

molecular biology 30th november - carlo ventura

On the website "heart math" there is publicity, they sell their apps to make everything quicker. There is another publicity even when you go to the hospital, in particular we are asking "who is going to take care of you when you are in the hospital?" "The doctors" is the answer, most of them are young and enrolled in a specialization course, gli "specializzandi" and they are supporting their company, their university studies, that are supporting their studies, like a hidden publicity.

List of many papers: most important from Nature - see on Virtuale

"Universal Structure of Normal and Pathological Heart Rate Variability" - Nature

There is an universal structure, the same for everybody, it can be normal or pathological heart rate variability.. But everybody has a personal variability, and if the variability is too much it's pathological, if it's too narrow it is pathological as well.

What's the fate for patients with severe acute myocardial infarction even if he/she survives? 55-65% of people die in the next 4 years. All these patients when the stratification of the risk of dying, other Heart variability, shows a lack of coherence. If this lack is not just a marker form, but a lack of coherence as the cause of a phenomenon in creating such a dramatic perspective for the patients, I will be led to bring back the heart rate variability to a coherent pattern making a difference in the surviving range. The chances will be reversed with 75% surviving. There is not just a marker for stratification, but this lack of coherence is also a cause of the phenomenon to get worst condition on patiences.

What's the difference from a clinical trial that demonstrates that something is working and convince everybody that this treatment is for everybody and people have to work with this? Another major issue is the part that makes its own electromagnetic field, the machine for recording the electrocardiogram is very primitive and the reason why you can detect electromagnetic is because the electric pattern, when the cell depolarizes, basically it has negative inside and positive outside, with the depolarization is just the opposite, when a cell depolarizes from negative charges outside, there is a positive charge inside. What is the association with this? Is the electric pole of resources on the heart, or on the skin, on the brain...

Another major discovery is that all the psychiatric pattern of severe depression can be dramatically ameliorated if you make your heart rate variability work on it. This affects the way the pattern of heart variability is moving, the major psychiatric depression has to be ameliorating affecting the IBG. This is well established that anyways the heart is sending info physically to the brain and vice versa.

Even the major psychiatric depression is not vanishing, but can be ameliorated by this. That institution that works with military people coming back from frontlines to solve the issue of massive suicide in the last 10 years have the evidence that it works for those that are in frontlines. Like training people in having super coherent heart rate variability, sustaining on the larger variation of the beats, to make them stay in the sinusoidal, demonstrating thai it works.

Whenever you have to use this treatment for everybody you have to build a business plan, that is different from the business model.

Business plan = how i can go further in studies to demonstrate something, the budget to provide for the labs...

Business Model = wherever it takes the results, has to be in a business model to promote this, dividing the percentage of the business, considering the side effect of the drugs, you have to watch the data of the future, everything has to be regarded with consciousness.

“Cell reports” - moderate heart reduction. If you fall in between a specific pattern of reduction of heart rate, which intends the heart rate variability, you have this metabolic switch in the heart that means the spontaneous heart regeneration, it may happen in patients.

There is a clinical syndrome, the hibernated myocardium. Means that when you do ultrasound analysis for patients with myocardial infarction there is an alteration of the pattern of motion of the ventricle. The part of the left ventricle with myocardial infarction is stuck, it doesn't move, it bangles, (banging of the heart = the myocardial contracts, there is a necrotic area that in systole doesn't follow and it extrudes outside, this is very dangerous. And a part that doesn't move is a dead part).

In Patients with hibernated myocardium, there was a necrotic part, where on one side there is no motion, on the other side you have a classic pattern of ICG with no electric pattern there, even at rest, like a dead part of the heart. The model theory is that there is a dead part, and in the other part that is not dead, the heart stops beating and in doing this it saves oxygen promoting this metabolic switch. By the time you have this metabolic switch you are saving enough ATP and enough energy that the heart is using for spontaneous regeneration. This mechanism is useful, having different chances to repeat the same message can be useful.

Basically, all you have is the pattern which the heart avoids rupture, fibroblast in the heart (which are the main component in the heart weight) start changing with a transition of myofibroblast; those are a few elongated cells in a matrix of type one collagen. This is very stiff, hard, prevents the heart from breaking, and creates diastolic infarction. So the heart doesn't feel properly in the diastole and still has some force of contraction that subsequently leads to heart failure. In this way the regenerative intervention with metabolic switch will transform the myofibroblasts back in another form, the matrix fibrocytes. These are very small and proliferate a lot, so you fill the space with many cells, the type 1 collagen is shift in type 3 that is softer, the cells stuck together and start proliferating hyaluronic acid very soft and resistant, good for the heart capability of compliance, stretch and come back to the initial position after stretch forces. With many cells becoming softer and softer, so there is no more stiffness, this matrix fibrocytes are electrically coherent, they do not create any disturbances on the flow of the electric signals to the heart, they have the possibility to contract, regenerating forces. Then the adult cardiac myocytes re-enter in the cycle, start to proliferate again, but this is a later phenomenon.

Paper: *Universal structures of normal and pathological heart rate variability.*

Here there is important the relevance of the electromagnetic field, because the pattern of heart rate variability is created by the electromagnetic field of the heart, which is so important, there is a matter of bioelectricity

If I change the heart rate variability, how is the sound produced by the myocardial cells affected?

And there's a huge shift. So the nanomechanical properties of the cells change in function of heart rate variability. We have specific libraries and banks where we can find normal and non normal patterns of heart rate variability, so this pattern is transformed to the right electric differentiation potential.

Through that change we move transducers, so that we can deliver mechanical waves that correspond to pathological or normal heart rate variability to microbial cells, coming from human. We start from human dermal fibroblast, reprogrammed into embryonic like stem cells, done with electromagnetic fields without any gene transfer. This cells became whatever, we pick the myocardial cells, then we act in these cells by delivering a mechanical pattern that corresponds to a normal or pathological heart rate variability, their fate is dramatically affected. So they can eventually proliferate affected by the pattern of these mechanical waves. It is not only simply that you have change in metabolic switch that makes the cardiac cells recover, but is a specific morphogenetic-genetic code driven by patterns of heart rate variability, but is more profound.

Lesson 4 - Microtubules and the Cytoskeleton a Bioelectronic Circuit Capable of Memory Switching and Intercellular Connectivity

By scanning tunneling microscopy we can follow the electro magnetic resonance pattern of tubulin dimers, they respond with an electromagnetic field in resonance to another field, but even when the field is switched off they continue to emit their field, provided that you are working with exactly those numbers of frequencies and there is a resonance frequency response.

Microtubules and the new frontiers of Mechanobiology.

The "memory switching" properties inherent in individual microtubules.

Dynamics of self-assembly of tubulin and three-dimensional visualization of microtubular electrical conductivity by means of tunneling microscopy (Scanning Tunneling Microscopy - STM)

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Multi-level memory-switching properties of a single brain microtubule

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We demonstrate that a single brain-neuron-extracted microtubule is a memory-switching element, whose hysteresis loss is nearly zero. Our study shows how a memory-state forms in the nanowire and how its protein arrangement symmetry is related to the conducting-state written in the device, thus, enabling it to store and process ~500 distinct bits, with 2 pA resolution between 1 nA and 1 pA. Its random access memory is an analogue of flash memory switch used in a computer chip. Using scanning tunneling microscope imaging, we demonstrate how single proteins behave inside the nanowire when this 3.5 billion years old nanowire processes memory-bits. © 2013 American Institute of Physics. [<http://dx.doi.org/10.1063/1.4793995>]

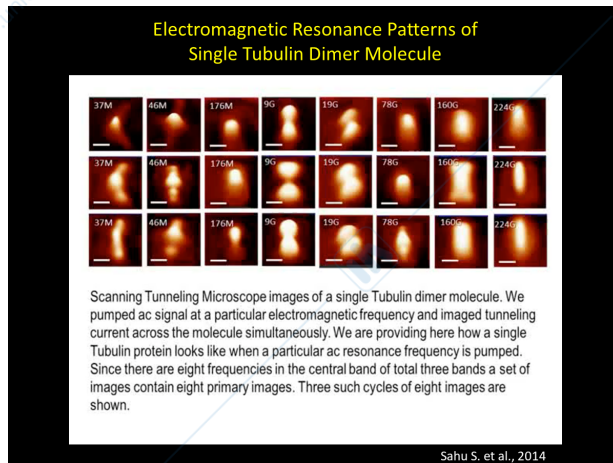
Microtubules, like aquaporins, play a crucial role in cellular dynamics. While aquaporins specifically facilitate water movement across cell membranes, microtubules are structural elements within cells that, among other functions, can experience various forces and deformations. Imagining water flowing through microtubules under high pressure helps grasp the complexity of intracellular environments.

Within cells, the water isn't a simple salt solution but behaves more like a gel due to the presence of various molecules and structures, including glycosaminoglycans (GAGs). These GAGs are pivotal in cellular regulation and communication processes. When water moves through microtubules, it creates non-homogeneous water distributions inside cells. This movement can influence the concentration of specific molecules within different subcellular compartments.

By altering water flow within a compartment, it's possible to affect the concentrations of numerous other molecules. Previously, GAGs were thought mainly to hydrate cells, but it's now understood that these polysaccharides interact extensively with proteins and signaling molecules. They help create and maintain constant extracellular pressure and store reserve water. These interactions underscore how the extracellular environment is not foreign but an integral part of the cell.

The interplay between microtubules, water flow, GAGs, and other molecules highlights the intricate relationship between cellular structures and their environment. Understanding these interactions is crucial for comprehending cellular dynamics, signaling pathways, and the impact of water movement on molecular concentrations within cells.

Electromagnetic resonance patterns of single tubulin dimer molecule



The motion of microtubules, the buckling of microtubules, a waving of electromagnetic forces where buckling is per se a form of information and communication.

Peter Agre : 2003 Nobel Prize in Chemistry. The change in local density at particular frequencies also accompanies local structural changes. From STM images, it is clear that there are fundamental structural changes. For each applied frequency we have three rows, so three possible states of resonance (of tubulin's electroconductivity). Thus not only were the microtubules responding to the incoming magnetic field and only to those specific frequencies, but they also were continuing to respond (this means that they had memory). The point is that microtubules contain an atomic water channel with a nuclear membrane of mitochondria of aquaporin. It's logic that we have water channels in our body. Infact, the atomic water channel controls remarkable properties of a single brain microtubule.

Buckling of microtubules: The microtubule buckling causes not only the elastic deformation of the filament network, but also the viscous flow of the cytosol. In turn, these two processes result in an external stress field that influences the microtubule buckling mode and kinetics. Microtubules are cylindrical structures found in cells and are composed of tubulin protein subunits. Buckling of microtubules refers to a structural instability where these cylindrical filaments can undergo bending or deformation when subjected to certain forces.

This phenomenon of buckling in microtubules is influenced by various factors, including:

External Forces: Mechanical forces applied to microtubules, such as compression or bending forces, can lead to buckling. For instance, during cellular processes like cell division or movement, microtubules can experience forces that might cause them to buckle.

Protein Interactions: Other proteins and molecules within the cell can bind to microtubules, affecting their stability and susceptibility to buckling. Regulatory proteins and motor proteins, for example, can interact with microtubules and alter their mechanical properties.

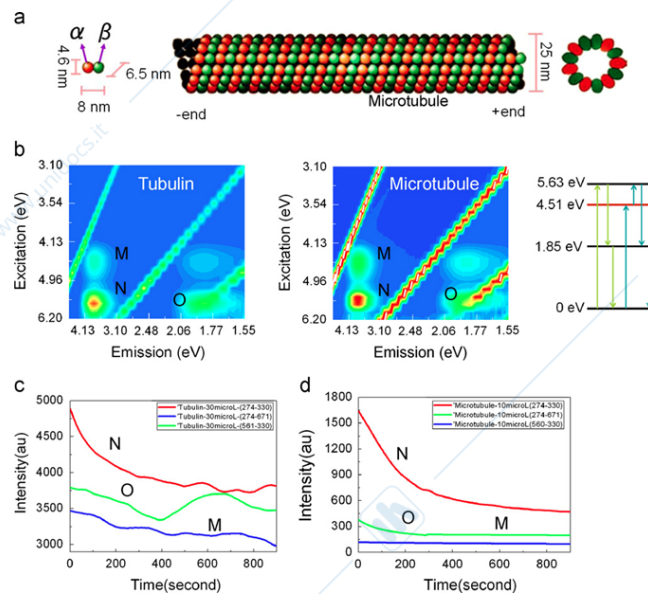
Dynamic Instability: Microtubules are dynamic structures that continuously grow and shrink by adding or losing tubulin subunits. Changes in their dynamics, such as rapid growth or sudden shortening, can influence their susceptibility to buckling.

Understanding the mechanics of microtubule buckling is crucial in various fields, including cell biology and materials science, as it contributes to comprehending cellular processes, cytoskeletal mechanics, and designing biomimetic materials inspired by biological structures.

We know that without water there is no life, but there is memory and other things so that water is not just a solution but is a gel water.

Another form of aquaporin are microtubules. Inside them water flows at a specific speed like 1.5 billions of water molecules for second. This turbulent regime is unknown.

experiment



In this study, they measured a single tubulin molecule and single brain-neuron extracted microtubule nanowire with and without water channel inside to unravel their unique electronic and optical properties for the first time. They demonstrate that the energy levels of a single tubulin protein and a single microtubule made of 40.000 tubulin dimers are identical, unlike conventional materials. Even more remarkable is that the microtubule nanowire is more conducting than a single protein molecule that constitutes the nanowire. To explain this, we have to think in terms of quantum physics:

50% of the energy of the cell is devoted

to maintaining the oscillation of the microtubule. If the energy of the intact microtubule was much larger than the energy content of its single component, the whole metabolism of the cell won't be enough to sustain this oscillation.

So the energy content of tubulin dimer is contemporary presents across the intact microtubules (this is a hypothesis but comes from a finding).

To allow the water that is trapped inside, to come out they broke the tip of the microtubule.


Once the water flow of the single microtubule is destroyed, they back to newton's physics.

The energy content of the single tubulin dimer is much lower than the energy content of the intact microtubule.

By changing the dilution of molecules you don't simply change concentration but you will also change the electronic configuration of these molecules and their interaction.

Peter Agre, an American physician and molecular biologist, was awarded the Nobel Prize in Chemistry in 2003 for his discovery of aquaporins, which are water-channel proteins that facilitate the movement of water molecules across cell membranes. This discovery greatly contributed to our understanding of how water and other molecules pass through biological membranes in living organisms.

His research focused on understanding the mechanisms of water transport in cells, particularly how these water-channel proteins allow water to pass through biological membranes while preventing the passage of ions and other molecules.


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CHARGE-BASED FORCES AT THE NAFION-WATER INTERFACE

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However, when considering Nafion, which is a perfluorinated polymer with sulfonic acid groups, the interactions at its interface with water involve electrostatic forces due to the charged nature of the sulfonic acid groups. These interactions influence the behavior of water molecules near the Nafion surface.

Agre's work, his study of water transport mechanisms across cell membranes contributes to the broader understanding of how molecules, including water, move through membranes, which can have indirect implications or relevance in understanding similar processes occurring at interfaces involving charged species, like those in Nafion-water interactions.

The article explores charge-based interactions occurring at the interface between Nafion, a synthetic polymer resembling hydrophilic substances, and water. This investigation draws parallels to the interaction between water and proteins inside microtubules, which serve as a prime example of protein-water interaction due to water movement through them.

To study these interactions in living systems, Atomic Force Microscopy (AFM) with a flexible Nafion tube is used. This technique aims to understand how microtubules, when isolated within cells, interact with water at their interfaces. The AFM allows observation of intracellular components without disturbing the plasma membrane, confirming the observations made inside the cell.

Two key experimental methods are employed: one measures proton distribution in bulk water using a pH-sensitive dye, confirming charge separation; the other uses a mechanical sensor to gauge electrostatic force-based deflection when a Nafion tube generating exclusion zones attaches to the sensor tip. These approaches correlate proton distributions with measured force data based on electrostatic interactions.


The setup involves a transparent box filled with liquid from a glass bottle. The Nafion tube, immersed in the box, connects to a flexible mechanical sensor, allowing observation of the Nafion tube's movement when pushed into the water upon charge separation generation.

The addition of pH-sensitive dye clearly demonstrates a color change, indicating charge separation at the interface. Negative charges accumulate around the Nafion tube, while positive charges are displaced, revealing the presence of electrical forces at the interface. This charge separation reflects the involvement of electrical forces between Nafion and water, akin to the interaction between proteins and water inside microtubules.

Furthermore, the use of the pH indicator is related to the cell's internal pH being more basic than the external environment. This causes cationic charges to enter the protein channel, generating electrical charges that contribute to electrical forces at the interface. This underscores the intricate nature of protein-water interactions in cellular environments.

Dor Ben Amotz

video: my stroke of insight jill bolte taylor

 My stroke of insight | Jill Bolte Taylor | TED

