'transient' types of adhesion.

The question arises: what functional properties of these molecules control the different dynamics of adhesion?

There is evidence that the dynamics of adhesion is coded by the physical chemistry of adhesion molecules, and not by cellular features such as deformability, morphology, or signaling.^{94,95}

Possible physicochemical properties that give rise to the various dynamic states of adhesion are rates of reaction, affinity, mechanical elasticity, kinetic response to stress, and length of adhesion molecules.

There are at least four distinct, observable dynamic states of adhesion (Fig. 5, from Ref. 73). In the 'no adhesion' state (Fig. 5a) cells are moving at a velocity greater than 50% of their hydrodynamic velocity V_H .

In 'transient adhesion' (Fig. 5b) cells move at $V < 0.5V_H$ but exhibit no durable arrests. In 'rolling adhesion' (Fig. 5c) cells travel at $V < 0.5V_H$ and experience durable arrests. Finally, in the 'firm adhesion' case (shown in Fig. 5d) cells bind and remain motionless.

The adhesion dynamics model of Chang *et al.*⁹⁶ defines molecular characteristics of firm adhesion, rolling adhesion and non-adhesion in the domain of leukocyte endothelium rolling interactions.

Quantitative analysis and modelling of the key molecular properties governing their action in regulating dynamic cell attachment and detachment events is crucial for advancing conceptual insight along with technological applications.

Adhesion is dependent on the magnitude of force applied to the cells.

Current concepts of the failure of adhesion molecules suggest that there is no single force for bond breakage (see e.g. Ref. 97). Bond failure might be governed by a series of transition states (not just one) and that these different transition states can be explored by exerting forces on adhesion molecules at different pulling rates (measured in pN s^{-1} ranging over several orders of magnitude).

The adhesion mechanism is also depending on the shear (see e.g. Ref. 97). At low shear, stabilisation through additional bonds is unlikely, because the probability of two selectins hitting two ligands is very low. At sufficiently high shear, shear mediated rotation of the cell over the substrate leads to the establishment of additional bonds.

Chang and co-workers started from the Bell model which considers functional properties of the adhesion molecules, relating the net dissociation rate $k_r(f)$ of a bond under applied force f with the unstressed dissociation rate constant k_r^0 , the thermal energy $k_B T$ and a parameter γ with units of length that relates the reactivity of the molecule to the distance to the transition state in the intermolecular potential of mean force for single bonds⁹⁸

$$k_r(f) = k_r^0 \exp(\gamma f / k_B T)$$

Bell model parameters for adhesion molecules can be determined using several methods: arrest duration distribution of cells on sparse coatings of adhesion molecules, microcantilever technique (see e.g. Ref. 99) and dynamic force spectroscopy (see e.g. Refs. 100 and 101).

In force spectroscopy, the adhesive interaction of the tip to the surface can be described by the differential equation

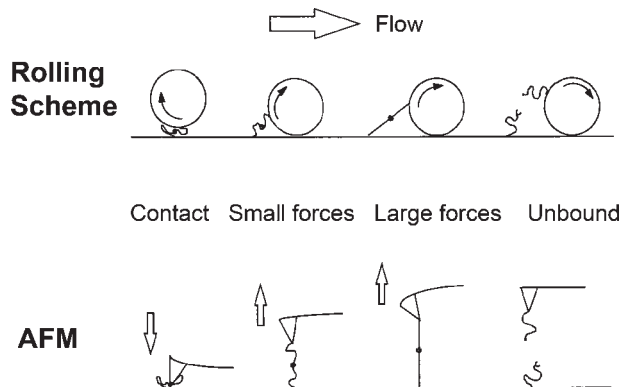
$$dP_{\text{adhesion}}(t)/dt = -k_r P_{\text{adhesion}}(t) + k_b [1 - P_{\text{adhesion}}(t)]$$

where $P_{\text{adhesion}}(t)$ denotes the probability of an adhesion event between AFM tip and surface during retraction. k_r and k_b are the molecular rupture and binding rate of the interaction under AFM conditions.

k_{rupture} directly corresponds to a forced dissociation rate k_r , and k_{bind} can be converted into an association rate via an effective concentration according to

$$k_{\text{bind}} = k_{\text{on}} c_{\text{eff}}(d)$$

The effective concentration c_{eff} describes the number of binding partners within the intersection volume of the accessible space for molecules on the AFM tip and on the surface and depends on the distance d between both. Since in the AFM experiments, immediately after rupture, c_{eff} equals zero (a rebinding after rupture of the stretched complex is inhibited because the molecules shrink to their equilibrium length and their binding sites are separated, Fig. 6) the above mentioned differential equation can be simplified to



6 Schematic representation of selectin ligand interaction during leukocyte rolling on endothelium and in AFM experiments: approach and retraction of AFM sensor simulates physiological rolling process; after binding, force on complex increases continuously with increasing sensor–surface distance; after rupture, chain-like molecules shrink to their equilibrium length, and their binding sites, both located close to aminoterminal ends of molecules, are separated; from Ref. 100, National Academy of Sciences, USA, 1998

$$dP_{\text{adhesion}}(t)/dt = -k_r P_{\text{adhesion}}(t)$$

By using the boundary condition $P_{\text{adhesion}}(t=0)=1$ the instantaneous binding at contact between tip and surface is taken into account and the missing k_{bind} term accounts for the inhibited rebinding

$$P_{\text{adhesion}}(t) = e^{-k_r t}$$

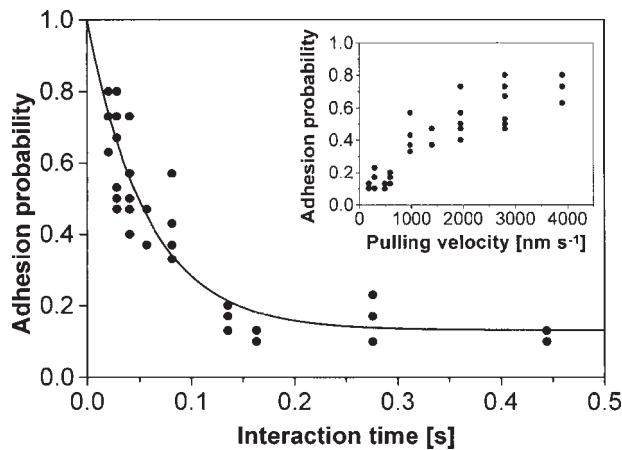
The time dependent adhesion probability between a selectin functionalised surface and an AFM tip functionalised with carbohydrate ligands reflects the fast forced off-rate $k_r(f)$ of the binding (Fig. 7).¹⁰⁰

The state diagram for leukocyte adhesion under flow⁹⁶ is shown in Fig. 8. The dynamic states of adhesion are controlled by bond physical chemistry (dissociative properties, association rates and elasticity). As already mentioned above, bond formation is a stochastic process. Knowledge of the responsiveness of a bond to force is important to complete understanding of molecular interactions.⁷³

Experimental k_r^0 and γ values from the literature for molecules that are known to mediate rolling adhesion mostly fall within the rolling region of the state diagram.

With the adhesive dynamics model, the dynamics of cell attachment, rolling and firm adhesion to a surface in flow can be simulated.¹⁰² The state diagram (which must be mapped for each receptor–ligand system) presents a concise and comprehensive means of understanding the relationship between bond functional properties and the dynamics of adhesion mediated by receptor–ligand bonds.

The scientific investigations of leukocyte endothelium adaptive adhesion interaction has already lead to the development of technological devices. Sakhalkar and co-workers engineered leukocyte inspired biodegradable particles that selectively and avidly adhere to inflamed endothelium *in vitro* and *in vivo*.¹⁰³ Leukocyte–endothelial cell adhesive particles exhibit up to 15-fold higher adhesion to inflamed endothelium, relative to non-inflamed endothelium, under *in vitro* flow conditions

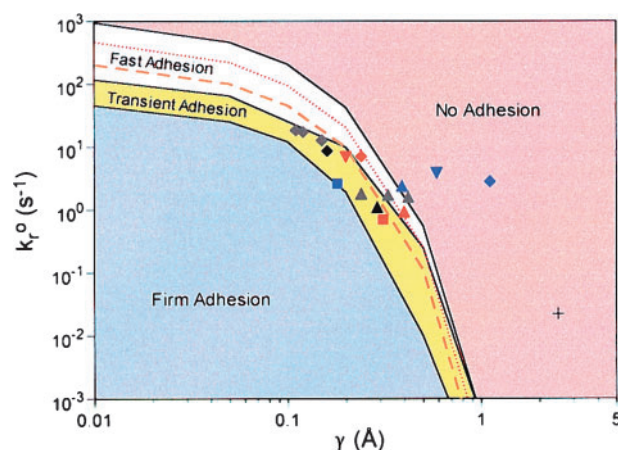


7 Time dependent adhesion probability between selectin functionalised surface and AFM tip functionalised with carbohydrate ligands reflects fast forced off-rate $k_r(f)$ of binding; interaction time was varied upon changing AFM pulling velocity (inset); each data point represents 30 approach retraction cycles; decrease in adhesion probability after long interaction times corresponds to lifetime of complex in AFM experiment of about 70 ms; from Ref. 100, National Academy of Sciences, USA, 1998

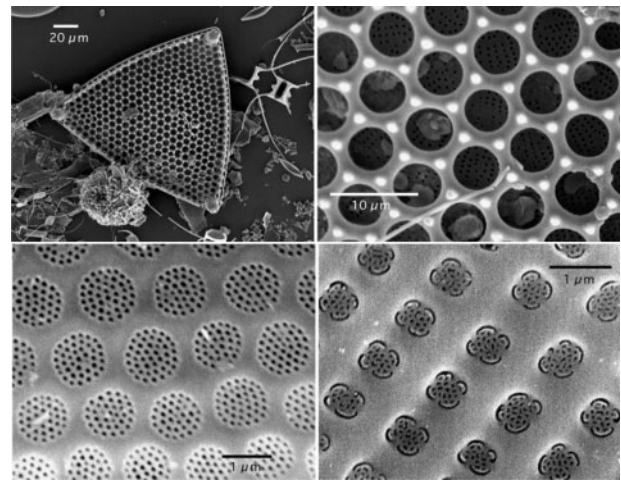
similar to that present in blood vessels. The leukocyte inspired particles have adhesion efficiencies similar to that of leukocytes and were shown to target each of the major inducible endothelial cell adhesion molecules that are up-regulated at sites of pathological inflammation. This opens the potential for targeted drug delivery to inflamed endothelium.

Recently, Chang and co-workers report a biomimetic technique for adhesion based collection and separation of cells in a microfluidic channel. By mimicking leukocyte endothelium adhesive interactions, cells can be captured and concentrated from a continuously flowing sample.¹⁰⁴

This chapter has demonstrated the intricate interweaving of fluid mechanics and the molecular mechanisms of cell adhesion that continuously occur in the blood stream. Our understanding of these mechanisms



8 State diagram for adhesion: four different states are labelled; dotted curve represents velocity of $0.3V_H$ and dashed curve represents velocity of $0.1V_H$; experimentally obtained Bell model parameters lie almost entirely within envelope for rolling; from Ref. 96, National Academy of Sciences, USA, 2000



9 Diatoms are micrometre small algae that biomineralise naturally nanostructured glass boxes: SEM shows delicate structure of these boxes; from Ref. 106, Maney Publishing, The Institute of Materials

and how they are modulated by shear stress is currently in the initial stages, but this knowledge is vital when we want to use the mechanisms for technological applications like switchable adhesives. Knowledge of the fundamental cellular and molecular mechanisms involved in adhesion and mechanical force modulation of metabolism under conditions that mimic those seen *in vivo* is essential for real progress in engineering.

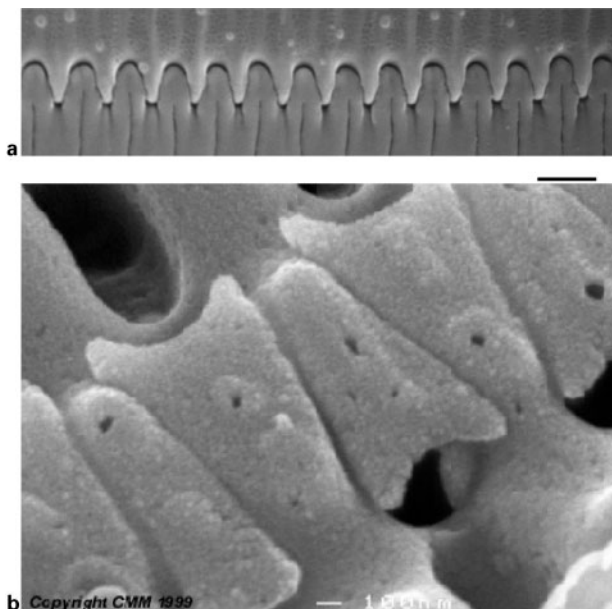
Diatom tribology

Diatoms are unicellular microalgae with a cell wall consisting of a siliceous skeleton enveloped by a thin organic case.¹⁰⁵ The cell walls of each diatom form a pillbox-like shell consisting of two parts that fit within each other like a shoebox. These micro-organisms vary greatly in shape, ranging from box shaped to cylindrical; they can be symmetrical as well as asymmetrical and exhibit an amazing diversity of nanostructured frameworks (Fig. 9, from Ref. 106).

Diatoms can serve as model organisms for micro- and nanotribological investigations.^{7,107–113} These organisms make (at ambient conditions) nanostructured glass surfaces of intricate beauty, some diatom species have rigid parts in relative motion acting like rubber bands and, furthermore, some diatom species have evolved strong, self-healing underwater adhesives.¹⁰⁶ Diatoms are small, mostly easy to cultivate, highly reproductive, and since many of them are transparent, they are accessible to different kinds of optical microscopy methods.

Diatoms are found in both freshwater and marine environments, as well as in moist soils, and on moist surfaces. They are either freely floating (planktonic forms) or attached to a substrate (benthic forms) via biogenic adhesives, and some species may form chains of cells of varying lengths. Individual diatoms range from $2\ \mu\text{m}$ up to several millimetres in size, although only few species are larger than $200\ \mu\text{m}$. Diatoms as a group are very diverse with 12 000 to 60 000 species reported.^{114,115}

Some of the diatom species that are of relevance for tribological research are presented below. Future work might add further interesting species to this list. The discussion of tribologists and nanotechnologists with diatomists has started some years ago. In 1999,



10 a structural details of *Ellerbeckia arenaria* (adapted from Ref. 119, The Royal Microscopical Society, 2003) and b another diatom species, possibly *Melosira sp.* (Centre for Microscopy & Microanalysis, University of Queensland, Australia)

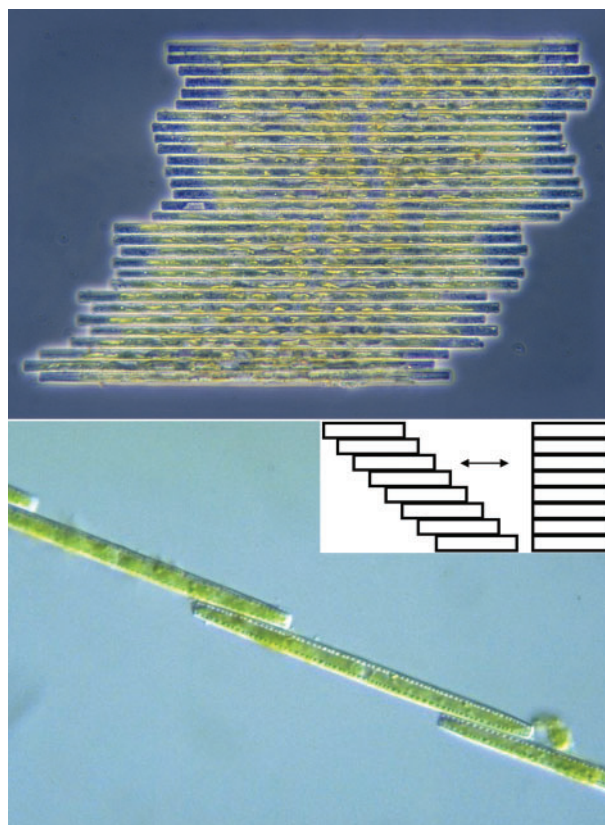
Parkinson and Gordon pointed out the potential role of diatoms in nanotechnology via designing and producing specific morphologies.¹¹⁶ In the same year, at the Fifteenth North American Diatom Symposium, Gebeshuber and co-authors introduced atomic force microscopy and spectroscopy to the diatom community as new techniques for *in vivo* investigations of diatoms.¹¹⁷ These scanning probe techniques allow not only for the imaging of diatom topology, but also for the determination of physical properties like stiffness and adhesion (see Refs. 106 and 118–122).

The January 2005 special issue of the Journal of Nanoscience and Nanotechnology (called ‘Diatom Nanotechnology’, edited by Richard Gordon) is a representative example for this fruitful exchange. No sign of wear has ever been found on diatom shells.¹²³

The first diatom species presented here is named *Ellerbeckia arenaria*. This freshwater diatom lives in waterfalls, the single cells are connected with each other, and they form stringlike colonies that can be several millimetres long. A microstructural example of an interconnection in *E. arenaria* (and one in another species found in a swimming-pool filter, possibly *Melosira sp.*) is given in Fig. 10.

The string-like colonies of *E. arenaria* are attached to moss and calcite particles, and have to be flexible at least in one direction to withstand the shear forces in the waterfall without breakage of the glass shells. Colonies of *E. arenaria* can be elongated by about one third of their original lengths. When released, they swing back like springs!¹⁰⁸ This interesting rubber band-like reaction results in parts in relative motion in this species, coping with friction.

In 2003 we reported atomic force microscopy investigations on three different freshwater diatom species *in vivo*.¹¹⁹ In one of these species, bead-like features on the edges of girdle bands (parts of the shoebox-like silica case that move against each other like



top photo: Wim van Egmond (<http://www.micropolitan.org>); bottom photo: Protist information server (<http://protist.i.hosei.ac.jp>); inset: own work

11 Light microscopy images of *Bacillaria paxillifer*, formerly called *Bacillaria paradoxa*: *B. paxillifer* is capable of active movement; single cells, about 100 μm long, slide against each other (see inset); shifting from stack of cells (top photo) to elongated band (bottom photo), and back again; movies on *B. paxillifer* motion can be found on the Internet

parts of a telescope while the diatoms elongate and grow) were found. These beads might act as lubricants, e.g. by means of ball bearings.

A friction coefficient of 0.0007 was once recorded under high load using hyaluronan acid (see above, section on synovial joints) as the carrier for SAPL, and this challenge has been taken up very recently.⁴⁶ A lubrication mechanism occasionally proposed envisages lamellar bodies, or rolls of SAPL and hyaluronan acid,^{48,50} acting as roller bearings (or dry lubricants), but usually, biological tissue would seem far too compliant (deformable) to act as the track for an effective ball race. The diatoms might be exceptions to this. This theory might be developed further once the material of the bead-like features on the edges of girdle bands mentioned above is determined.

Some diatom species are capable of active movement. Examples for this are *Pseudonitzschia sp.* and *Bacillaria paxillifer* (the former name of this diatom is *Bacillaria paradoxa*, because of its unusual behaviour, Fig. 11). *B. paxillifer* shows a remarkable form of gliding motility: Entire colonies of five to 30 cells expand and contract rhythmically and – as it seems – in coordination.¹²⁴ Anomalously viscous mucilage excreted through a fissure that covers much of the cell length, may provide the means for the cell to cell attachment.¹²⁵

Consequently, *Pseudonitzschia sp.* and *Bacillaria paradoxa* join *Ellerbeckia arenaria* and the unknown species with the bead-like features as our candidates for bionanotribological investigations.

As mentioned above, diatoms may occur freely floating in the water, or attach to substrates via biogenic adhesives. There are even diatom species that attach to ice via ice binding proteins.¹²⁶ Understanding natural adhesives opens opportunities to tailor new synthetic adhesives. Advances in composites have emphasised the need for durable adhesives that work in wet environments. Systematic investigation of the relationship between modular structure and adhesive function could lead to generic glue that can be modified at the molecular workbench for any number of different moist environments.¹²⁷ Diatoms have evolved adhesives that are stable and strong in wet environments¹⁰⁶ and scientific investigation of these adhesives might lead to important contributions to a new kind of underwater glue. Also, the winter tire industry would greatly benefit from a switchable adhesive functioning in wet environments.

The production of biominerals (such as calcium carbonate in snail shells, strontium sulphate in radiolaria, silicon dioxide in diatoms, and about 50 more in various kinds of organisms) always involves proteins. Silaffins, the proteins involved in silica formation in diatoms, were recently used as structuring agents to produce holographic nanopatterning of silica spheres.¹²⁸

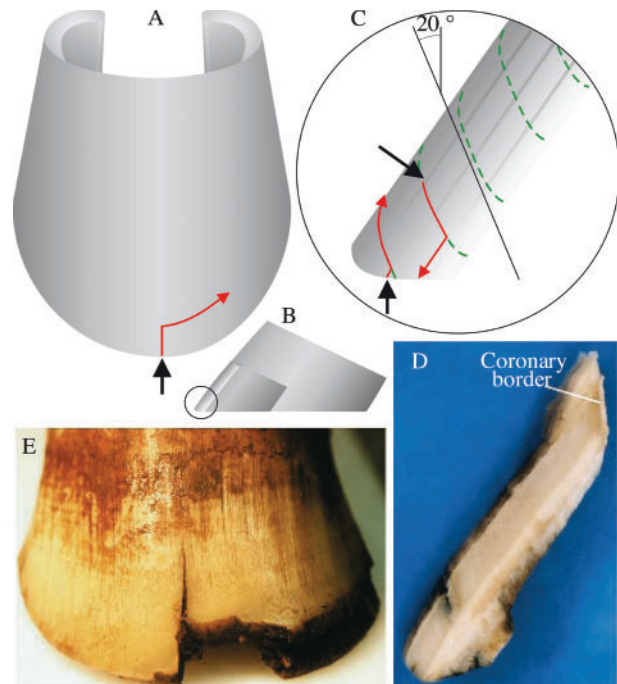
Leuwenhoek (1632–1723) used the distinct patterns on diatoms to test the resolution of his light microscopes. The diatom *Pleurosigma angulatum* has been among the microscopist's favourite specimens for more than 100 years. The 0.65 μm spacing of its pores in hexagonal arrangement makes it a suitable test object for objectives.

In the near future, we might even be able to develop the kind of nanostructure we want (e.g. via a compustat, see Refs. 129 and 130) and replicate them in large numbers via the natural way diatoms replicate – cell division. This conveyor belt type production will yield nanostructures that can be used in technological applications. The material of the diatom nanostructures is silicon dioxide, but as Sandhage and co-workers have shown, the silicon and oxide atoms can stepwise be replaced, yielding exactly the kind of material we want.^{131,132} Summing up, diatoms are perfect little beauties, offering a thesaurus to science and technology.

Other biological model systems of possible interest to tribologists

Horse hoof – tailored shape of wear particles

The toughest materials are known to raise the energy required for tearing by diverting cracks away from their preferred directions of propagation. This is relevant concerning the macroscopic wear particles that originate from horse hoofs: more often than not they are of rectangular shape. A horse's hoof is difficult to split vertically (in the direction up the horse's leg, Fig. 12, from Ref. 133). Hoof material contains keratin, a protein based fibre reinforced nanoscale composite, which is also the major component in horn, nail, claw and feather (Fig. 13, from Ref. 134). In the hoof, the keratin is arranged in an ordered three-dimensional array such that a crack initiated by a vertical cut will



(A) circumferential redirection of cracks; (B) side view of hoof wall with portion of toe and quarter removed; (C) magnified view of circled portion in (B) showing two other example directions of crack initiation and likely routes of crack redirection; (D) block of hoof tissue; (E) example for redirection of crack in hoof

12 Functional design for crack control: equine hoof, from Ref. 133, The Company of Biologists Limited, 1999

turn and split the material at right angles to the vertical direction (circumferentially in the hoof).^{133,134} Studies of the mechanisms of synthesis of hoof material in the horse can be expected to provide hints for the industrial fabrication of such complex three-dimensional fibrous materials.

Biomolecules

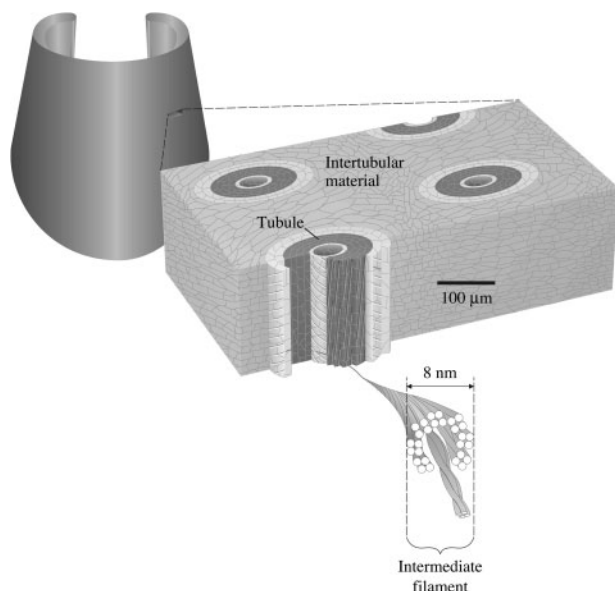
Biomolecules such as proteins and amino acids are defined in their structure down to the atomic level. They are materials built with molecular precision. In many cases, small changes in their three-dimensional structure would render them unfunctional.

Chaperones are large biomolecules that help other proteins to fold correctly. Generally, chaperones consist of a bucket like part and caps, and when a protein is repaired by the chaperone, the cap and bucket enclose the misfolded protein, and refold the protein correctly in a chain of conformational changes.¹³⁵

This molecular nanomachine is determined in its structure down to the single atoms. Wear in such a system during conformational changes would change the composition of the proteins.

Discussion, conclusions and outlook

Current man-made adhesives and lubricants are not perfect, and the low friction coefficients in many natural systems are yet to be achieved in man-made systems. Biotribologists gather information about biological surfaces in relative motion, their friction, adhesion, lubrication and wear, and apply this knowledge to technology.



- 13 Keratin is nanoscale composite that is main component of hoof material: Keratins have filamentous and matrix phases that are believed to have analogous roles to those in phases of fibre reinforced composites; from Ref. 134, The Company of Biologists Limited, 1999**

Innovations, completely new ideas, unconventional approaches, all this we can learn from nature. These approaches have been tested and improved for millions of years; they are continuously being optimised regarding their function and environment.

Natural systems occupy niches and specialise more and more inside them, yet in many cases keep open backup options in case of changed environmental conditions.

However, the thermal and hydrolytic sensitivities of biological material limit their applicability in many important synthetic materials applications. Furthermore, organisms cannot choose the materials they use, but are subject to phylogenetic restrictions. A real technological breakthrough requires an understanding of the basic building principles of living organisms and a study of the chemical and physical properties at the interfaces, to control the form, size and compaction of objects. Generalisation of the methods of controlled synthesis to new classes of monomers thus becomes an important objective.

Engineers and materials scientists can learn by watching, imitating, understanding and generalising natural approaches to challenges concerning processes, materials as well as structure and function.

The perfect material comprises the following aspects in varying amounts:

- (i) it can be controlled over time
- (ii) it has the capacity of self-repair
- (iii) it disintegrates after use (can be integrated in bio-geo-chemical cycles)
- (iv) it is non-toxic and environmentally safe
- (v) it has 'smart', dynamic, complex and multi-functional properties
- (vi) it is energy efficient
- (vii) it shows heterogeneity
- (viii) it shows hierarchical structure
- (ix) it shows gradient properties.

Another recurring feature in natural systems is the high level of integration: miniaturisation whose object is to accommodate a maximum of elementary functions in a small volume, hybridisation between inorganic and organic components optimising complementary possibilities and functions and hierarchy. Hierarchical constructions on a scale ranging from nanometres to micrometres to millimetres are characteristic of biological structures introducing the capacity to answer the physical or chemical demands occurring at these different levels.¹³⁶

New technology produced by man must in the future respect the environment, be reliable and consume little energy during production and/or use (e.g. the biomimetic straw bale screw).¹³⁷ By elucidating the construction rules of living organisms, the possibilities to create new materials and systems will be offered.

The investigation of tribological principles in biological systems may be a path for realising lubricants and adhesives that comprise some of the above mentioned features.

A biomimetic and bioinspired approach to tribology should therefore be considered further.

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