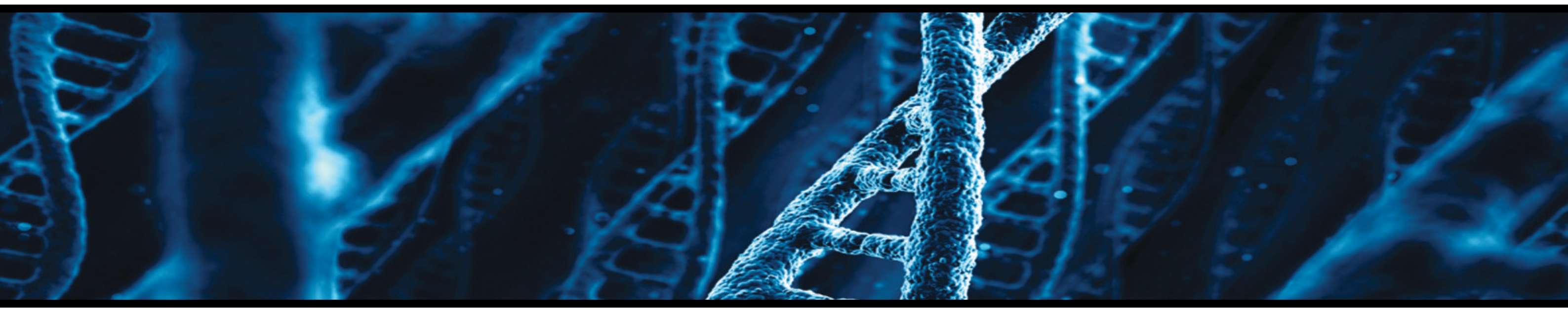
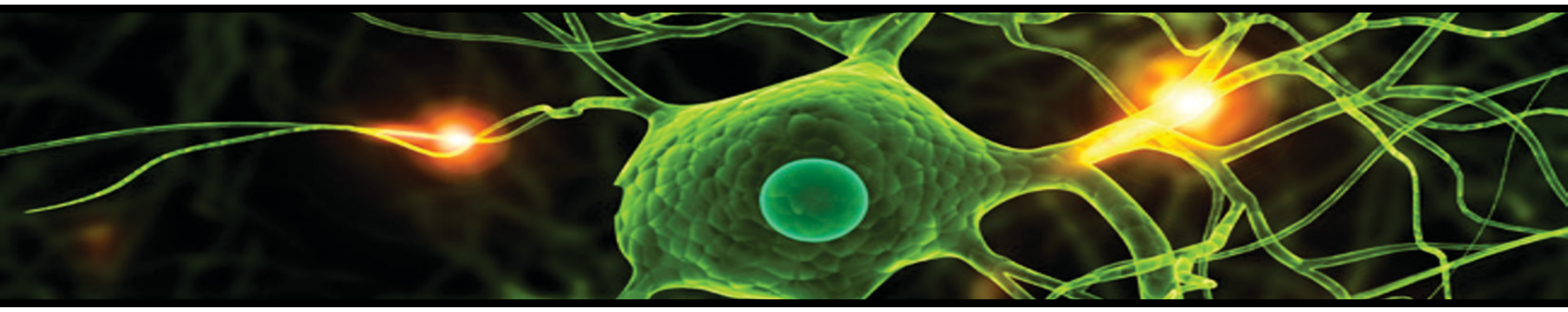
THE WORLD OF BIOPHYSICS





$$V(\vec{R}) = \frac{1}{4\pi\varepsilon}\left[\frac{q_i q_j}{R} + \frac{q_i\left(\vec{\mu}_i \cdot \hat{R}\right) - q_j\left(\vec{\mu}_j \cdot \hat{R}\right)}{R^2} + \frac{\vec{\mu}_1 \cdot \vec{\mu}_1 - 3\left(\vec{\mu}_i \cdot \hat{R}\right)\left(\vec{\mu}_j \cdot \hat{R}\right)}{R^3} + \sum_{\alpha,\beta=1}^{3} \hat{R}_\alpha \hat{R}_\beta \left(q_i Q_{j,\alpha\beta} + q_j Q_{i,\alpha\beta}\right)\frac{1}{2R^3} + \dots\right]$$

$$\frac{\partial}{\partial t}\rho_e(t)_{mn} = -\frac{i}{\hbar}\left[H_e, \rho_e\right]_{mn} - 2\delta_{mn}\sum_r \gamma_{rn}\left[\rho_e(t)_{nn} - \rho_e(t)_{rr}\right] - \left(1-\delta_{mn}\right)\left[\sum_r\left(\gamma_{mr} + \gamma_{rn}\right)\rho_e(t)_{mn} - \bar{\gamma}_{mn}\rho_e(t)_{mn}\right]$$

$$\dot{\rho}_e(t)_{mn} = -\frac{i}{\hbar}\left[H_e, \rho_e(t)\right]_{mn} - \sum_{pq} R_{mn,pq}\rho_e(t)_{pq}$$

SOUTH AFRICAN INSTITUTE OF PHYSICS

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THE VOICE OF PHYSICS IN SOUTH AFRICA

THE WORLD OF BIOPHYSICS

INDEX

EDITOR'S NOTE

Welcome to the 2nd 'World of Biophysics' booklet!

For this edition we have collected a completely new set of articles, all written by active South African physicists. This booklet doesn't only introduce you to some of the basic concepts and powerful experimental techniques used in biophysics, but you will also get a glimpse of frontier research of international quality. Read the personal stories of two students to know what motivated them to study biophysics

If you're fascinated by life and intrigued by the fact that all biological processes are actually based on physics, then this booklet is for you. Biophysics is an extremely promising research field with mind-boggling technological applications

Enjoy your journey through just a tiny part of the World of Biophysics!

Tjaart Krüger
Chair of the SAIP Biophysics Initiative

SOUTH AFRICAN INSTITUTE OF PHYSICS

SAIP BIOPHYSICS INITIATIVE

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what is
BIOPHYSICS?

Biophysics is the branch of physics that applies the methods and theories of physics to study biological systems. In short, biophysicists study the physics of living systems.

Studying the patterns in life using state-of-the-art physics experimental techniques and complex computational models is the most powerful way to find out how life works at the fundamental level. This is not an easy task, though. Living systems are exceedingly rich in variety and complexity, while the laws of physics are often best studied in simple, well-controlled circumstances.

The challenge of biophysics lies exactly here: to bridge the complexity of life and the simplicity of the mathematical laws of nature. Biophysics combines the complex beauty of biology with the rigour of physics.

what tools are used by
BIOPHYSICISTS?

Many interesting biological phenomena occur on the scales ranging from micrometres to nanometres. These phenomena can be probed and visualised using, for example, electromagnetic radiation to obtain information about the structure, function, and dynamics of the biological systems on all levels of complexity.

The interesting properties that determine behaviour include conductivity and binding energy, which can only be measured and described using physical methods. Much of the discipline of experimental biophysics is devoted to overcoming the problems of obtaining reliable measurements of the exquisite and delicate nanoscale machines in the cells of living organisms, without destroying them.

Biophysics has undergone rapid advances over the past two decades due mainly to the development of new technologies. These technologies enable multiscale imaging ranging from cellular to atomic resolution and allow us to record events on ultrafast (picosecond to femtosecond) timescales.

Biophysics pushes back barriers that once seemed insurmountable.

what do
BIOPHYSICISTS study?

Biophysicists study life at every level, from the molecular scale to cells, whole organisms and even ecosystems. This involves developing new experimental and computational tools to understand at a fundamental level the structure, interactions, dynamics, and ultimately the function of biological systems.
The biological questions of interest to biophysics are as diverse as the organisms of biology and the properties of all their components, for example:

- How does the brain process and store information?
- How does the heart pump blood?
- How do viruses invade cells?
- How do plants harness sunlight to make food?
- How are genes switched on and off?
- How do nature's nano-machines (like motor proteins and enzymes) move to do their work?

Biophysics discovers how to modify micro-organisms for producing biofuel (replacing gasoline and diesel fuel) and bio-electricity (replacing petroleum products and coal for producing electricity). It discovers the biological cycles of heat, light, water, carbon, nitrogen, oxygen and the organisms involved throughout our planet. Biophysics harnesses micro-organisms to clean our water and to produce lifesaving drugs.

how can
BIOPHYSICS be used?

Biophysics is a wellspring of innovation and instrumentation for any high-tech economy. The previous century has evidenced great progress in treating diseases. Biophysics helped to create powerful vaccines against infectious diseases. It described and controlled diseases of metabolism, such as diabetes. Biophysics provided both the tools and the understanding for treating the diseases of growth known as cancers. With the help of biophysics we are witnessing in the 21st century a rapid progress in the understanding of diseases at a fundamental level.

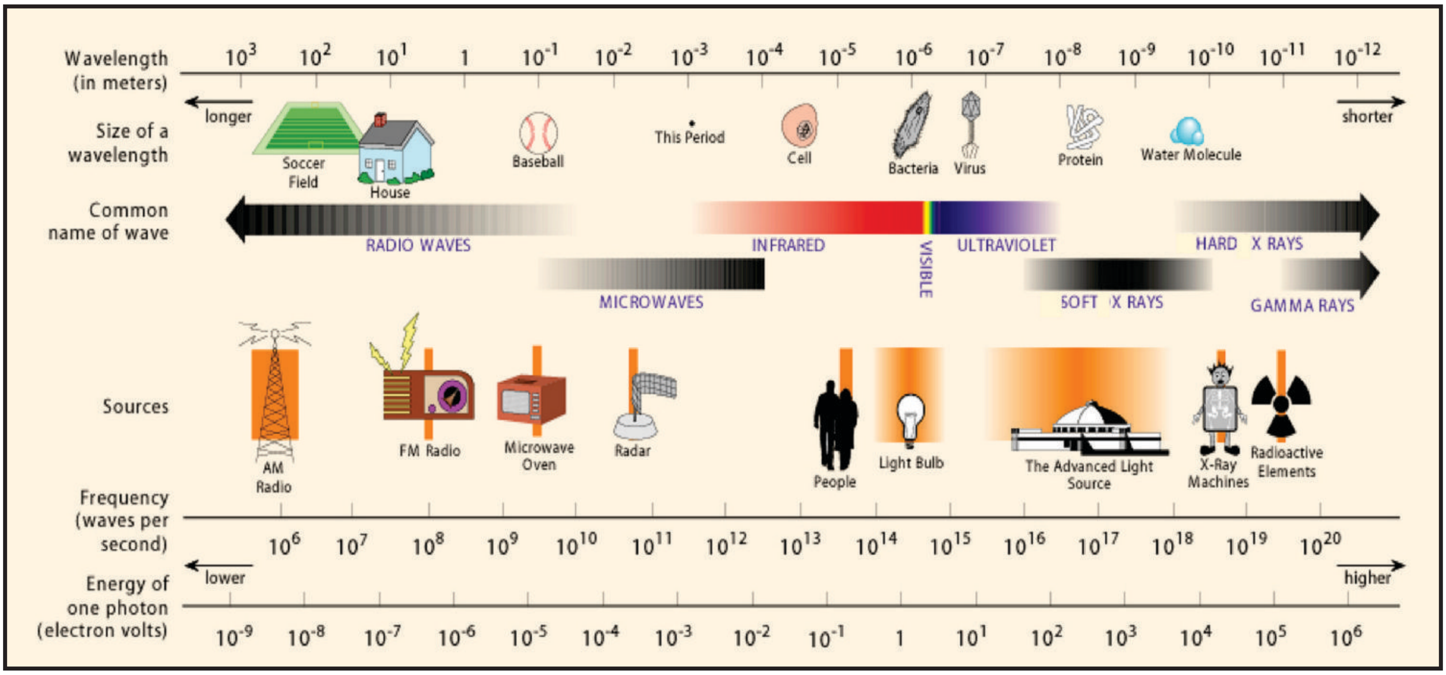
Society is facing physical and biological problems of global proportions. How will we continue to get sufficient energy? How can we feed the world's population? How do we remediate global warming? How do we preserve biological diversity? How do we secure clean and plentiful water? These are crises that require scientific insight and innovation. Based on the principles of physics and the mechanisms of biology, biophysics provides valuable insight and technologies for meeting these challenges.

Inspiration obtained from the Biophysical Society.

ELECTROMAGNETIC RADIATION

Electromagnetic (or EM) radiation is a quite peculiar form of energy. We can describe it classically as a self-propagating wave consisting of electric and magnetic fields that oscillate exactly in phase. According to the Theory of Quantum Mechanics, EM radiation is composed of photons, i.e., small packets of energy. These photons can have virtually any energy and are classified into different classes according to their energy, as shown by the EM spectrum. According to the wave theory, each value of energy can be converted into a distinct frequency and wavelength of the corresponding EM wave.

ELECTROMAGNETIC SPECTRUM



EM radiation exhibits numerous remarkable properties. You will encounter a few of them in the other articles in this booklet. For example, the phenomenon of **diffraction** is explained and applied to X-rays on p. 4 and applied to visible light on p. 10. The **quantum nature** of EM radiation brings about a number of exotic properties, as highlighted on pp. 6-8. A lot of interesting effects arise when EM radiation interacts with a sample. These effects can be investigated using a set of techniques known as **spectroscopy**. The two most commonly studied spectroscopic effects are **absorption** of the EM radiation by the sample, and spontaneous emission, also known as **fluorescence**, whereby EM radiation with a slightly lower energy is emitted.

Raman spectroscopy is a frequently used technique to study molecular vibrations and is introduced on p. 9. This technique is based on the **inelastic scattering** of EM radiation by a sample whereby the energy of the EM radiation changes due to its interaction with the vibrations of the molecules in the sample. Molecular vibrations normally correspond to energy in the near-infrared region of the EM spectrum. When a molecule's electron cloud responds non-linearly to the electric field of an EM wave, this property can be exploited to bring about interesting **non-linear effects**, as explained on p. 10. Finally, one can actively modify the waveform of an EM wave; for example, shaping the phase or intensity of the wave front in a predetermined way (see also on p. 10).

With all its fascinating features, EM radiation is an extremely powerful and versatile tool to study biological systems. Visible light, which covers only a small fraction of the EM spectrum, is the most commonly used form of EM radiation simply because we can guide and observe it the best.

The year 2015 is known as the UNESCO International Year of Light and is therefore an opportune moment to publish this edition of 'The World of Biophysics' brochure.

UNESCO

INTERNATIONAL YEAR OF LIGHT 2015

PROTEIN STRUCTURE & BIOTECHNOLOGY

Trevor Sewell, University of Cape Town

Applications of biological molecules have a huge commercial potential, but scientists first have to understand the structures of proteins at the deepest atomic level. Being able to unlock these secrets locally is an important component in the global economic success of South Africa.

South Africa has a long history of involvement in biotechnology. The "first-generation" biotechnology used organisms to grow one of the world's largest brewing companies, a globally renowned wine industry, and important programmes in plant and animal breeding. The "second generation" went a step further and introduced useful characteristics into micro-organisms. Now the "third generation" engineers molecules and cells, creating products like industrial enzymes (i.e., the chemical "reactors"), therapeutic agents, pesticides, and vaccines. To tap into this potential one needs to have a detailed knowledge and understanding of proteins. This starts with the structure of the protein.

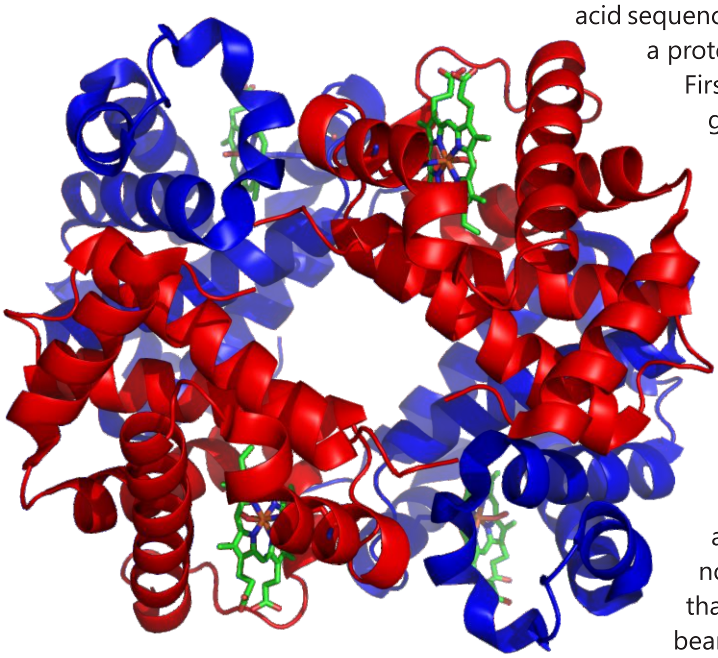
What are proteins and why are they important?

A protein is a chain of amino acids. Only 20 different amino acids are generally used in nature, yet when arranged in sequences of differing length they fold into a specific pattern having interesting and useful properties. Each type of protein has its own specific sequence of amino acids. Each amino acid has a different side chain giving specific properties to that amino acid. The amino acid chain generally folds in a manner determined by the amino acid sequence, producing a specific 3D (three-dimensional) structure. It is this 3D structure that gives the protein its unique properties. Proteins are the macromolecules that do most of the work in a cell, taking part in essentially every structure and activity of life. They catalyse reactions, transport molecules around, detect and respond to the environment in which the cell is situated, and controls the way in which genetic material is expressed in the formation of cells. They make cells into well organised, exquisite and efficient machines. Studying the 3D structure of a protein provides insights into how proteins work, how they interact with each other and other biomolecules, and how the higher order complexities enable cells to function.

Knowing the protein structure, we can engineer proteins to make new chemicals. This is the heart of industrial enzymology. We can also now design molecules that interfere with the life-giving reactions of harmful pathogens or pests (i.e., drugs and pesticides). South Africa has a huge biodiversity, which opens the possibility of various new discoveries. Unfortunately, South Africa has so far been slow in taking up this opportunity.

How to find the structure of a protein

Despite decades of intensive research, we are still unable to predict the unique folded structure of a protein even when its amino acid sequence is known. In fact, the research needed to work out the structure of a protein is complex and has many stages, each with its own challenges. First, a sufficient amount of the protein is required. This is often done by genetically engineering a laboratory friendly bacterium to produce large amounts of the protein. After extraction and purification of the protein, a visual image of its atomic structure needs to be obtained. One commonly used technique is X-ray crystallography. For this to work, the protein needs to be crystallised to high purity, the right shape, size and quality. Once this has been achieved an intense beam of X-rays is focused onto the crystal.



The X-rays are then diffracted into a pattern of spots with different intensities and positions. From this pattern computer programmes can be used to generate a 3D image of the crystal's atomic structure that scientists can understand and interpret. This is no trivial exercise, because the equipment has not yet been invented that would give us all the information we need to recombine these beams into an atomic resolution, 3D image of the protein.

***Original article:** "Treasure from the molecules of life" Quest 2(1) 2005. Synopsis by Raymond Sparrow and Tjaart Krüger.*

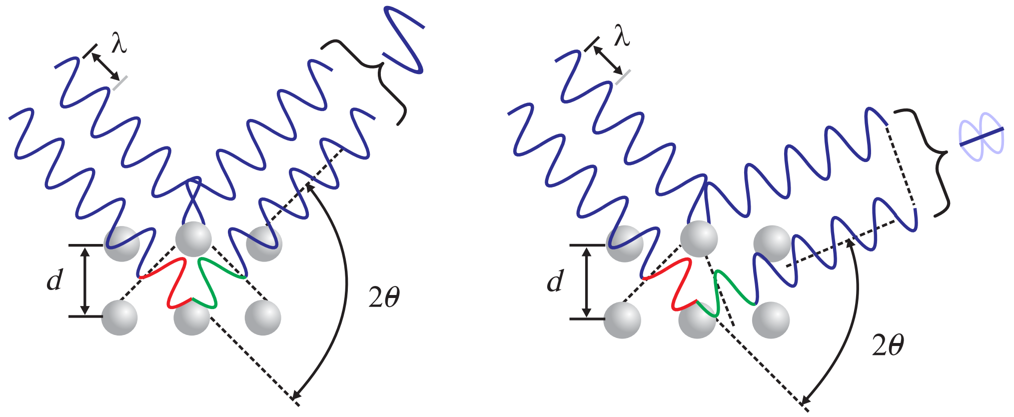
X-RAY CRYSTALLOGRAPHY

At the age of only 22, William L. Bragg realised that, because of their extremely short wavelengths, X-rays can be used to determine the arrangement of individual atoms inside solid crystals. For this insight, three years later he became the youngest ever physicist to receive the Nobel Prize.

The key to Bragg's discovery is the phenomenon known as **diffraction**. When a wave hits an atom, it bends around the atom and gives rise to a spherical wavelet. The spherical wavelets emanating from each atom in the molecule meet again and interfere with each other. The result of interference depends on the distance travelled by two such wavelets (see diagram below). When the two wavelets are exactly in phase they will add up and produce a strong wave. This is known as constructive interference. If the two wavelets are exactly out of phase they will cancel out, a process known as destructive interference. Projection of the interfering wavelets onto a detector gives a particular diffraction pattern.

In crystals the protein molecules are lined up in a regular array, like soldiers on a parade ground, and so the signals due to the diffracted beams are greatly amplified. These amplified signals can be detected and recorded. Because the physics of diffraction is well understood it is possible for the recorded signal to be processed by a computer to produce an image of the electron density in the protein that can be interpreted in terms of the precisely located atoms.

Diffraction: Two layers of equally spaced atoms diffracting two X-rays incident from the left



Bragg's law relates all the symbols:

$$2d\sin\theta = n\lambda$$

where n = 1,2,3,...

Constructive interference *occurs at an angle where the emerging wavelets are in phase.*

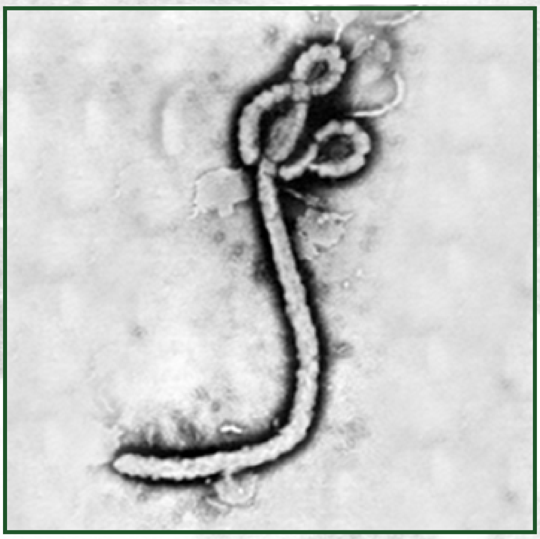
Destructive interference *occurs at another angle where the emerging wavelets are exactly out of phase, resulting in the cancellation of the two wavelets*

ELECTRON MICROSCOPY

Electron microscopy is another technique that can be used to obtain near-atomic resolution of a specimen. Electrons differ from X-rays in that they are charged particles and thus they can be bent by magnetic fields and focussed with electromagnetic lenses. The wavelength of an electron is a function of its momentum. When an electron is accelerated by a 300 kV potential difference it has a wavelength of 1.97 pm – much smaller than the size of an atom!

The images formed are the projections of the molecules being examined. The projections down different axes can be combined into 3D images by a technique called electron tomography that was invented by Aaron Klug. He was educated at the Universities of Witwatersrand and Cape Town but did his Nobel Prize winning work in Cambridge.

By averaging thousands of identical single-particle images, the resolution can be increased even further. Although electron microscopy still cannot always match the resolution provided by X-ray crystallography, its big advantages are that crystals are not required and only a small amount of sample can be used.



Electron micrograph of an Ebola Virus

PLANT POWER

Tjaart Krüger, University of Pretoria

How do you envision the power plant of the future? What will electricity be like in fifty years?

Imagine using trees as the future street lamps (with the special feature that they direct the light only onto the street and not into your bedroom). Or the possibility of growing grass on your roof and using part of the absorbed solar energy to run your household devices...

Did you know that plants are miles ahead of our best solar energy technologies? Plant leaves contain billions of tiny photosystems, which are responsible for collecting sunlight and ensuring that the energy is stored in useful forms for later use. A plant photosystem works pretty much like a satellite dish: it contains a large antenna to absorb as much of the sunlight as possible and directs the absorbed energy to a reaction centre. The reaction centre is the "receiver" where the signal is converted into another form – in this case into a potential difference across one of the membranes in the chloroplast. The potential difference is formed by rapidly transporting a proton to one side of the membrane and an electron to the other side. This temporary state constitutes a powerful nano-scaled battery, which drives subsequent reactions to stabilise the energy. The harvested energy is eventually stored in chemical bonds – the most compact and efficient way of storing energy.

Most plants are designed to thrive in rather dim light conditions. Under these conditions, a so-called photosystem uses the energy of essentially every absorbed photon – the smallest unit of light – to eject an electron and transport it across a membrane. This whole process occurs within a few picoseconds, that is 10^{x12} times faster than a second, or one-trillionth of a second.

What do the photosystems actually look like? They contain a lot of molecules which our bodies are also made of. That's why it's good to eat your vegetable salad! First, the main component is proteins. Proteins are in fact the molecular machines of all living systems. Second, there are lipids that help with the assembly and functional regulation of the photosystem. Third, everything is located inside a membrane – a huge, structured soapy layer – that controls the movement of substances between the inside and outside. Finally, the molecules that absorb the photons are called pigments, because they are responsible for the distinct colouration of the leaves. The two types of pigments in plants are called chlorophylls and carotenoids. Carotenoids have a few different functions, amongst which is to act as antioxidants: they deactivate dangerous forms of oxygen and oxygen-containing molecules and in this way protect the photosystems, and ultimately the cells, from being destroyed. The proteins act as a scaffold to position the pigments in a precise and dense arrangement to ensure efficient and fast light harvesting. The arrangements are such that relatively small disturbances can significantly alter the amount of light that eventually reaches the reaction centre. This feature is used by the proteins in a magnificent way to very precisely tune the light harvesting efficiency of the photosystems, depending on all environmental conditions, such as the light intensity and temperature. Imagine a solar cell that can similarly adapt perfectly to almost any environmental condition...

Only very recently have scientists started to understand how this energy regulation works. Each protein can switch rapidly and efficiently between different functional states: a light-harvesting state and a light-protecting state. This constitutes a switch of a few nanometers in size, hence a nanoswitch. Under normal conditions these switches are performed frequently and randomly due to the intrinsic disorder of the proteins. This property of proteins is quite related to what Nobel Laureate Richard Feynman once said, "Everything that living things do can be understood in terms of the jiggling and wiggling of atoms." A photosystem senses the intensity of the incident solar light and based on this, controls how the protein nanoswitches operate. This means that a natural safety valve is regulated to safely dissipate just the right amount of excess energy that would otherwise damage the photosystem.

In other words, a property that in conventional nano-engineered materials is tried to be avoided as far as possible – disorder – is used by plants in an ingenious way. This is not all: the intrinsic disorder actually promotes the light harvesting efficiency too. Let's take silicon semiconductors as a counter-example. These materials are designed to be perfect crystal lattices, because defects trap the excitations, which results in energy losses. Plant photosystems, in stark contrast, are much more irregular, random, and defect-filled than these materials, and yet they perform energy harvesting in a far superior way.

So it should start to dawn that physics plays a very important role when one desires to understand the fundamental functioning of natural photosystems, which are in fact very complex systems to investigate. Once these processes are understood, the principles can be used to develop the next generation of solar cells. One powerful method to probe the very fast motion of energy within a photosystem makes use of femtosecond lasers. Pulses as short as a few femtoseconds are used, that is 10^{x12} times faster than a second! One new exciting development in our lab is to manipulate and control the energy transfer within a photosystem by laser light with special properties. This will enable scientists to control externally the light harvesting ability of these miniature biological solar cells.

QUANTUM BIOLOGY:
WHERE QUANTUM PHYSICS MEETS BIOLOGY

Adriana Marais, Betony Adams, Maria Schuld, Ilya Sinayskiy, Francesco Petruccione, University of KwaZulu-Natal

What is Quantum Biology?

Quantum biology studies biological processes necessary for the functioning of living systems where there exists evidence that a description in terms of classical physics is insufficient. [Let's define 'classical physics' as the kind of physics we are used to in everyday life.] In its current state, the primary importance of the field of quantum biology lies in the identification and mimicry of the ingenious feats of engineering taking place in systems ranging from bacteria to birds. If exotic quantum phenomena (often called 'non-trivial quantum effects' – see the Box on the right) on a macroscopic scale play a role in getting the job done better in immensely complex systems, then there exists before our very eyes a wealth of information in the biological world from which to draw inspiration for our own technologies. In the following, three examples of Quantum Biology will be given: (1) quantum effects in energy and electron transfer in photosynthesis; (2) the quantum radical pair mechanism in magnetoreception in birds; and (3) biologically inspired quantum computation in the area of neural networks.

Exotic Quantum Phenomena

For more than 100 years, the somewhat puzzling behaviour of very small objects observed in isolation is studied in the field of quantum physics. Particles like atoms, photons and electrons can be described surprisingly accurate through wave functions that contain probabilistic information on the particle's state (such as its momentum, position and energy).

These 'probability waves' can interfere, giving rise to a highly unintuitive behaviour of small particles that has been observed in countless experiments up to today. For example, quantum objects can be in different states at the same time (called a 'superposition') as long as they are not disturbed. 'Coherence' describes a distinct, well-determined relationship between such states. 'Quantum entanglement' means that such states interact even though the particles might be light years apart.

1. QUANTUM EFFECTS IN PHOTOSYNTHESIS

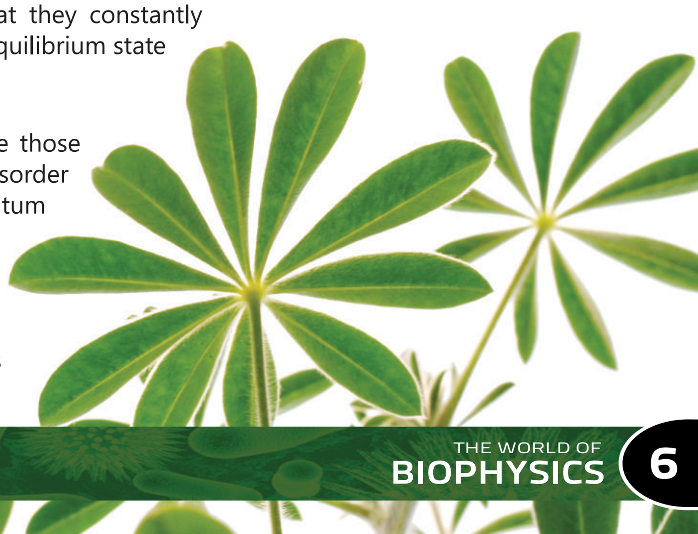
There is a large class of living systems that has perfected a method of synthesising organic compounds from carbon dioxide and an electron source using the sunlight energy continuously incident on the surface of the earth: the process is known as photosynthesis. Photosynthetic organisms are the source of carbon-based structures which form the elementary building blocks for all known life.

Solar radiation accounts for nearly all of the renewable energy available on earth, with on the order of 10^{17} Watts of incoming radiation at the upper atmosphere, which far exceeds current human consumption. Photosynthesis is an extremely efficient process for harvesting light energy from the sun. But how this efficiency is achieved, although pivotal to our very existence, is not yet well-understood.

Photosynthesis is initiated when the light-harvesting antennae in the photosynthetic apparatus absorb incoming photons of sunlight. This light energy is transferred with almost no energy loss (i.e., near-perfect quantum efficiency) through a series of electronic excitations to the reaction centre, where it is stored as the electrochemical potential energy necessary for subsequent chemical conversions. Understanding photosynthesis on a molecular scale is necessary to engineer biologically inspired artificial photosynthetic systems, which would allow us to harness renewable sunlight energy with greater efficiency than is presently possible.

Vast scale separation has meant a traditional distinction between quantum mechanics and biology. However, recent evidence of quantum coherence (see the Box about Exotic Quantum Phenomena) in the primary stage of energy transfer in photosynthetic light-harvesting complexes at physiological temperatures, has raised the intriguing question of whether non-trivial quantum effects play a role in the efficiency of this process. While evidence of quantum effects in the subsequent stage of primary electron transport in photosynthesis were identified nearly 50 years ago, aspects of this stage of the process are also not yet fully understood microscopically. Biological systems are open systems, which means that they constantly exchange energy and matter with the environment to maintain the non-equilibrium state synonymous with living.

It is necessary to use the theory of open quantum systems to describe those biological processes for which classical physics fails. Protein structural disorder creates a "noisy" environment, which can either destroy or sustain quantum coherence. Understanding how environmental noise can sustain rather than destroy coherence has important implications for the drive towards building the legendary "quantum computer" and for quantum information processing and transfer in general, where the decohering effect of the environment on the quantum systems in which information is stored is considered one of the most serious challenges.



2. THE AVIAN MAGNETIC COMPASS

The incredible feat of navigation that birds perform so easily in their seasonal migration is an intriguing puzzle. From the sheer distance covered every year by the Arctic Tern to the ability of certain species to find their way home even when transported far off their normal course, avian migration testifies to the intricate genius design of biological systems. But it is a question that is still not perfectly understood.

There are currently two models that have been proposed to explain the phenomenon. The first model suggests a magnetite-based receptor located in the beak of the bird would provide map information about the bird's position. The second, more feasible model is the so-called radical pair mechanism, taking place in the eye of the bird. The latter model accounts for compass information through the orientation of the bird relative to the geomagnetic field.

The radical pair mechanism operates through the following steps. A donor molecule absorbs a photon, which results in one of its electrons moving to an excited state and then being transferred to a nearby acceptor molecule. The donor and acceptor molecules now form the radical pair as each has an unpaired electron. Before transfer, the electrons are in a so-called singlet state. This state depends on the relative spin orientations of the electrons and it is this correlation that introduces quantum mechanics into the model.

Due to the interaction between the electrons and the surrounding nuclei, the electron spin can flip, bringing the electron into a so-called triplet state. An external magnetic field, like that of the earth, can strongly affect the interconversion between singlet and triplet states. This interconversion depends on the alignment of the radical pair with the magnetic field and finally results in a specific signalling state, which gives information on the bird's orientation in the magnetic field.

There are various reasons why the radical pair mechanism is accepted as a model to describe bird navigation during migration. One piece of evidence is that migration is light dependent, which corroborates the photon-induced electron transfer; another indication is that an oscillating magnetic field of specific frequency influencing the singlet-triplet conversion results in disorientation in birds. Furthermore, whereas the magnetite model does not show noticeable effects for weak magnetic fields, the radical pair mechanism shows significant effects at fields comparable to the geomagnetic field. In addition to this, predictions made by the model agree with characteristics discovered by behavioural tests.

Being a relatively new model, there are still various open questions. For example, what is the special biological molecule allowing magnetoreception? Is it cryptochrome, a light-receptor protein also found in plants and animals? Why do different wavelengths of light induce more or less successful migratory responses in birds? Is this an indication of two interacting receptors? How does the singlet-triplet conversion translate into a signalling state? How do specific quantum effects such as coherence, decoherence, and entanglement contribute to the functioning of the radical pair mechanism and thus the ability of birds to navigate in a magnetic field?

The magnetoreception model has similarities with some key processes in photosynthesis and might therefore give added insight into the way energy is harvested in photosynthesis. In addition to this, the research will address more widely relevant questions in that it will need to consider the effects of 'decoherence' and 'dissipation', both of which remain challenges in the ongoing quest to build a quantum computer.

Finally and most generally, this research aims to marry quantum mechanics, one of the most successful theories used to describe the physical world on its most fundamental level, with an attempt to understand that most fundamental question, "what is life?".

3. QUANTUM NEURAL NETWORKS

Quantum neural networks is a rather exotic research area that combines probably the most fascinating and active fields in biology and physics, namely neuroscience and quantum computing.

Despite its long tradition, neuroscience is still confronted with the open question of how information is processed in our brain. By extracting, classifying and remembering patterns from input stimuli we are able to make sense of large amounts of data relatively fast and efficiently. Similar tasks pose a serious problem to common computers. The foundations of the connectivity of neural cells and their chemical transmission of electric signals are thereby fairly well established, and neuroscientists try to simulate these processes in simplified mathematical models, so called artificial neural networks. It has been comprehensively shown that these models recover fundamental principles of how the brain operates. However, the power of our central organ, especially the problem of how the mind emerges from neurophysiology, largely remains a mystery.

Equally mysterious seems to be another, recently developed paradigm of information processing: quantum computing. Quantum computing uses the quantum effect of superposition (see the Box about Exotic Quantum Phenomena) to do a large number of computations in parallel. Although we are currently only able to control small numbers of 'quantum bits' without destroying their quantum nature by disturbing them too much, there is no lack of theoretical proposals and algorithms for a future quantum computer. The most famous is the solution to the prime factorisation problem which has not been accomplished on a classical computer yet. The reason for the importance of this formal problem is that our daily digital communication is based on our inability to solve it. The potential power of quantum computers is consequently beyond doubt.

Quantum neural networks merge insights from quantum computing and artificial neural network research. This can either refer to artificial neural networks that fulfil the paradigms of quantum mechanics, or quantum computing algorithms inspired by neural networks. The basic approach when merging both fields is the so-called McCulloch-Pitts neuron, a reductionist neuroscientific model from the 1940s that understands neurons as binary objects with the two possible states 'resting' and 'active'. Although being far from the complexity of chemically induced action potentials, this simplification allows the construction of surprisingly powerful artificial neural networks. In quantum neural network research, these binary neurons are interpreted as two-level quantum objects. A quantum neuron can consequently be in a superposition of the two states 'resting' and 'firing'. This superposition is responsible for the power of quantum computing, as both possibilities feed into the calculation in parallel.

Recent developments to explore new algorithms of quantum machine learning promise to link the two emerging fields in an overall discipline of quantum artificial intelligence, in which the exploitation of quantum effects for methods of 'intelligent' data processing is studied.

Quantum neural networks also border the controversial debate around the 'quantum brain', i.e., whether our brain uses quantum effects to increase its performance. Quantum brain models are still disputed and it is questionable if quantum effects can be observed in the macroscopic process of neural signal transmission that is currently believed to be the central mechanism of information processing. However, we now know from quantum biology that physiological temperatures can very well provide an environment to quantum objects that is useful for certain tasks, and we cannot exclude that similar phenomena as in photosynthesis are found for our central organ as well. Exploration of new ways of information processing consequently also serves to establish potential quantum brain models, even though such ideas still are in their infancy and a fair amount of fundamental research is needed.

SURFACE ENHANCED RAMAN SPECTROSCOPY
NANOTECHNOLOGY & LASERS SHED LIGHT ON BIOLOGICAL PROCESSES

Pieter Neethling, Laser Research Institute, Stellenbosch University

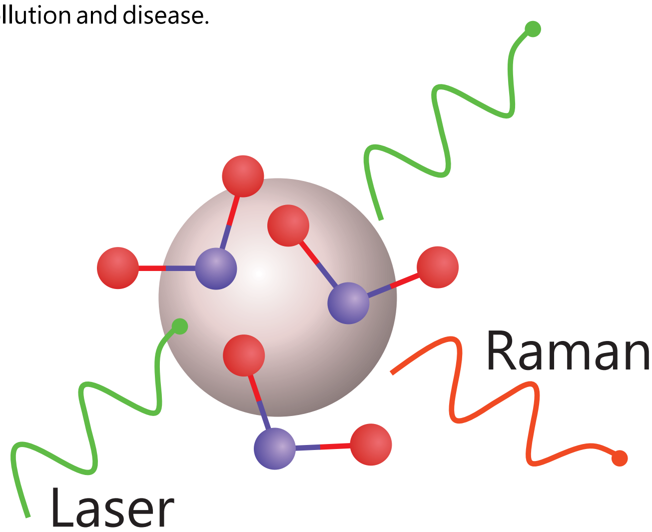
Raman spectroscopy is an invaluable tool to study materials and molecules and to identify compounds within a sample. Much like a human's fingerprint is unique and cannot be duplicated, so the Raman spectrum from a molecule acts as a fingerprint. In this way if one can record the Raman spectrum of an unknown sample, one can in principle identify all the molecules that are present in the sample, even in very small quantities.

Now this might make Raman spectroscopy sound like the Holy Grail for analytical chemists, enabling the identification of mixtures of compounds with unprecedented accuracy. Unfortunately, it is not quite that simple. Raman scattering, the principle behind Raman spectroscopy, is an extremely weak process. This means the measured signals needed to identify molecules are hard to measure. This is simply because of the nature of Raman scattering which is the inelastic scattering of photons by a molecule. When photons with a specific energy (specific wavelength or colour) scatter off a molecule, about one in a billion scatter inelastically, leaving some energy behind. These few scattered photons now have less energy and hence a different wavelength or colour. The shift in wavelength is small and one needs very high resolution and very sensitive detectors to distinguish them from the elastically scattered photons. This then explains the serious limitation of conventional Raman spectroscopy, namely, the signal is very weak.

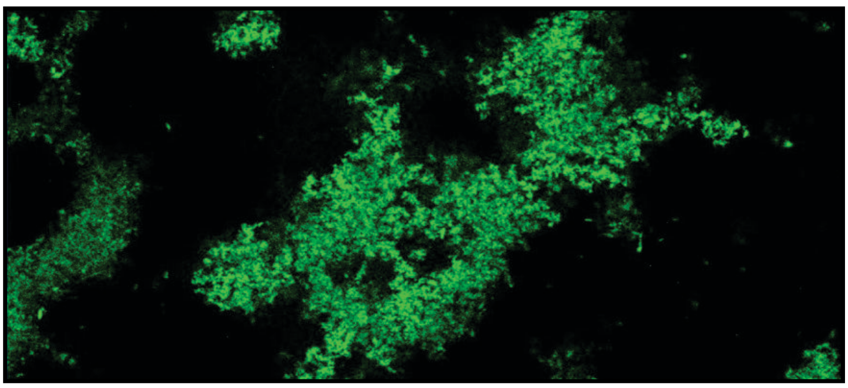
In 1973 however, it was first reported that the Raman signal measured from a molecule adsorbed on a metal surface is orders of magnitude bigger than predicted from theory. This was the first reported instance of surface enhanced Raman spectroscopy (SERS). It seemed that the inelastic scattering process is significantly enhanced by the close interaction between the metal surface, the molecule being investigated, and the laser beam. Latching on to this phenomenon, scientist began experimenting with different metal surfaces and structures. One of the most promising variations is using metal nanoparticles (metal spheres on the order of a millionth of a millimetre in diameter). These tiny metal balls can come into extremely close contact with many more of the molecules that are in the solution one is investigating compared to a metal surface, thereby enhancing the Raman signal even more.

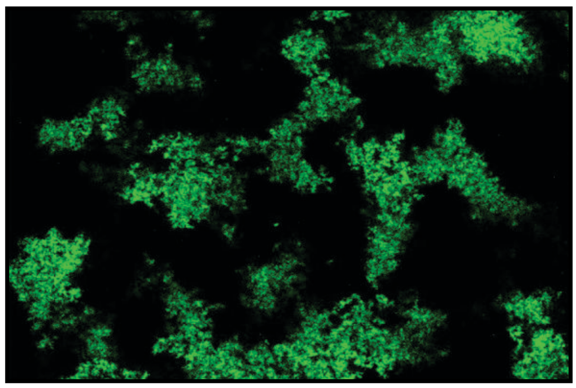
These breakthroughs have led to the application of SERS to a variety of fields, none more so than the field that I am most interested in, namely Biophotonics. The easy synthesis of a variety of metal nanoparticles together with the SERS technique has allowed researchers to gain insight into the biochemical processes occurring within cells, non-invasively and non-destructively. This means we can monitor which biochemical products (carbohydrates, proteins, enzymes, etc.) are formed under particular conditions inside living organisms. My current research focusses on biofilms. Biofilms are colonies of bacteria that occur all around us, in our bodies and in our water supplies. The bacteria excrete a slime which provides an environment in which the bacteria can thrive.

Some of these biofilms van be very harmful and it can be very expensive and time consuming, if not impossible, to remove them. Our research focusses on the slime these bacteria excrete. By using nanoparticles and the SERS technique, we can identify the molecules present in this excreted slime. Once we have identified these molecules, our colleagues over at Biochemistry can use this knowledge to turn the once ideal slimy environment of the bacteria inhospitable. In this way nanotechnology and lasers combine to help us fight against pollution and disease.



Raman signal originating from molecules close to a metal nanoparticle (depicted in grey). The Raman photon has a longer wavelength than the incident laser wavelength.





Fluorescence micrographs of biofilms in their initial growth state.

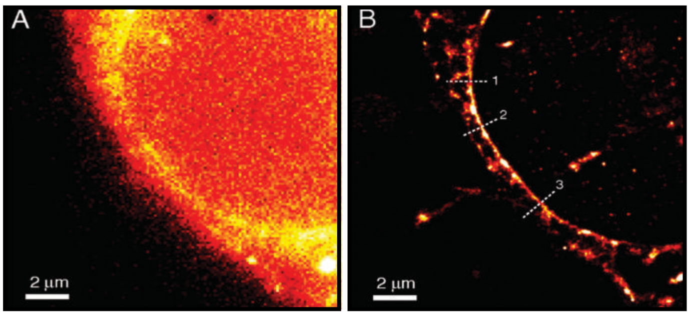
OPTICAL MICROSCOPY

Tjaart Krüger, University of Pretoria

Optical microscopy is probably the most commonly used tool to study biological systems. It is one of the very few techniques by which a physiologically active sample can be studied with high spatial resolution. With 'resolution' we mean the ability to distinguish two objects as separate entities instead of seeing them blurred together. The added resolution is the key asset of a microscope, because mere magnification does not add any information, just as enlarging a small photograph will only have a blurring effect. In optical microscopy, mainly visible light is used, having wavelengths of roughly 400 nm to 700 nm (where nm stands for nanometre, which equals 10^{-9} m). Even when using only this tiny part of the electromagnetic spectrum, there are numerous microscopy techniques available and new ones are still being developed.

Diffraction (see p. 4) sets a fundamental limit to the resolution of an image, restricting it to about half the wavelength of the light that is used. For blue light, this is about 200 nm, which may look impressive, but with this resolution one can hardly discern the interiors of biological cells. This law of physics did not prevent scientists improving the optical resolution, though. Various ingenious approaches have been developed during the last decade, which make it possible to get a resolution as high as 1 nm, using only light. This resolution is sufficient to resolve small biological molecules and even subunits of larger molecules like proteins and DNA. The 2014 Nobel Prize in Chemistry was awarded for this incredible feat. Interestingly, all three Nobel Laureates received a solid training in physics – yet another illustration of how far physics can bring you in the field of biology.

Many of the sub-diffraction imaging techniques make use of fluorescent (spontaneously light-emitting) molecules that switch their emission on and off and using this information to locate the position of each individual molecule with nanometre precision. Some other techniques make use of specially tailored light beams. This brand new basket of techniques is known as 'super-resolution microscopy' or simply 'nanoscopy'.



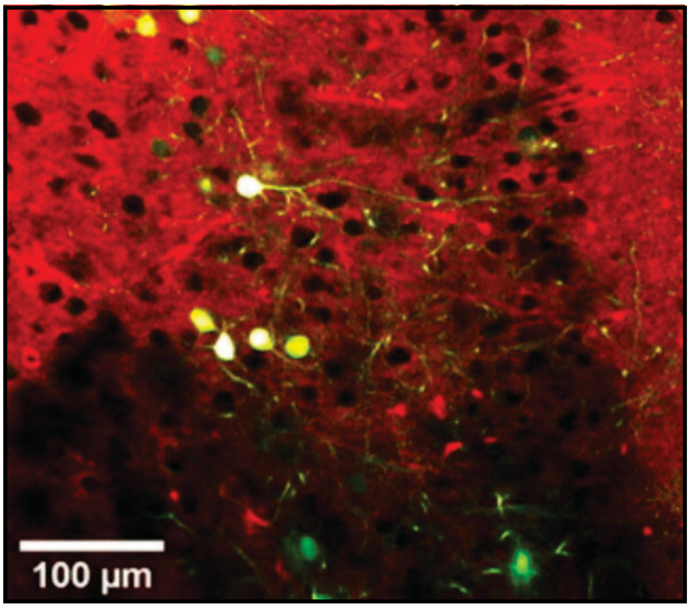
HIV-infected cell imaged with conventional light microscopy (left) and using super-resolution reconstruction (right).
Courtesy: Christophe Zimmer, Institut Pasteur, France

Light exhibits many fascinating features. An interesting phenomenon occurs when a molecule absorbs two photons of the same wavelength at exactly the same time. When the energy is emitted a short instant later, the emitted radiation has double the frequency of the two absorbed photons. This phenomenon is called 'second-harmonic generation' or 'frequency doubling' and is one of the many so-called non-linear optical effects.

Non-linear effects are typically only observed at very high light intensities. This is readily achieved using a laser beam consisting of extremely short pulses (with a pulse duration of typically 10^{-11} - 10^{-13}s), giving a very high energy per pulse. The energy density can be increased even further by focussing the beam tightly, such as is done by a microscope lens. Scanning across a specimen under a microscope brings us to the technique known as 'non-linear microscopy'.

Non-linear optical effects occur only in a non-linear medium, which is a medium whose optical properties are modified by an intense beam of light. Some biological structures are non-linear, for instance muscle myosin, a motor protein moving along filaments and involved with muscle contraction. Such structures can be studied directly using non-linear microscopy or can be used to stain other biological structures to make them non-linear. One commonly used non-linear staining molecule is the Green Fluorescent Protein extracted from a particular jellyfish.

Non-linear microscopy holds several advantages over conventional microscopy, enabling deeper penetration into the sample, less scattering of the light, less damage of the sample, efficient light detection, and useful colour contrasts.



Non-linear fluorescence image of a mouse prefrontal cortex, where frequency doubling (red) and frequency tripling (green) were used.
Courtesy: Stefan Witte, VU University Amsterdam

Profile: ALEXANDER PARADZAH

GENERAL BACKGROUND

I come from the remote district of Chirumanzu in Zimbabwe. I received my early education in Zimbabwe and graduated with an Honours degree in Physics from the University of Zimbabwe in 2010. In 2012 I started studying for a Masters degree in Physics at the University of Pretoria where my research focused on semiconductor materials.

CURRENT STUDIES

Currently, I am busy with my PhD studies at the University of Pretoria, specialising in Biophysics. Instead of continuing with Semiconductor Physics, I decided to go for an entirely different challenge. I believe it is good to challenge oneself and also to diversify one's own knowledge base. Biophysics at the University of Pretoria and in South Africa as a whole is a new field of physics research and I wanted to be part of the pioneering group of students in this exciting research field.

My studies are aimed at understanding the ways in which energy is transferred between different molecules of the light harvesting apparatus in photosynthetic organisms. These processes occur on extremely short timescales, typically in the order of femtoseconds to picoseconds from the time a photon is absorbed by the photosynthetic organisms. I carry out my experiments at the CSIR, using femtosecond lasers and optics to get an insight in these ultrafast energy transfer processes. If these processes are well understood, it will be a major step in revolutionising the energy industry towards cleaner renewable energy. It is this positive impact on humanity that motivated me to be involved and contribute in this research area.

STUDYING BIOPHYSICS

After last studying biology in high school, it has been a challenge to learn again some biology as biophysics requires some knowledge of biology. However, it has been a worthy challenge, and this is mainly because I have much respect for the positive impact that the kind of research I am involved in has. This research is undertaken in collaboration with other institutions and I have had opportunities to travel and carry out experiments abroad. This makes the research less difficult and more enjoyable.

LOOKING FORWARD

As I continue with my PhD studies and beyond, I aim to focus my research more towards hybrid structures made up of semiconductors and natural light harvesting complexes. Energy transfer studies in these structures are very important as we move closer to utilising natural light harvesting systems in real devices. This is even more important as my MSc expertise will be integrated with my current PhD studies. This shows the interdisciplinary nature of Biophysics.

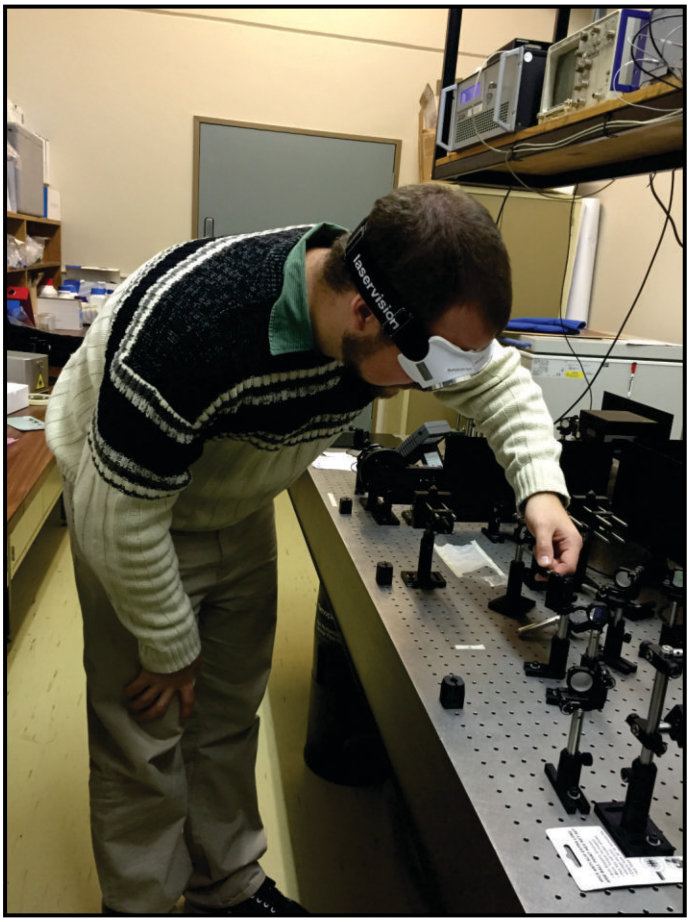
Profile: JOSHUA BOTHA

GENERAL BACKGROUND

I grew up in a small town called Newcastle in KwaZulu Natal. As a young high school pupil I believed that my difficulty with mathematics would be a limiting factor on my future, but through hard work and dedicated parents my weakness grew into a tool that has made possible the path I have taken thus far. A love for questioning all the wondrous phenomena we find around ourselves drove me towards the sciences.

ACADEMIC BACKGROUND

After matriculating from High School Rustenburg in 2008 I completed a BSc degree majoring in Physics and Chemistry followed by a BSc Hons. in Physics, both at the North-West University. A chance encounter with Dr. Krüger towards the end of my Honours led to my discovery of Biophysics, which I had an immediate affinity for. I've always believed that interdisciplinary science is the way forward: humanity has always benefited from working together towards a common goal. Biophysics is precisely that - a common goal. The following year Dr. Krüger started a Biophysics group at the University of Pretoria and I enrolled for my MSc in 2014. I was fortunate to have been given the opportunity to spend two months at the Vrije Universiteit of Amsterdam. Presently I am attempting to complete my MSc by the end of 2015, and am hopeful to be given the opportunity to continue with a PhD next year.



GETTING INTO PHYSICS

In a way I happen into physics without realising it, and I have realised that this often has been the case with physicists in general. There are a select few that knew beforehand that studying physics was their dream vocation. Whether by active planning or happenstance, physicists seem always to be passionate about their work. This to me seems to be a rare thing that few people achieve in life. I recall being told many a time that to become a scientist I would need great resolve and be passionate about science, as the science itself would be my greatest reward. I agree wholeheartedly. I would encourage any young minds to take a second look at the world of physics; there truly are many opportunities in South Africa.

"BIOPHYSICS?"

This question seems to be the inevitable reply when I tell people that I study Biophysics, so allow me to motivate why one would want to study Biophysics and what it is. If one were to consider a living organism, you would realise that as an object made of matter it needs to obey all the rules, say, a rock has to. But unlike a rock, a living organism is dynamic and functional. In a sense the 'purpose' of a rock is to be, whereas a living organism can survive and thrive. To my mind this is what sets Biophysics apart from mainstream Physics; we study a system that makes use of the physical word objectively instead of only being a part of it. Nonetheless, it remains a study of physics, and fundamental physics at that. Thermodynamics, electrodynamics, spectroscopy (i.e., the interaction of light and matter), quantum mechanics, polymer physics..., to name but a few of the areas of physics that are found in biological systems. In concert with genetics, physical and organic chemistry, bioinformatics, biotechnology, etc., Biophysics provides a foundation to our understanding of life and living things.

Consequently, Biophysics has a myriad of possible applications. Once we truly understand how living organisms function, avenues open up that have always been closed to our imaginations. Synthetic photosynthesis is the one application that has captivated my interest. Imagine, if you will, a future in which rural areas can grow genetically altered algae that adhere to a cheap metallic surface and provides a flow of electricity through the day. This truly is exciting to me as a physicist! It might still be 'Sci-Fi' at the moment, but in the words of Albert Einstein, "Imagination is more important than knowledge."

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