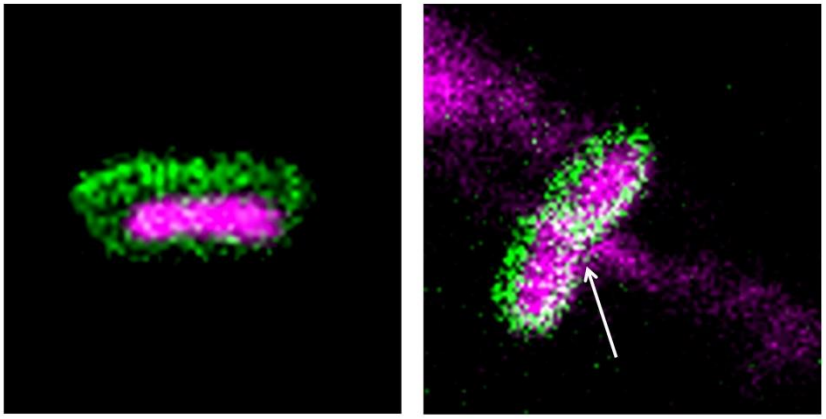
Nanomaterials as broad-spectrum antimicrobial agents

-Priti Bangal

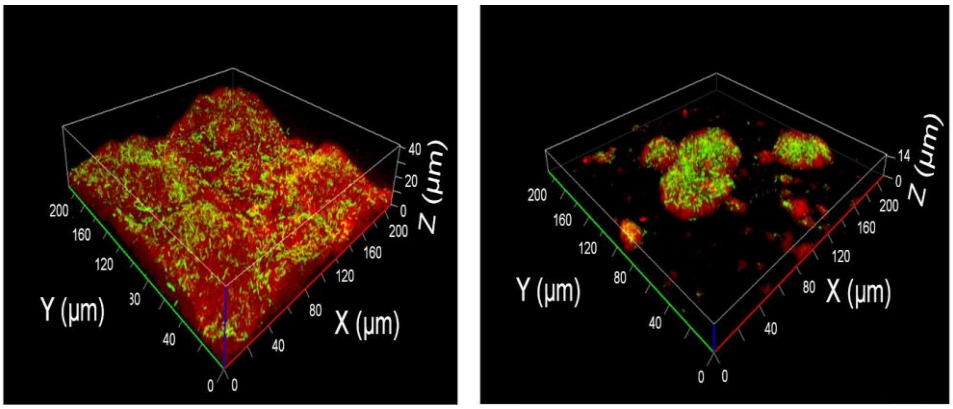
In a significant breakthrough in the battle against antibiotic resistance, a research team from the Indian Institute of Science (IISc) has synthesised a nanomaterial that mimics an enzyme and can disintegrate the cell membranes of a range of disease-causing bacteria. The study, published in the journal *ACS Applied Bio Materials,* is a collaboration between researchers from the Department of Inorganic and Physical Chemistry (IPC) and the Department of Microbiology and Cell Biology (MCB).



*Confocal microscopy images showing bacterial DNA (magenta) and cell membrane (green) in normal bacterial cell (left). DNA oozes out of bacterial cells when treated with nanozyme (right) which disrupts the cell membrane (Credits: Kritika Khulbe and Kapudeep Karmakar)*

The discovery of antibiotics revolutionised the field of medicine. By the 1960s, many health experts even believed that the fight against infectious diseases was in its final stages. However, recent decades have seen a new challenge – the evolution of resistance to antibiotics in pathogenic bacteria.

Antibiotics typically work by interfering with the cellular activities of the bacteria. Over many generations, thanks in large part to misuse and overuse of antibiotics, several bacteria have developed resistance to antibiotics by producing their own enzymes that target the drugs.




*3D images showing bacteria (green) inside a biofilm matrix (red) with nanozyme*

*treatment (right) and without nanozyme treatment (left). The nanozyme kills the bacteria and inhibits the formation of biofilm (Credits: Kritika Khulbe and Kapudeep Karmakar)*

The cell membranes of all organisms, including bacteria, have two layers of lipids containing phosphate molecules. “Phospholipid is an essential component of the cell membrane,” explains Kapudeep Karmakar, a former PhD student at MCB and the joint first author on this paper along with Kritika Khulbe, former PhD Student at IPC. Therefore, the researchers decided to target these phospholipids with the help of nanomaterials that would break the bonds holding the membrane bilayer together. These nanomaterials are known as nanozymes. According to the authors, since the nanozymes directly target the chemical integrity of the phospholipids to destroy the cell membrane, bacteria are less likely to be able to develop resistance against them.

To develop this novel compound, the team synthesized a cerium oxide based nanozyme using what is known as a chemical co-precipitation method. In the next step, they carried out a reaction between cerium oxide and sodium polyacrylate in a basic solution to coat the nanoparticles with polymers. The polymer coating allows the nanozyme to disperse onto any surface or material and boosts its activity.

The nanomaterial was then tested in the lab on several potentially pathogenic bacteria such as *Salmonella* Typhi, *Shigella flexneri*, *Escherichia coli*, *Vibrio cholerae* and *Klebsiella pneumoniae*, which cause typhoid, gastroenteritis, dysentery, cholera and pneumonia respectively. What the team found was that the nanozyme stopped their growth and subsequently inhibited the formation of biofilm – a densely packed community of bacteria.

“Most antibiotics are not able to penetrate through biofilms. Our nanomaterials were able to penetrate even a 10-day old, well-developed biofilm and showed anti-bacterial activity inside the biofilm because of their small size,” says Khulbe.

The researchers also tested the nanozyme on urinary catheters. These medical devices are vulnerable to formation of pathogenic biofilm on their surfaces, leading to infections in patients. In a laboratory setting, the team found that the bacterial attachment to the catheter surface significantly reduces on treatment with the nanozyme. Because the nanozyme does not distinguish between human and microbial cells, the researchers strategically coated only the inner surface of the catheter to kill the microbes. In order to use their nanomaterial in other medical devices, more research would be required to ensure that there is no contact between human cells and the nanozymes.

# Prawn exoskeleton – a rich source of efficient sunscreen filters

Aniket Majumdar

Commercially available sunscreen products usually contain chemically active ingredients to absorb ultraviolet (UV) radiation. But these chemicals are not eco-friendly and are inefficient UV absorbers. Besides, long-term use of such products can even lead to hazardous side-effects such as allergy and hypersensitivity of the skin. As a result, the focus is now shifting towards natural sunscreens, since they do not have such adverse effects. Notable examples include mycosporine-like amino acids with a central aromatic ring such as tryptophan, phenylalanine, and tyrosine, which are found in marine-based mucus and can absorb the entire range of UV radiation.

A good source of these amino acids is the prawn exoskeleton, which is the external shell that covers the entire body of the prawn. Previous skincare studies have already shown that proteins extracted from prawn shells enhance anti-ageing effects in the skin because of their anti-microbial and skin regeneration properties. In their latest work, researchers from the Indian Institute of Science (IISc), led by Bikramjit Basu, Professor at the Materials Research Centre, in collaboration with those from the National Institute of Technology Karnataka (NITK) Surathkal, have conducted a detailed study on the prawn exoskeleton to understand the nature of the proteins. Their results showed that amino acids present in prawn shells absorb the entire range (200-400 nm) of UV radiation and hence serve as excellent sunscreen filters.

The team collected shells of the Arabian Sea prawn (*Fenneropenaeus indicus*) from the market, cleaned them with hot water and dried them overnight. The chemical composition of the compounds present in the shell was examined using X-ray spectroscopic techniques, which revealed that the prawn shells are primarily composed of calcite, α-chitin and proteins. Thermal analysis of the prawn shell further confirmed that it contains 6 percent moisture, 42 percent calcite and the remaining 52 percent organic matter, which includes α-chitin and proteins. Microscopic imaging of prawn shells showed regular spherical calcites embedded into the α-chitin protein structure. The team also carried out X-ray photoelectron spectroscopic (XPS) measurements on the prawn shells to identify the organic compounds, and hence the amino acids present in them. UV-visible spectroscopy results confirmed the presence of mycosporine-like amino acids with a central aromatic ring (namely tryptophan, tyrosine, phenylalanine) in prawn exoskeleton.

The team concluded that extraction of UV-absorbing proteins from prawn shells can have potential applications as permissible eco-friendly sunscreen filters in polymer coatings, cosmetics, textiles, food, pharmaceuticals and biodegradable packaging products.

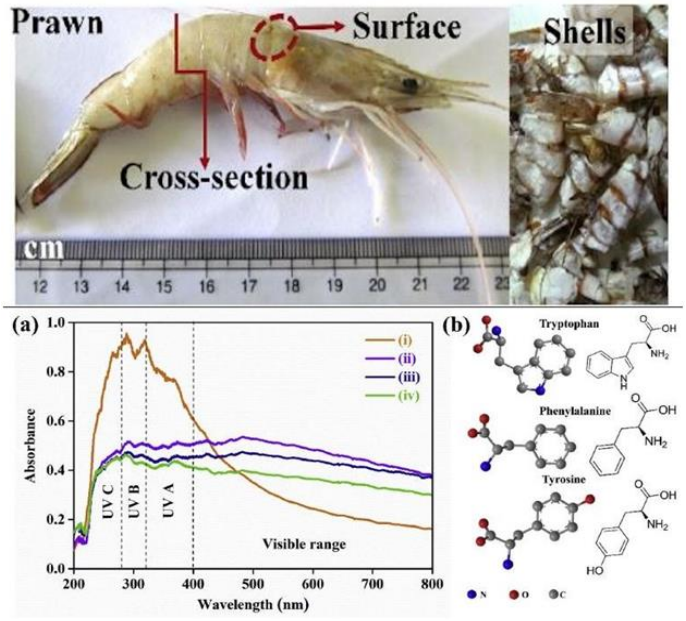



**Figure:** (Top Panel) Image of an Arabian Sea prawn and its exoskeleton/shell, discarded as food waste. (Bottom Panel) UV absorbance spectra of prawn shell, showing wide absorption of UV irradiation in the range of 200–400 nm

**Reference:**

Komalakrushna Hadagalli, Rahul Kumar, Saumen Mandal, Bikramjit Basu, Structural, compositional and spectral investigation of prawn exoskeleton nanocomposite: UV protection from mycosporine-like amino acids, *materials Chemistry and Physics,*249 (2020) 123002. https://doi.org/10.1016/j.matchemphys.2020.123002

**Lab Website:** http://www.mrc.iisc.ac.in/bikramjit-basu/

## Unfolding the connection between electronic and thermal transport

Various forms of electron and ion interactions in materials are broadly responsible for the observed electronic and thermal transport properties. Despite the overlapping origin, there is lack of clear connection between these two transport properties. In this work, we have used machine learning (ML) to establish a connection between otherwise independent electronic and thermal transport properties, whereinbonding features (BF)are found to be the bridging link.

By creating a comprehensive database, electronic and thermal transport properties of 135 materials are calculated. Analysis of independent prediction models for these transport properties reveals the potential of elemental and bonding descriptors in predicting them. Hence, to find a possible connection, we employed electronic transport properties along with chemical bonding driven elemental and structural descriptors to predict the thermal transport properties. These descriptors are electronegativity, volume, coordinationnumber, bond distances, and bond strength. Employing these descriptors, the prediction model for thermal transport property, gives root mean square error (RMSE) of 0.19/0.19 and $R^2$ of 0.99/0.99 for the train/test data. The scatter plot for the variationof DFT versus ML predicted log-scaled is shown in Fig. 1 (a).

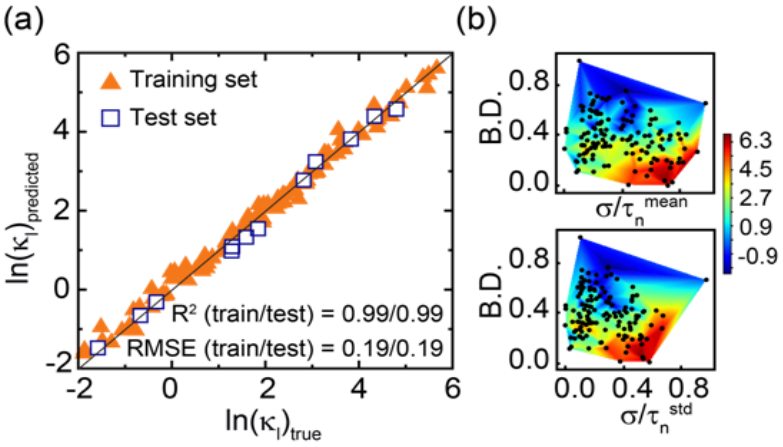



Fig. 1: (a) Scatter plot for DFT calculated versus ML-predicted log-scaled , (b) Contour plots showing the variation of  as a function of electronic transport properties and chemical bonding driven property.

This relationship with bonding is further substantiated by the contourplots, corresponding to the variation of  as a function ofelectronic transport and bonding properties. Among these, thecombination of mean bond distances (BD) and electronic transport properties partitions the dataset into the regions of low andhigh , as shown by the blue and red regions in Fig. 1 (b). Hence, the developed model can be used to screen materials with desired lattice thermal conductivity by looking at electronic transport and bonding attributes.

**Reference :**

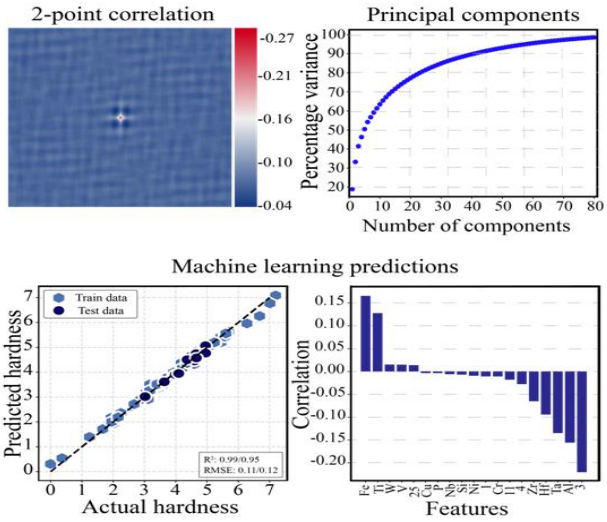
Unraveling the role of bonding chemistry in connecting electronic and thermal transport by machine learning*J. Mater. Chem. A,* 2020, 8, 8716-8721

Website URL : http://mrc.iisc.ac.in/abhishek/

## Hardness prediction from microstructures using machine learning

The application of machine learning (ML) has accelerated the process of developing novel materials for a wide variety of applications. ML algorithms are used to learn from patterns in past data and use it to predict future events. In a new study, IISc researchers led by Abhishek Kumar Singh, Associate Professor at the Materials Research Centre, have developed highly accurate ML models to predict the Vickers hardness of nickel and cobalt-based superalloys.

Superalloys are materials possessing excellent mechanical strength and creep resistance at high temperatures, high surface stability and high corrosion resistance. Due to these properties, they are heavily employed in the aerospace, marine, chemical and petrochemical industries.




*Top row: Images representing the 2-point correlations and the variance captured by the principal components obtained using electron micrograph. Bottom row: Results of the machine learning model developed using 2-point correlations and compositions.*

To develop the ML model, a database was generated initially, comprising of the microstructures, compositions and Vickers hardness of several cobalt and nickel-based superalloys. SEM microstructures were denoised and thresholded to obtain binary microstructure. The binary microstructure was then used to calculate 2-point correlations. 2-point correlations are statistically derived parameters, which give the probabilities of finding different phases in microstructure at a specified distance. Further, principal component analysis (PCA) was performed on these correlations to select the most dominant correlations. These PCA-derived correlations along with composition of the superalloys are used as descriptors for building the ML models.

The approach developed in this study can be generalised for any material property, making it highly useful and adaptive.

**Reference:**

N. Khatavkar, S. Swetlana, A. K. Singh, Accelerated prediction of Vickers hardness of Co- and Ni-based superalloys from microstructure and composition using advanced image processing techniques and machine learning, *Acta Materialia*, In press, (2020)

**Website:** http://mrc.iisc.ac.in/abhishek/

# Molecular cages that mimic enzymes and kill bacteria in water

– Gouri Patil

Researchers from the Departments of Inorganic & Physical Chemistry and Organic Chemistry at IISc have synthesised molecular architectures that can kill pathogenic bacteria in water, including the infamous methicillin-resistant *Staphylococcus aureus* (MRSA). They fashioned these molecules to mimic enzymes – proteins found in living organisms regulating the rate of chemical reactions – using the principles of supramolecular chemistry, which deals with how molecules assemble spatially, and the intermolecular forces responsible for their organisation.

In one of their studies, the researchers designed a “molecular cage” called PMB1 via self-assembly of abenzothiadiazole-based ligand and platinum-based units. The benzothiadiazole unit is a photosensitiser, which absorbs light efficiently and produces reactive oxygen species that disrupt the bacterial cell membrane. The positively charged PMB1 cage also enhances the adhesion of the bacteria to the cage and damages the bacterial cell membrane.

The authors believe that this is the first time a water-soluble molecular cage antibacterial agent has been designed where a single entity utilises two pathways to degrade bacteria — both in the presence and absence of light.

Though these nano-sized supramolecular assemblies are being used in applications like catalysis, smart materials, drug delivery, light-harvesting and sensors, they have rarely been employed in disinfecting water. Therefore, this work could help develop more such antibacterial agents in the future.

The team, in a related study, proposes a water-soluble nanozyme cage structure consisting of benzothiadiazole-based and palladium-based units. Nanozymes are nanomaterials mimicking the properties of the natural enzymes. The molecular cage here imitates the activity of an enzyme called ‘oxidase’ and generates reactive oxygen species due to the light absorption by benzothiadiazole unit. These free radicals kill the bacteria present in water.

Nanozymes have an advantage over natural enzymes because they are more stable and are easier to synthesise on a largescale. Hence, they have found potential applications in biochemical tests, biosensors and therapeutics.

**REFERENCES:**

Soumalya Bhattacharyya, Mangili Venkateswarulu, Jagabandhu Sahoo, Ennio Zangrando, Mrinmoy De, and Partha Sarathi Mukherjee, Self-Assembled PtII8 Metallosupramolecular Tubular Cage as Dual Warhead Antibacterial Agent in Water, *Inorganic Chemistry,* 2020, 59, 17, 12690–12699.

https://pubs.acs.org/doi/10.1021/acs.inorgchem.0c01777

Soumalya Bhattacharyya, Sk Rajab Ali, Mangili Venkateswarulu, Prodip Howlader, Ennio Zangrando, Mrinmoy De, and Partha Sarathi Mukherjee, Self-Assembled Pd12

Coordination Cage as Photoregulated Oxidase-Like Nanozyme, *Journal of the American Chemical Society,* 2020, 142, 44, 18981–18989

https://pubs.acs.org/doi/full/10.1021/jacs.0c09567

**LAB WEBSITES:**

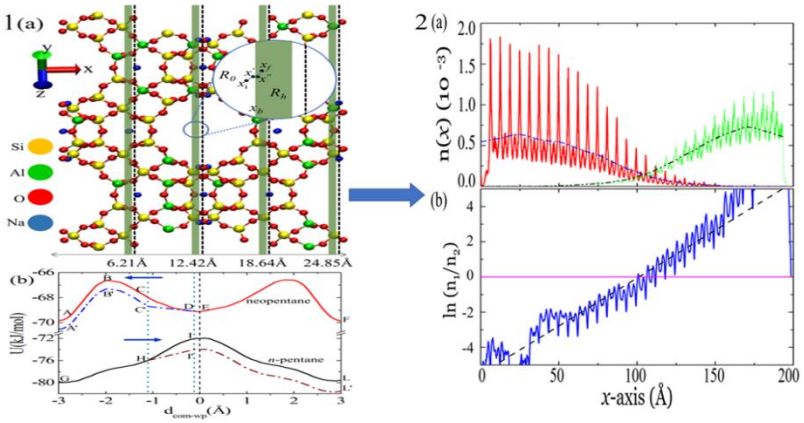
https://orgchem.iisc.ac.in/mrinmoy_de/
http://ipc.iisc.ac.in/~psm/

---

## A green separation method capable of giving high purity components

A novel separation method has been proposed by IISc researchers to separate molecular mixtures to very high purity, which is not possible with existing approaches. It also requires very low energy, making it environment-friendly.

Methods such as distillation, crystallization and filtration separate the components of a mixture by driving them to move at different speeds along the same direction in a column of porous solid such as zeolite. They usually lead to an impurity of 1 molecule in 100. The proposed new method, on the other hand, causes movement of different types of molecules to opposite ends of the column, resulting in better than 1 in $10^{10}$ separation.




The method judiciously combines two well-studied phenomena: levitation effect and blow torch effect. Levitation effect is an anomalous diffusion phenomenon which occurs in a porous solid, where the bigger particle has higher diffusivity than the smaller one. Blow torch effect alters the relative population in a bistable potential by placing a hot zone in the region between the two potential minima.

This method has been demonstrated for a mixture of a linear hydrocarbon called n-pentane and its branched isomer, neopentane. The mixture was separated using a zeolite to very high purity. Such separations are routinely carried out in petroleum refineries, but consume large amounts of energy. This new method is more energy-efficient by several orders of magnitude. The method will also be useful in green chemistry where high purity reactants are required.

**Reference:**

S. Nag, G. Ananthakrishna, Prabal K. Maiti and S. Yashonath, *Separating Hydrocarbon Mixtures by Driving the Components in Opposite Directions: High Degree of Separation Factor and Energy Efficiency*, Phys. Rev. Lett., **124**, 255901, 2020.

DOI: https://doi.org/10.1103/PhysRevLett.124.255901

**Website:** http://nsayuja.sscu.iisc.ac.in/

---

## A novel low temperature dynamic correlated paramagnet on a randomly diluted lattice

A lattice of interacting spins usually leads to a unique ferro- or anti-ferromagnetically ordered arrangements of those spins at a low temperature. There are certain lattice types where such orderings are strongly suppressed. A prototypical example is the Ising spin-½ system on a triangular lattice with a nearest neighbour antiferromagnetic interaction where the triangular arrangement results in competing interactions leading to a large number of distinct states with the same ground state energy. In recent times, there is an increasing focus on such magnetically frustrated systems, in search of quantum spin liquids which relieves the frustration by entangling the spins instead of ordering. Another approach to a ground state without order is to introduce sufficient magnetic disorder in a lattice. Such systems may get stuck in a differently disordered "glassy" state. In this letter, we explore what happens with extensive disorder introduced in the frustrated triangular lattice such that elements for both spin "liquid" and "glass" coexist.

$Y_2CuTiO_6$ has magnetically coupled spin-½ $Cu^{2+}$ on a triangular lattice with 50% of the sites randomly replaced by nonmagnetic $Ti^{4+}$. We establish that this system does not achieve either a magnetic ordering or a pure glassy state down to 50 mK, though the magnetic interaction strength is nearly 3000 times larger than this temperature. Various experiments and specific scaling behaviours of thermodynamic properties with temperature and magnetic fields suggest that the system remains in a disorder driven, dynamic cooperative paramagnetic state, opening new possibilities to explore the field of frustrated magnetism aided by disorder.

**Publication :**

S. Kundu, Akmal Hossain, Pranava Keerthi S., Ranjan Das, M. Baenitz, Peter J. Baker, Jean-Christophe Orain, D. C. Joshi, Roland Mathieu, Priya Mahadevan, Sumiran Pujari, Subhro Bhattacharjee, A. V. Mahajan and D. D. Sarma, Phys. Rev. Lett. **125**, 117206 (2020)

(**DOI**:10.1103/PhysRevLett.125.117206)

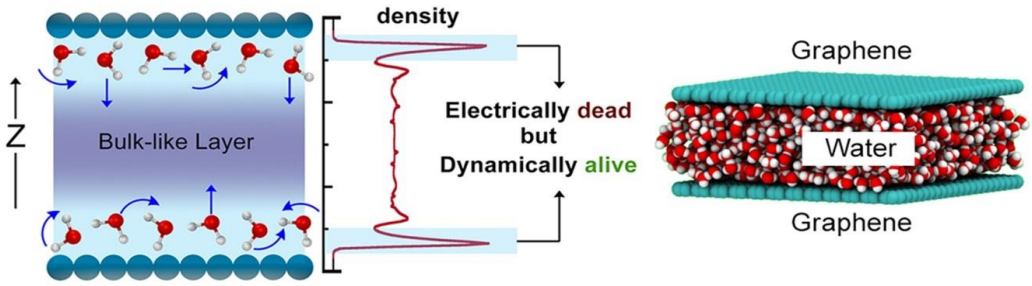
**Relevant References :**

[1] L. Balents, Nature (London) 464, 199 (2010).

[2] I. Kimchi, A. Nahum, and T. Senthil, Phys. Rev. X 8, 031028 (2018).
[3] T. Furukawa, K. Miyagawa, T. Itou, M. Ito, H. Taniguchi, M. Saito, S. Iguchi, T. Sasaki, and K. Kanoda, Phys. Rev. Lett. 115, 077001 (2015).

---

## Water layer at hydrophobic surface: Electrically dead but dynamically alive?




Water confined between parallel graphene sheets exhibits several interesting anomalies. This work unravels the origin of the *surprisingly low static dielectric constant* of such systems by employing linear response theory, a mean-field capacitor model and computer simulations. We find that the interfacial water layer, with a substantially attenuated dielectric permittivity, makes a disproportionately large contribution to the effective value. *This is partly because the observed dielectric constant is a harmonic mean of the grid-wise dielectric constants*. In addition, we study the dynamics of water molecules at a microscopic level. We find that the water molecules residing in the so-called “electrically dead layer” become orientationally ordered yet dynamically active, with a finite residence time in the layer. While these water molecules display timescales not substantially different compared to the water molecules at the distant layers, their dipole moment fluctuations are quenched. Our study provides new insights into the dielectric anomaly of nanoconfined water, which has been a topic of great current interest.

**REFERENCE:** https://pubs.acs.org/doi/10.1021/acs.nanolett.0c04312

**WEBSITE:** https://sscu.iisc.ac.in/bagchi/