

# Nature Inspired Hay Fever Therapy

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## Abstract

The survival oriented adaptation of evolved biosystems to variations in their environment is a selective optimization process. Recognizing the optimised end product and its functionality is the classical arena of bionic engineering. In a primordial world, however, the molecular organization and functions of prebiotic systems were solely defined by formative processes in their physical and chemical environment, for instance, the interplay between interfacial water layers on surfaces and solar light. The formative potential of the interplay between light (laser light) and interfacial water layers on surfaces was recently exploited in the formation of supercubane carbon nanocrystals. In evolved biosystems the formative potential of interfacial water layers can still be activated by light. Here we report a case of hay fever, which was successfully treated in the course of a facial rejuvenation program starting in November 2007. Targeting primarily interfacial water layers on elastin fibres in the wrinkled areas, we presumably also activated mast cells in the nasal mucosa, reported to progressively decrease in the nasal mucosa of the rabbit, when frequently irradiated. Hay fever is induced by the release of mediators, especially histamine, a process associated with the degranulation of mast cells. Decrease in mast cells numbers implies a decrease in the release of histamine. To the best of our knowledge this is the first report on the treatment of hay fever with visible light. This approach was inspired by bionic thinking, and could help ameliorating the condition of millions of people suffering from hay fever world wide.

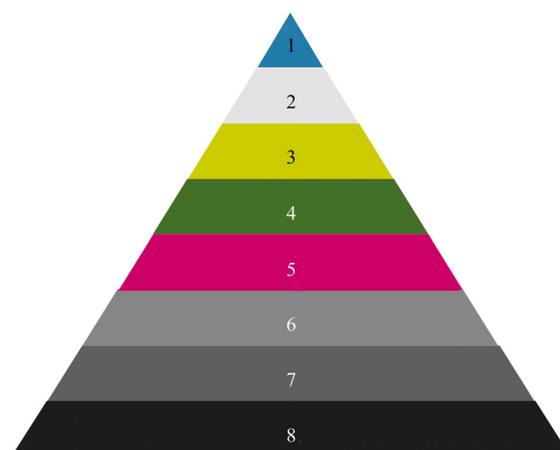
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## 1 Introduction

### 1.1 The biomimetic triangle

Earlier we introduced the biomimetic triangle, a hierarchic catalogue comprising eight precisely quantifiable physical and chemical determinants of biocompatibility (Fig. 1)<sup>[1]</sup>, allowing us to predictably design biomaterials. Here we demonstrate its versatility and show that it is not only instrumental in the design of biomaterials but also in the exploration and explanation of basic processes in biology and evolution. Apparently, the synthesis of first prebiotic polymers on earth occurred on hydrogenated diamonds by the interplay of six out of the eight determinants, i.e., the interfacial water layer, nanostructure, surface charge, chemistry, hardness and biodurability<sup>[2]</sup>. The remaining two determinants, the microstructure and elasticity are the typical fingerprint of evolved biosystems, which formed later. By a systematic analysis of different combinations of the



**Fig. 1** The biomimetic triangle is subdivided into three blocks consisting of long, medium and short term determinants of biocompatibility. The basic block includes biodurability (8), hardness (7) and elasticity (6); the second covers microstructure (5), chemistry (4), surface charge (3) and nanostructure (2); the third is the interfacial water layer (1) – the top of the biomimetic triangle. Determinants 2–8 have been characterized in a variety of laboratory experiments; their specific biological impacts have been studied individually. Determinant 1 has been only recently accessed experimentally.

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eight elements of the biomimetic triangle on the one hand, and by establishing a connection between the functions of these elements and anticipated primordial structures on the other hand, we introduce here a novel approach in bionic thinking, which is potentially capable to provide insight into a variety of actual complexes and offers unforeseen solutions to evolutionary, biological and biomedical problems.

Information on the nature of the top-element of the biomimetic triangle, i.e., the interfacial water layer, was extracted from experiments performed on synthetic (nanocrystalline) diamond<sup>[3]</sup>. The experiments indicated the presence of an ordered, crystalline water layer on hydrogen-terminated diamond. The relevance of the physical picture emerging from studies conducted on the surface of diamond can be understood by realizing that diamond is chemically inert. Chemical stability of the substrate is a precondition for the intrinsic inspection of interfacial water layers. It is known that their molecular structure is sensitive to both the substrate quality and means of observation.

## 1.2 Synthetic and natural diamonds

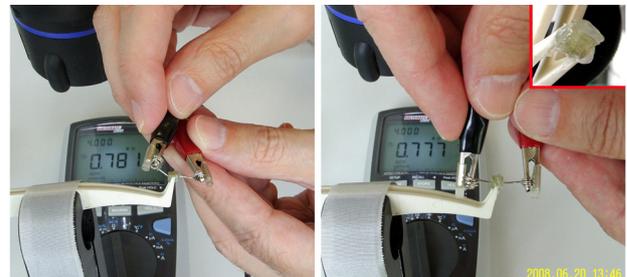
Remarkably, the currently accepted model of the surface conductivity on hydrogenated diamond, i.e., the transfer doping model<sup>[4]</sup>, demands the presence of a water layer on the diamond but does not specify its structure. On the basis the transfer doping model, the surface conductivity should increase with increasing relative humidity – and not decrease as reported in our previous work<sup>[3]</sup>. The interpretation of the tendency observed by us led to the discovery of a nanoscopic crystalline water layer on hydrogenated diamond. Unexpectedly, the prevalence of a crystalline water layer on the diamond, and its manifest implication in the phenomenon of surface conductivity, resulted in a new physical picture, which is incompatible with the current models. The new paradigm was subsequently severely challenged, specifically by the supposition that our results were unique to the synthetic diamond employed in our experiments<sup>[5,6]</sup>. Noting the key-experiment character of our previous work, in particular with regard to the crystalline structure of interfacial water layers on hydrogenated diamond, we recently repeated the surface

conductivity measurements, using a natural diamond cube, hydrogenated according to the aforementioned protocol. Clearly, there was no difference between the synthetic and natural diamond in the tendency of the dependence of the conductivity on the relative humidity<sup>[7]</sup>.

## 2 Material and methods

### 2.1 Physical section – water and diamonds

For additional clarity and to complete the work, we hydrogenated a natural diamond cube and measured its transversal conductivity by applying the platinum electrodes of an ohmmeter at two of its opposite sides (Fig. 2, left). We obtained in air resistances on the order of 1 M $\Omega$ . In order to interrupt a potential water layer adsorbed from the air onto the diamond, according to the transfer doping model a prerequisite for surface conductivity on hydrogenated diamond, we applied an equatorial belt of a Baysilone paste (a highly insulating viscous material) onto the diamond (inset in Fig. 2, right) and repeated the measurement by applying the electrodes at the same sides of the diamond cube, i.e., the paste-free sides normal to the Baysilone belt.



**Fig. 2** Conductivity measurements on a hydrogen-terminated natural diamond cube – before (left) and after application of an insulating belt consisting of a Baysilone paste (right). The platinum electrodes contact the paste-free facets of the diamond cube.

### 2.2 Biomedical section – A case study

In the model analyzing the formation of the first prebiotic polymers on Earth, we exploited the interplay of sun light with the top element of the biomimetic triangle (interfacial water layers) in the presence of five of the total of eight elements. Interestingly, in bionic modelling the analysis of the interplay of light with components of evolved biological systems does not inescapably involve the complete set of eight elements, as

opposed to the systematic design of biocompatible materials. On the basis of ample experimental evidence that interfacial water layers are tuneable by visible light applied at intensities of the terrestrial solar radiation<sup>[8,9]</sup>, we designed a facial rejuvenation program using an array of light emitting diodes (WARP 10, Quantum Devices, Inc. WI). Operating in the range 600 nm to 720 nm (central wavelength 670 nm, 50% relative spectral output 660 nm to 680 nm), it covers an area of 10 cm<sup>2</sup> with an integral light intensity of 728 W·m<sup>-2</sup>. The wavelength range used by us is outside the 760 nm to 1440 nm near-infrared window, found to possibly contribute to photoaging<sup>[10]</sup>. To exclude a possible inhibition of cellular functions, irradiation times were adjusted to local doses around 4×10<sup>4</sup> J·m<sup>-2</sup>, known to activate cellular functions and to transiently increase blood circulation<sup>[11]</sup>. Using this protocol, one of us started irradiating facial areas bilaterally, once per day (Fig. 3, left). The experiment started in November 2007. The initial expectation of the ongoing program was to reduce wrinkle levels by liberating elastin fibres from an osmiophilic interlayer, a cladding encouraging the conversion of the hydrophobic elastin to hydrophilic and promoting the formation of a viscous interfacial water layer<sup>[12-14]</sup> that is supposed to be involved in both loss of stretchability and immobilization of the fibres by the surrounding tissue matrix. In their liberated state the hydrophobic fibres necessarily carry a crystalline interfacial water layer, separating them from the matrix. Wrinkling, in particular



**Fig. 3** Photograph shows irradiation of facial area with WARP 10, a devise originally developed for self-aid administration under severe battlefield conditions, for instance, pain alleviation<sup>[26]</sup> (left) and raindrops on leaves (right). Even without a superhydrophobic structure, the interplay between leaf position, raindrops, moderate hydrophobicity and gravity equips many plant leaves with an efficient self-cleaning program. The images provide means to combat emerging allergies, the left using advanced technology, and the right using nature.

in the face, naturally a manifestation of aging, potentially accelerated by environmental factors, is thought to be partially triggered by the progressive deposition of osmiophilic groups (polar amino acids, fatty acids and calcium salts) on elastin fibres<sup>[15]</sup>. Using an experimental model, we demonstrated that crystalline water layers perform on hydrophobic surfaces a lubricating function and reduce dissipative effects<sup>[9]</sup>. Their biological functions, including lubrication, have been envisaged by Szent Györgyi in 1971<sup>[16]</sup>. Presumably, they are the key factor in maintaining the structural integrity of the elastin fibres, thereby granting their unique functionality. Whereas first results show a clear tendency of reduced wrinkle levels in response to the successively repeated irradiation, we observed as a manifest result of a change in the recurrent immune response.

### 3 Results and discussion

#### 3.1 Water structure on diamond

Although the diamond cube used in our experiment had an edge length of 5 mm, we observed resistances on the same order as without Baysilone belt (Fig. 2, right). Because of the electrically insulating belt interrupting the water layer on the diamond surface, we can safely assume that in the present scenario, the conductivity cannot be understood on the basis of the transfer doping model, which prerequisites a superficial water layer at the hydrogenated site of the diamond. Importantly, in both material forms, synthetic and natural diamond, the conductivity decreased in response to an increase in relative humidity<sup>[3,7]</sup>. Additional humidity reduces the crystalline order in the chains of the polarized proton conductive water molecules spanned between the platinum electrodes and diamond. Presently, this correlation – in conflict with the finding of others<sup>[5]</sup>, and their interpretation of our results<sup>[6]</sup> – is the strongest experimental confirmation for the prevalence of a crystalline water layer on a hydrophobic surface<sup>[3]</sup>. Its implication in the phenomenon of surface conductivity<sup>[17,18]</sup> is a strong challenge for the validity of the transfer doping model.

#### 3.2 Hay fever therapy – A bionic approach

Laboratory experiments performed by us suggest

that the synthesis of first prebiotic polymers on Earth occurred on diamonds<sup>[2]</sup>. Polymerisation of amino acids, the building blocks of proteins, is regarded as the most basic event in the formation of primordial life. The new paradigm was inspired by the coincidence of three observations: (1) Virtually all cells, including those of plants, animals and humans, respond to their irradiation with visible light, when applied at intensities in the range of the terrestrial solar radiation ( $\sim 1000 \text{ Wm}^{-2}$ ), (2) water becomes ordered at solid interfaces, and (3) light at intensities in the range of the terrestrial solar radiation interacts with interfacial water layers on both hydrophilic and hydrophobic surfaces, changing their order<sup>[19]</sup>. Physically, the interplay of non-destructive intensities of visible light with interfacial water layers on relevant biological surfaces (for instance the extra and intracellular membranes and proteins) is an ordering process, probably affecting cellular programs. The actual susceptibility of cells, genetically and evolutionary as different as those of plants, animals and humans, to similar light intensities is indeed a clear indication for an active role of the sun in the process of genesis on Earth. This excludes theories claiming that primordial life emerged from sun-deprived deep-sea volcanoes, and leaves room to the presumption that the actual susceptibility of different cells to light intensities in the range of the terrestrial solar radiation, even of those dormant in plant seeds<sup>[20]</sup>, is an evolutionary effect. The evolutionary perspective deserves attention and merits further study, in particular the potential of activation of programs in intact cells. In 2008 in the course of the facial rejuvenation routine all the characteristic symptoms of hay fever – very intense in previous years – disappeared in response to the daily WARP 10 irradiation. Hay fever is induced especially by histamine, a mediator released in association with the degranulation of mast cells. Targeting primarily the interfacial water layers on elastin fibres in the wrinkled areas of the face, we presumably also activated mast cells in the nasal mucosa – an interface directly interacting with the environment. Mast cells were reported to progressively degranulate and/or decrease in the nasal mucosa of the rabbit, when frequently irradiated with similar levels of light, likewise on the tongue of the mouse<sup>[21]</sup>. Decrease in mast cell

numbers implies a similar tendency in the release of histamine. It is worth noting that there is evidence for a climate change related rise in hay fever globally<sup>[22]</sup>. From this perspective, the bionic approach presented by us could help ameliorating the condition of millions of people suffering from hay fever world wide. Previously we proposed a nature inspired strategy to simultaneously cool the air and reduce  $\text{CO}_2$  concentrations and fine and ultrafine particle levels in it<sup>[23]</sup>. As illustration for its performance, we presented a photograph of a leaf with a large number of pollen on its surface. Elevated  $\text{CO}_2$  concentrations, and fine and ultrafine particle levels are blamed to worsen the body's response to pollen<sup>[22]</sup>. Consequently, spray irrigation of plant walls erected in suitable green zones promises reducing allergies and could be especially beneficial in highly polluted megacities. The functional interplay between the self-cleaning capacity of plant leaves (Fig. 3, right) and their scavenging capacity for airborne micro and nanoparticles operates with virtually all leaves, even without the lotus effect. Notably, both approaches – internal with light and external using plant walls – exploit not only the properties of interfacial water layers on surfaces but also the impact of light on them. The interaction of light wavelengths that are practically not absorbed by bulk water with interfacial water layers on solid surfaces was recently confirmed experimentally<sup>[24]</sup>. The ordering effect of interfacial water layers in combination with laser light has been exploited in the process forming supercubane carbon nanocrystals<sup>[25]</sup>. Experiments to test our model on a physiological level are in preparation.

#### 4 Conclusions

Machiavelli recommended to disoriented troops to return to the origin, i.e., to first principles. It is worth noting that the current strategy in bionic thinking is more or less restricted to the discovery of actual biological patterns and their conversion into products. Our approach suggests that bionic thinking can be considerably enriched by studying not only actual biological patterns but also by attempts to go back to the ancient principles of their emergence. Their study necessarily involves a strong speculative element. Nevertheless, even with the meagreness of the currently available authenticable data

and inevitably incomplete picture, we can design powerful predictive models and confirm them, *a posteriori*. Starting from the premise that the universal susceptibility of cells to light intensities of the order of the terrestrial solar radiation has its origin in the early days of evolution and is related to the ordering interplay between interfacial water layers – present on all surfaces – and light, we arrived to a powerful strategy to treat hay fever. More research is needed before the whole picture and its further implications become clear.

## References

- [1] Sommer A P, Zhu D, Wiora M, Fecht H J. The top of the biomimetic triangle. *Journal of Bionic Engineering*, 2008, **5**, 91–94.
- [2] Sommer A P, Zhu D, Fecht H J. Genesis on diamonds. *Crystal Growth and Design*, 2008, **8**, 2628–2629.
- [3] Sommer A P, Zhu D, Brühne K. Surface conductivity on hydrogen-terminated nanocrystalline diamond – Implication of ordered water layers. *Crystal Growth and Design*, 2007, **7**, 2298–2301.
- [4] Maier F, Riedel M, Mantel B, Ristein J, Ley L. Origin of surface conductivity in diamond. *Physical Review Letters*, 2000, **85**, 3472–3475.
- [5] Angus J C, Chakrapani V, Anderson A B, Wolter S D, Stoner B R, Sumanasekera G U. Response to A. P. Sommer et al.'s E-Letter. *Science Online*, [2008-2-28], <http://www.sciencemag.org/cgi/eletters/318/5855/1424>
- [6] Angus J C. Diamond is an insulator. *Chemical and Engineering News*, 2008, **86**, 6–10.
- [7] Sommer A P, Zhu D, Franke R P, Fecht H J. Biomimetics – Learning from diamonds. *Journal of Materials Research*, 2008, **23**, 3148–3152. Focus issue on biomimetic and bio-enabled materials science and engineering.
- [8] Sommer A P, Franke R P. Modulating the profile of nanoscopic water films with low level laser light. *Nano Letters*, 2003, **3**, 19–20.
- [9] Sommer A P, Pavláth A E. The subaquatic water layer. *Crystal Growth and Design*, 2007, **7**, 18–24.
- [10] Schroeder P, Lademann J, Darvin M E, Stege H, Marks C, Bruhnke S, Krutmann J. Infrared radiation-induced matrix metalloproteinase in human skin: implications for protection. *The Journal of Investigative Dermatology*, 2008, **128**, 2491–2497.
- [11] Sommer A P, Pinheiro A L, Mester A R, Franke R P, Whelan H T. Biostimulatory windows in low-intensity laser activation: lasers, scanners, and NASA's light-emitting diode array system. *Journal of Clinical Laser Medicine and Surgery*, 2001, **19**, 29–33.
- [12] Goertz M P, Houston J E, Zhu X Y. Hydrophilicity and the viscosity of interfacial water. *Langmuir*, 2007, **23**, 5491–5497.
- [13] Jinesh K B, Frenken J W M. Capillary condensation in atomic scale friction: How water acts like a glue. *Physical Review Letters*, 2006, **96**, 166103.
- [14] Li T D, Gao J, Szoszkiewicz R, Landman U, Riedo E. Structured and viscous water in subnanometer gaps. *Physical Review B*, 2007, **75**, 115415.
- [15] Stadler R, Orfanos C E. Maturation and aging of elastic fibers. *Archives of Dermatological Research*, 1978, **262**, 97–111.
- [16] Szent-Györgyi A. Biology and pathology of water. *Perspectives in Biology and Medicine*, 1971, **14**, 239–249.
- [17] Sommer A P, Zhu D. Conductivity of diamonds. *Chemical and Engineering News*, 2008, **86**, 6–11.
- [18] Sommer A P, Zhu D, Försterling H D. Breathing Conductivity into Diamonds. *Science Online*, [2008-2-28], <http://www.sciencemag.org/cgi/eletters/318/5855/1424>
- [19] Sommer A P, Caron A, Fecht H J. Tuning nanoscopic water layers on hydrophobic and hydrophilic surfaces with laser light. *Langmuir*, 2008, **24**, 635–636.
- [20] Sommer A P, Franke R P. Plants grow better when seeds see green. *Naturwissenschaften*, 2006, **93**, 334–337.
- [21] Trelles M A, Mayayo E. Mast cells are implicated in low power laser effect on tissue: A preliminary study. *Lasers in Medical Science*, 1992, **7**, 73–77.
- [22] Williams R. Climate change blamed for rise in hay fever. *Nature*, 2005, **434**, 1059.
- [23] Sommer A P, Zhu D, Jaeger B. Other side of climate change: Nanoparticle emission. *Energy and Fuels*, 2008, **22**, 2869–2870.
- [24] Sommer A P, Zhu D, Försterling H D, Scharnweber T, Welle A. Crystalline water at room temperature - Under water and in air. *Crystal Growth and Design*, 2008, **8**, 2620–2622.
- [25] Liu P, Cui H, Yang G W. Synthesis of body-centered cubic carbon nanocrystals. *Crystal Growth and Design*, 2008, **8**, 581–586.
- [26] Mester A R, Sommer A P. How it all started: Dr. Endre Mester's pioneering work. *Proceedings of the 2nd International Conference on Near-field Optical Analysis: Photodynamic Therapy & Photobiology Effects*, Johnson Space Center, *NASA Publication*, 2002, CP-2002-210786, 11–13.