Biotribology inspires new technologies

This review deals with natural biotribological systems and how they have inspired novel micro- and nanotechnological applications. The biogenic devices presented here have functional units in the micro- and nanometer regime and have been evolutionarily optimized over millions of years. The examples discussed comprise natural micromechanical systems made of nanostructured silica (diatoms produce hinges and interlocking devices on the micrometer scale and below), adhesive molecules (selectin and integrin) that can switch states and account for white blood cell rolling in endothelial cells, dry adhesives as they occur on the Gecko foot and certain insect attachment pads, and single molecules that serve as strong self-healing adhesives (diatom underwater adhesives, abalone shell proteins).

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All organisms face tribological challenges. Surfaces in relative motion occur, for example, in joints, in the blinking of an eye, or a fetus moving in a mother's womb. While humans have researched the field of tribology for several thousand years, nature has been producing lubricants and adhesives, as well as optimizing materials and junctions, 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 miniaturization of technological devices such as hard-disk drives and biosensors increases the necessity for a fundamental understanding of tribological phenomena at the micro- and nanometer scale[1–3]. In micro- and nanotribology, at least one of the two interacting surfaces in relative motion has a 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[4]. Biological systems also excel at this scale and might serve as templates for developing the next generation of tools based on nano- and micrometer scale technologies[5].

Materials found in nature combine many inspiring properties such as sophistication, miniaturization, hierarchical organizations, resistance, and adaptability. The hydrodynamic, aerodynamic, wetting, and adhesive properties of natural materials are remarkable and often

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converge on limited constituents or principles. Elucidating those selected by evolution allows for the development of more reliable, efficient, and environment-respecting materials[6].

Another recurring feature in natural systems is the high level of integration: miniaturization, the object of which is to accommodate maximum elementary functions in a small volume; hybridization between inorganic and organic components to optimize complementary possibilities and functions; and hierarchy.

However, the thermal and hydrolytic sensitivities of biological materials limit their applicability in many important synthetic materials applications. Secondly, organisms cannot choose the materials they use, but are subject to phylogenetic restrictions (i.e. they have to pertain to evolutionary history). A real 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[6].

Life itself is still a miracle. Organisms are open complex systems riding on a trajectory far away from the thermal energy minimum. Engineers and materials scientists can learn by watching, imitating, understanding, and generalizing natural approaches to challenges. The new technology we build in the future should be recyclable and sustainable, reliable and energy efficient. By elucidating the delicate and intricate assembly of living organisms, it will be possible to create new materials and systems.

The following sections focus on four biological examples with amazing tribological properties. Diatoms are algae just a couple of micrometers in size that have rigid surfaces in relative motion and have evolved self-healing adhesives, nanostructured amorphous silica surfaces, and interconnected junctions[7]. White blood cells serve as the police of the body's immune system. 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 controlled deployment of anti-inflammatory agents in our bodies[8]. The Gecko can easily climb up walls and run on ceilings. The measurement of the adhesive force exerted by a single Gecko hair[9] has opened a new field of research: dry adhesives. Tough underwater adhesives produced by diatoms[10] and the molecular mechanistic origin of the 'glue' responsible for the high fracture resistance of the abalone shell[11] conclude the biological examples.

These and other natural systems show great potential as model systems for innovations in micro- and nanotechnology. This review will describe some of the first devices based on bioinspired materials:

- A diatom-based sensor for nitric oxide gas;
- A technique for cell separation inspired by the selectin/integrin complexes;
- Some devices inspired by the Gecko's foot, such as wall-climbing robots; and
- Artificial hierarchical, as well as novel, adhesives.

Biotribological model systems

Diatoms – creators of glass castles

Diatoms are unicellular microalgae with a cell wall consisting of a siliceous skeleton enveloped by a thin organic case[7]. The cell walls of each diatom form a pillbox-like shell consisting of two parts that fit within each other. These microorganisms 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[7,12] (Figs. 1–3).

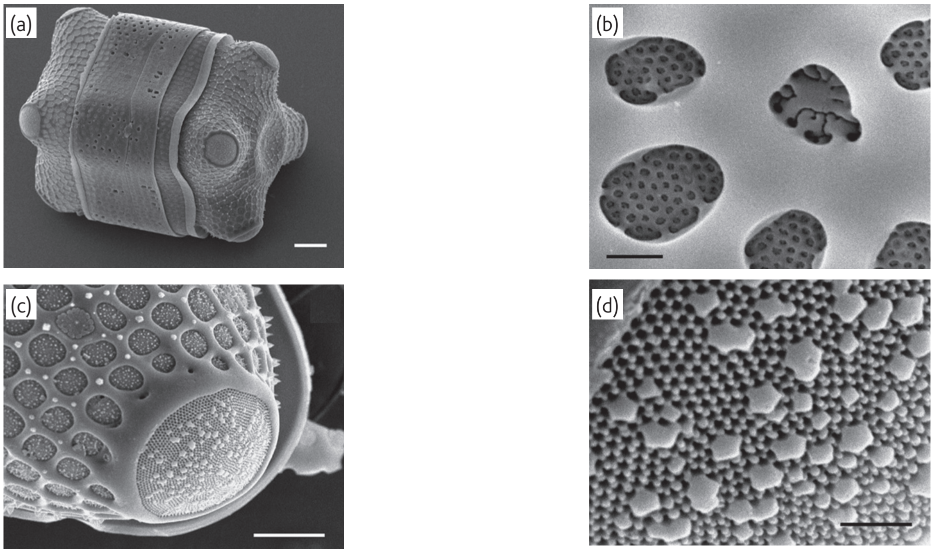

Fig. 1 Scanning electron microscopy (SEM) images of the diatom species Amphitetras antidiluvianum Ehrenburg. The sample was obtained from seaweed in Point Dume State Park, California. The whole cell can be seen in (a). The other images are close-ups of this cell. Scale bars: 20 μm (a), 1 μm (b), 5 μm (c), and 1 μm (d). (Reproduced with permission. © M. A. Tiffany.)

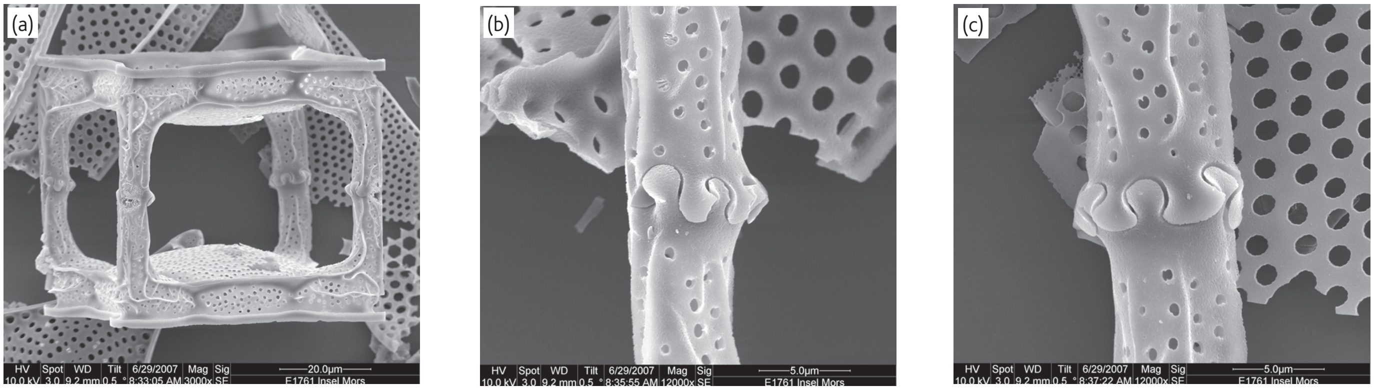

Fig 2. SEM images of an Eocene fossil (45 million years old) from a deposit at Mors, Denmark. (b) and (c) show the linking structures in more detail. Scale bars: 20 µm, 5 µm, and 5 µm, respectively. The sample is from the Hustedt Collection in Bremerhaven, Germany, # E1761. (Reproduced with permission. © F. Hinz and R. M. Crawford.)

Diatoms are found in both freshwater and marine environments, as well as in damp soils and on moist surfaces. They are either free 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 in size from 2 µm up to several millimeters, although only a few species are larger than 200 µm. Diatoms as a group are very diverse, with 12 000 to 60 000 species reported[12,13].

Diatoms can serve as model organisms for micro- and nanotribological investigations[14–16] and as templates for novel three-dimensional microelectromechanical systems (MEMS)[17,18]. In ambient conditions, these organisms produce nanostructured amorphous silica surfaces. Some diatom species have rigid parts that in relative motion act like rubber bands when elongated and subsequently released, whereas other diatom species have evolved strong, self-healing underwater adhesives[10]. Diatoms are small, mostly easy to cultivate, highly reproductive, and, since many of them are transparent, are accessible using optical microscopy methods.

The discussion of tribologists and nanotechnologists with diatomists started some years ago. No sign of wear has ever been found on diatom shells[19]. In 1999, Parkinson and Gordon[20] pointed out the potential role of diatoms in nanotechnology via designing and producing specific morphologies. In the same year, at the 15th North American Diatom Symposium, Gebeshuber and coauthors[21] introduced atomic force microscopy and spectroscopy to the diatom community as new techniques for *in vivo* investigations of diatoms. These scanning probe techniques not only allow for the imaging of diatom topology, but also for the determination of physical properties like stiffness and adhesion[10,22–26]. A representative example of the fruitful exchanges in the area of diatom nanotechnology can be found elsewhere[27].

Some diatom species are even capable of active movement. Examples of this are *Pseudo-nitzschia sp*. and *Bacillaria paxillifer* (the former name of this diatom is *Bacillaria paradoxa* because of its unusual behavior, Fig. 3). *B. paxillifer* shows a remarkable form of gliding motility: entire colonies of 5–30 cells actively move through the water by rhythmical expansion and contraction of the whole cell colony. The single cells glide against each other – as it seems – in coordination[28]. Anomalously viscous mucilage excreted through a fissure that covers much of the cell length may provide the means for the cell-to-cell attachment[29].

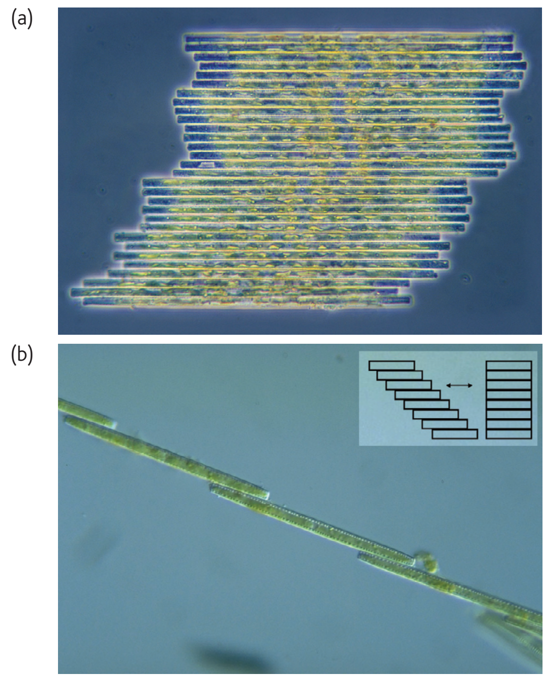

Fig. 3 Light microscopy images of Bacillaria paxillifer. The single cells, which are about 100 µm long, slide against each other (see inset). The movement goes from a stack of cells (a) to an elongated band (b), back to the stack, and then to an elongation once more. Movies on B. paxillifer motion can be found on the internet. (Part (a) Reproduced with permission. © Wim van Egmond, http://www.micropolitan.org. Part (b) Reproduced with permission. © Y. Tsukii, http://protist.i.hosei.ac.jp/. Inset is author's own work.)

Hinges and interlocking devices in diatoms are very stable and can still be seen in fossil deposits millions of years old. In 2006, Gebeshuber and Crawford[17,18] presented scanning electron microscopy (SEM) images of extinct and recent diatom species with linking structures with the aim of showing a correlation between structure and function. Fig. 2 shows four connections of two *Solium exsculptum* sibling cells that lived 45 million years ago and are still in good condition.

Perhaps we might even soon be able to evolve the kind of nanostructures we want and replicate them in large numbers via the way diatoms naturally replicate – cell division: a compustat[30,31] could monitor diatom properties and selectively destroy cells that do not evolve in the desired direction. In this way, directed evolution is taking place. This conveyor belt-type production could yield nanostructures for use in technological applications.

Switchable adhesives

The understanding of adhesives on the molecular level is important for engineering tailored synthetic adhesives. Depending on the application, either increased adhesion or effective anti-adhesive mechanisms are necessary. For example, nanorobots floating in the blood stream, acting as microsurgeons, should not aggregate and must therefore exhibit strong nonadhesive properties with regard to the environment[32]. On the other hand, good adhesive interaction of implant surface with surrounding tissue is a necessity. Furthermore, implants should not cause immune reactions via the generation of small wear particles[33].

The interaction of white blood cells with blood vessels shows adaptive adhesion features. Physiologically, white blood cells 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 liter of healthy adult blood. The size of a white blood cell is about 10–20 μm. White blood cells are capable of active amoeboid motion, a property that allows their migration from the blood stream into tissue[34].

White blood cells in the circulation may stop at a particular site as a result of interactions with the layer of cells that lines the blood vessel walls (the endothelium) or the subendothelial matrix[35].

Traditionally, the endothelium is thought to be specialized to resist adhesive interactions with other cells. However, such interactions do occur during certain important biological events like blood cell migration through the blood vessel to the site of inflammation. Further details of these interactions can be found elsewhere[36].

White blood cell adhesion to the endothelium plays a central role in inflammation. Adhesion molecules on the white blood cells and the endothelium regulate cell interactions during this process. The adhesion of white blood cells is mediated by adhesion molecules and also by the force distribution present in the blood vessel[37]. The specific molecular mechanisms of adhesion often vary with the local wall shear stress[38,39]. 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. Physiological levels of venous and arterial shear stresses range between 0.1–0.5 Pa and 0.6–4 Pa, respectively.

Initially, white blood cells move freely along with the blood stream. White blood cell adaptive adhesion involves a cascade of adhesive events[40] 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[8] (Fig. 4). After initial tethering, white blood cells may detach back into the free stream or begin to roll in the direction of the blood flow[37]. Their rolling velocity is typically 10–100 times lower than a nonadherent white blood cell moving next to the vessel wall.

The rolling velocity is not constant and the cells tend to speed up and slow down as they roll along the endothelium. At some point, the white blood cell may become activated, i.e. adheres firmly to the endothelium, and might migrate through the blood vessel to the site of inflammation.

Lawrence and coworkers[39,41,42] have examined white blood cell adhesion to certain endothelial cells under well-defined flow conditions *in vitro*. The initial flow studies were followed by many further studies both *in vitro*[43–47] and *in vivo*[48–51], which clearly distinguish separate mechanisms for initial adhesion/rolling and firm adhesion/white blood cell 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 white blood cell migration are mediated primarily by integrin/peptide interactions (at the site of inflammation)[52].

Integrins are the most sophisticated adhesion molecules known. They can be found, for example, on the surface of a white blood cell. In less than a second, signals from other receptors on the cell are transmitted to its integrin extracellular domains, which undergo

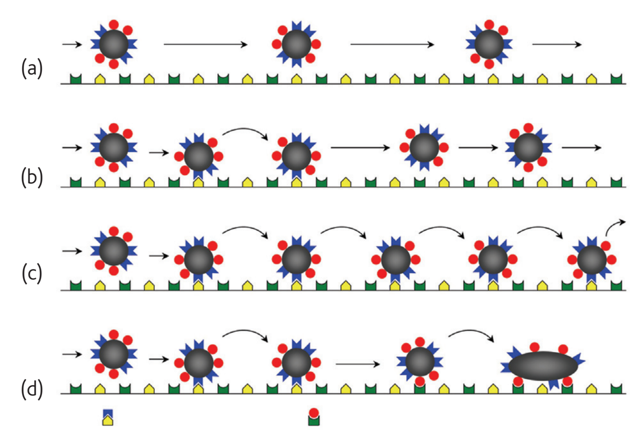

Fig. 4 White blood cell adhesion to the endothelium. (a) No adhesion: the cells contact the surface but do not bind. (b) Transient adhesion mediated by selectin molecules: the cells bind very briefly and then lose contact again. (c) Rolling adhesion mediated by selectin molecules: cells bind and translate along the surface at a reduced velocity compared with bulk fluid velocity. (d) Firm adhesion mediated by integrin molecules: the cells bind strongly to the surface and move at a very slow rate. (Blue: selectin; yellow: selectin ligand; red: integrin receptor; green: integrin ligand.) (Adapted from[8].)

conformational movements (changes in their molecular arrangement) that enable ligand binding (i.e. the adhesives switch from a nonadhesive to an adhesive state). These unique, switchable adhesives rapidly stabilize contacts between white blood cells in the bloodstream and the endothelium at sites of inflammation[53].

Characterization of the molecular and cellular properties that enable such a transient form of adhesion (which would be of interest for a variety of technological applications, e.g. for grippers) under the high forces experienced by cells in blood vessels has been investigated by a multitude of groups, experimentally as well as theoretically[53–58].

In inflammation, firm adhesion can be mediated by activated integrins once the white blood cells have been slowed by selectin mediated rolling[42,50]. Integrins can also mediate firm adhesion when activated[59,60] 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 are coded by the physical chemistry of adhesion molecules, and not by cellular features such as deformability, morphology, or signaling[61,62]. 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. Adhesion is also dependent on the magnitude of the force applied to the cells.

Gecko attachment pads

The Gecko is an amazing animal. It can rapidly climb up vertical glass surfaces, it can climb on ceilings. Microscopy shows that the Gecko foot (Fig. 5) has about 14 400 hairs (setae) per square millimeter, covered with even smaller projections only hundreds of nanometers in diameter. The adhesive force of a single Gecko foot-hair is 600-fold greater than that of frictional measurements of the material. On the other hand, highly orientated setae reduce the detachment force of the foot by simply detaching above a critical angle with the substratum[9]. There is strong evidence that the adhesion force in the Gecko is mediated via van der Waals interactions[63].

The Gecko foot also exhibits self-cleaning properties. Autumn and coworkers[64] have found that the self-cleaning effect is simply a result of the attraction for dirt being slightly less than for the surface on which the Gecko is walking. This results in a net cleaning effect. Their mathematical models suggest that self-cleaning in Gecko setae is a result of geometry not chemistry, thereby opening up the possibility of constructing synthetic self-cleaning adhesives from a wide variety of materials.

Self-healing adhesives

Diatoms may be free floating or attached to substrates in seawater, fresh water, or on moist surfaces. Diatoms have evolved adhesives that can mediate stable and strong attachment in wet environments[10]. There are even diatom species that attach to ice via ice-binding proteins[65]. Understanding natural adhesives such as the ones produced by diatoms opens up opportunities to tailor new synthetic adhesives for specific applications.

Atomic force spectroscopy investigations of the adhesives certain diatoms produce to attach to surfaces have shown a multimodular structure and self-healing behavior[10,21]. As Dugdale and coworkers[66]

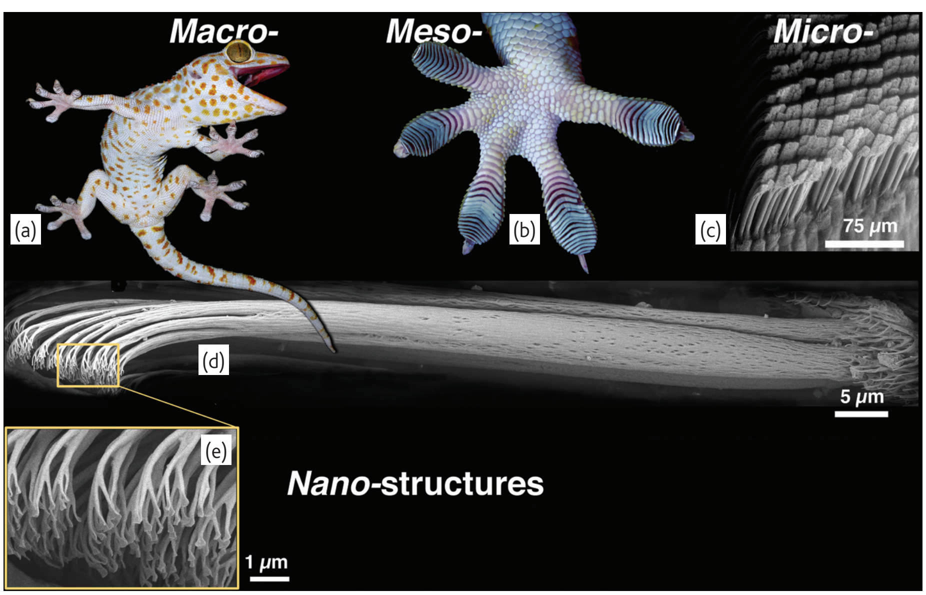

Fig. 5 The Gecko foot shows a hierarchical adhesive system. (a) Gecko climbing a glass surface. (Photograph courtesy of M. Moffett). (b) Gecko foot. (Photograph courtesy of M. Moffett). (c) Microstructure of the Gecko foot. There are about 14400 hairs (setae) per square millimeter. (d) and (e) show the nanostructure of the Gecko foot: each single Gecko seta has hundreds of tiny spatular tips. (Photograph reproduced with permission from K. Autumn and S. Scherf.)

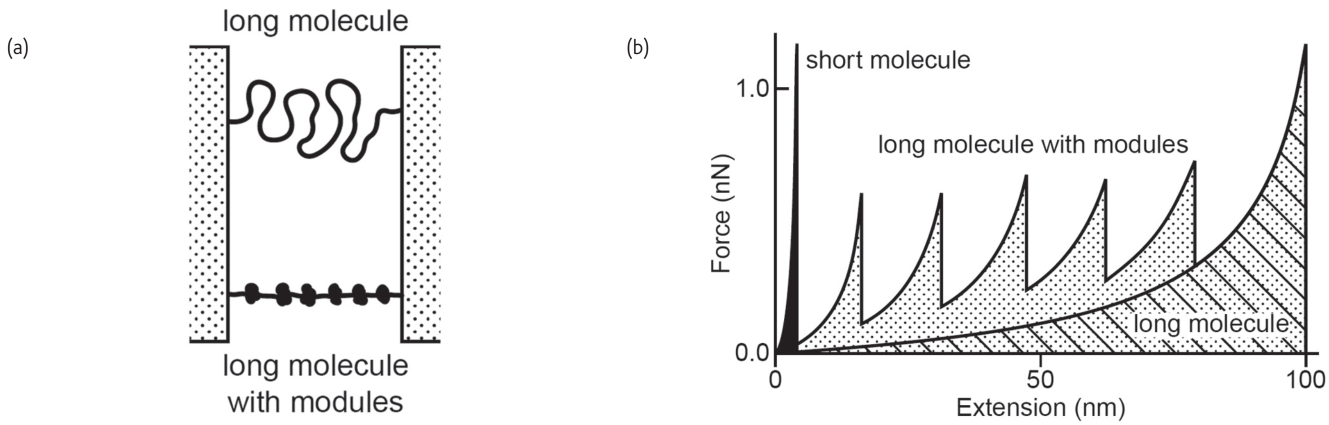

Fig. 6 (a) Two surfaces held together by long molecules. The lower molecule has modules, i.e. it has compacted modules in which domains are held together with sacrificial bonds. (b) Force-extension curves. Short molecules can only be extended for a small amount and then break. A long molecule can be extended considerably further until it breaks. A long molecule with modules, however, resists pulling even at small extensions. Before the molecule breaks, other modules unfold and the energy required to break the molecule (dotted and striped areas under the curves) is large. (Reproduced with permission from[11]. © 1999 Nature.)

showed in 2005, single adhesive nanofibers from a live diatom have the signature fingerprint of modular proteins: their force-extension curves have regular sawtooth patterns.

Another biological system where multimodular self-healing molecules can be found is the abalone shell. The main constituent of the abalone shell is calcium carbonate. Only about 3% of the shell is made up of organic components. Nevertheless, the fracture resistance of the nanocomposite nacre is about 3000 times higher than for the pure inorganic material. The nanocomposite nacre is formed by organic polymer adhesive molecules with sacrificial bonds and hidden lengths (unfoldable modules, Fig. 6) that hold together the hard calcium carbonate elements. In molecules with sacrificial bonds, molecular segments can be reversibly stretched by the breaking and rebonding of weak bonds (such as Coulomb, van der Waals or hydrogen bonds), dissipating large amounts of energy and thereby preventing the whole molecule from breaking[11] (Fig. 6).

Advances in composites have emphasized the need for durable adhesives that work in wet environments. Systematic investigation of the relationship between adhesive modular structure and function could lead to a generic glue that can be modified at the molecular workbench for any number of different moist environments[67].

Biologically inspired technical systems

Diatom-based gas sensor

Sandhage and coworkers[68-71] have reported methods to produce pure Si replicas of diatom silica shells. In this way, micro- and nanostructured Si units with high surface area (>500 m^2g^{-1}) are obtained. These Si structures show rapid changes in impedance when exposed to gaseous nitric oxide with concentrations as low as 1 ppm[71] (Fig. 7). Such fast response and sensitivity cannot be matched by mesoporous silicon NO(g) sensors[72]. Furthermore, the bias voltage applied to the nanosensor developed by Sandhage and coworkers only

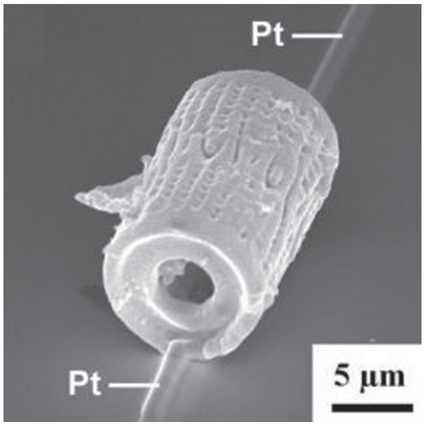

Fig. 7 A nitric oxide gas sensor created from a nanoporous Si structure converted from the shell of a single diatom. (Reproduced with permission from[71]. © 2007 Nature.)

needs to be about 100 mV, which is considerably smaller than the bias voltage needed in mesoporous devices.

Selectin/integrin-inspired technique for cell separation

Research of the white blood cell-endothelium adaptive adhesion interaction has already led to the development of technological devices.

Separating and isolating different cell types or molecules from a raw sample is a basic step in bio(nano)technology, especially in lab-on-a-chip (LOC) devices. LOC devices integrate multiple laboratory functions on a single chip of only a few square millimeters to a few square centimeters in size and are capable of handling extremely small fluid volumes down to less than picoliters. LOC devices are used in medical diagnostics, chemical analysis, and environmental monitoring, but also in synthetic chemistry, where they perform rapid screening or serve as microreactors for pharmaceutics[73].

Chang *et al*.[74] have reported successful adhesion-based capture and subsequent concentration of cells bearing ligands for selectin from a continuously flowing sample in a microfluidic channel that has been functionalized with selectin molecules. Captured cells show rolling adhesion and tethering before resuspension and are enriched on the substrate several hundred fold compared with the concentration in the original solution. Arrays of micropillars (made from Si prepared via deep reactive ion etching) with characteristic spacings somewhat larger than the size of cells (some tens of micrometers in diameter) were used. The Si surface is subsequently functionalized with physisorbed selectin. Control experiments show no nonspecific adhesive interactions between the cells and the microchannels[74].

Sakhalkar and coworkers[75] have reported engineered white-blood-cell-inspired biodegradable particles that selectively and avidly adhere to inflamed endothelium *in vitro* and *in vivo*. White blood cell endothelial cell adhesive particles exhibit up to 15-fold higher adhesion to inflamed endothelium relative to non-inflamed endothelium under *in vitro* flow conditions similar to that present in blood vessels. The white-blood-cell-inspired particles have adhesion efficiencies similar to that of white blood cells and are shown to target each of the major inducible endothelial cell adhesion molecules that are up-regulated at sites of pathological inflammation. This opens up the potential for targeted drug delivery to inflamed endothelium.

Gecko-inspired adhesives

Adhesion, as it is mediated by the Gecko foot, is attractive for technological applications because it is dominated by the intermolecular van der Waals forces that exist between all materials. A nanostructure can be applied directly to a surface – therefore it is conceivable that Gecko-like structures could replace screws, glues, and interlocking tabs in many applications[76].

A batch-fabricated, biomimetic, dry adhesive based on massively parallel MEMS processing technology has been introduced by Northen *et al*. in 2005[77] (Fig. 8). This multiscale fine hair adhesive system shows significantly improved adhesion compared with nonhierarchical organorod-covered substances.

Recently, the first synthetic dry adhesives with anisotropic frictional adhesion[78] and limited self-cleaning[79] properties have been developed. At the moment, no synthetic Gecko-foot-inspired device reaches the extraordinary properties of the biological template. Performance requirements for the synthetic adhesive are high attachment and low detachment forces, rough surface adaptation, self-cleaning ability, and durability[80].

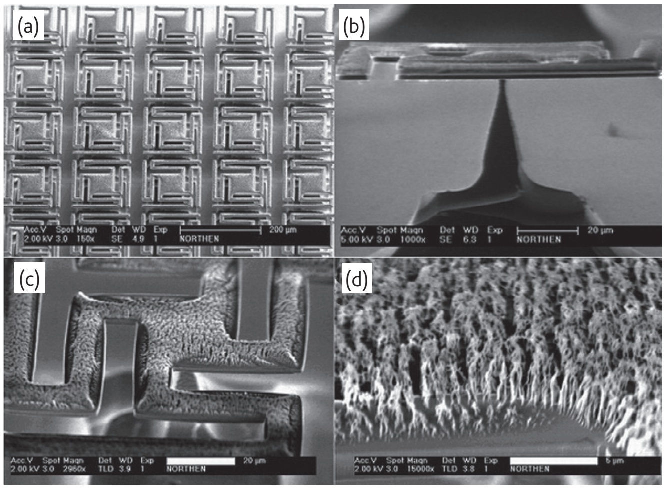

Fig. 8 SEM images of a biomimetic dry adhesive. (a) Large flexible SiO_2 platforms (scale bar 200 μm) are supported by (b) single high aspect ratio Si pillars (scale bar 20 μm). The platforms (c) are coated with 200 nm diameter organorods (d) approximately 2 μm tall and 50–200 nm in diameter (scale bars 20 μm and 5 μm, respectively). (Reproduced with permission from[77]. © 2005 IOP Publishing Ltd.)

Self-healing adhesive inspired synthetic adhesives

In 2007, Hansma and coworkers[81] reported how bioinspired optimized adhesives combined with carbon nanotubes or graphene sheets can yield strong, lightweight, damage-resistant nanocomposite materials. The inspiration came from their work on the abalone shell[11], diatom adhesives[10,21], and bone[82]. A basic common feature of all these biological nanocomposites is the small amount of adhesive needed. Excess adhesive can weaken the material. In an optimized synthetic nanocomposite, the amount of adhesive is just enough to fully transfer the desired load to the strong elements.

Discussion, conclusions, and outlook

Current synthetic adhesives and lubricants are not perfect, and the low friction coefficients in many natural systems are yet to be achieved in artificial systems. Technological innovations, completely new ideas, and unconventional approaches can all be learned from nature. These approaches have been tested and improved upon for millions of years; they are continuously being optimized with respect to their function and environment. The perfect material is not pure, homogenous, and with constant parameters, but can be controlled over time, has the capacity to self-repair, and disintegrates after disposal. Living systems possess all these abilities.

Biomicro- and nanotribology, the investigation of micro- and nanoscale tribological principles in biological systems, may be a path to realizing simultaneously 'smart', dynamic, complex, environmentally friendly (nontoxic, biodegradable, able to be integrated in biogeochemical cycles without sinks), self-healing, and multifunctional lubricants and adhesives. A biomimetic and bioinspired approach to tribology should therefore be considered further. nt

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