From medical imaging to new microscopy techniques, physics can be applied in many ways to biological sciences. Discuss how this multidisciplinary approach is useful, giving specific examples.

The intricacies of the physical and biological disciplines, on the surface, appear to have very limited overlap. However, the widening frontiers of modern science are fostering the collaboration of the biological sciences and physics. By drawing together ideas from multiple disciplines, problems that are outside of normal boundaries can be explored and solutions can be discovered, due to a new understanding of complex situations.

Quantum Biology and Solar Energy

Surprisingly, the quantum world – an aspect of science that seems to be solely found within physics - can actually be found in several areas within biology, from the sense of smell believed to be driven by quantum mechanics, or the possible release of biophotons associated with high intelligence,[1] the two disciplines are more intricately intertwined than one may originally think. A central goal of quantum biology would be to elucidate new design principles to create new devices and technology.[2]

Over billions of years, photosynthetic organisms have evolved using a unique strategy to harvest solar energy with nearly perfect efficiency, possibly due to quantum phenomena. At the nano-meter scale, thylakoids act as the 'engines' of photosynthesis, containing molecules of chlorophyll. They hold antennae-like pentagonal plates which are light-harvesting molecules called chromophores.[3] Chlorophyll molecules contain a magnesium atom, in which the valence electron can be easily knocked into the surrounding carbon cage, by the absorption of a photon, creating a positively charged gap or electron hole. This leaves the rest of the magnesium atom neutral whilst a system, called an *exciton*, of the escaped negative electron and a positive hole has been created. This is unstable as the electron and hole feel an attractive electrostatic force. If they recombine, the solar energy would be lost as waste heat. A process called charge separation occurs and the electron is rapidly transferred to the neighbouring molecule, aided by the tightly packed nature of these chlorophyll molecules. The transfer of this energy from a chlorophyll antenna molecule to the reaction centre has one of the highest efficiency of any known reaction. Using a powerful technique called 'two-dimensional Fourier transform electron spectroscopy' (2D-FTES), the inner structure and dynamic of the tiniest molecular systems can be studied by targeting them with highly-focused short-duration laser pulses.[3] Three successive pulses of laser light were fired at a photosynthetic complex called the Fenna-Mathews-Olson (FMO) protein made by green sulphur bacteria which lives in cold temperatures. This deposited energy in very rapid and precisely timed pulses, generating a light signal that can be detected. From analysation, it was found that oscillations were produced, forming an interference pattern, similar to that produced by 'Young's Double Slit experiment'. From this, it may be deduced that the exciton doesn't take one single route but rather multiple routes simultaneously, showing that chlorophyll molecules cooperate by applying the principle of quantum superposition.[4] Energy is shared by all the chlorophyll molecules at once.

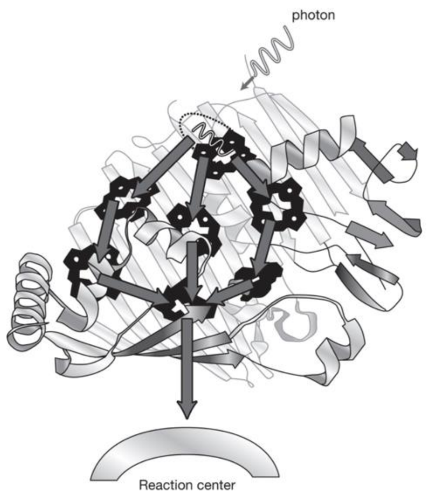

Figure 2: The exciton moves through the FMO via multiple routes simultaneously. [3]

However, this 'quantum coherence' is extremely delicate and random molecular motion can quickly disrupt this carefully aligned quantum mechanical system – known as decoherence, and it occurs more rapidly at higher temperatures. 'Quantum beating', however, has also been detected in spinach[5] and so the concept that warm living bodies maintain these quantum states is extremely impressive. Quantum coherence may be a factor in optimising energy transfer efficiency as it is very different from the random hopping motion associated with classical mechanisms of energy transfer.[6] Another aspect contributing to the rapid energy transfer include the fact that chlorophyll molecules are optimally spaced, to allow energy transfer but also to prevent concentration quenching. The supramolecular organisation of antenna again contributes to this efficient process by allow a multitude of energy delivered pathways.[6] Once at the reaction centre, a particular pair of chlorophyll molecules, P680, release electrons, which are sourced, using the energy provided by the exciton, from the oxidation of *water* – the only natural process known to do this. The electrons are captured and transported by NADPH, which is more stable than an exciton, to a chain of enzymes that pump protons out of the chloroplast membrane. This can then be used to produce ATP molecules and eventually power lots of processes within the plant cell.[3]

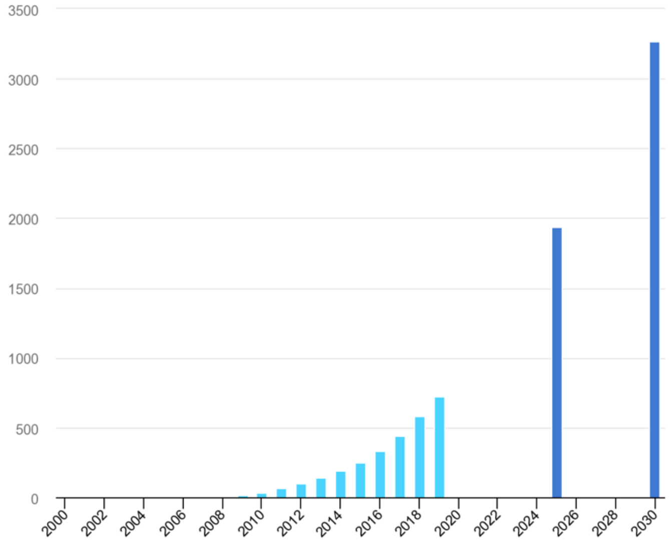

Figure 1: Solar photovoltaics power generation in the Sustainable Development Scenario, 2000-2300.[7]

Considering the interior of cells is a very noisy environment with random molecular vibrations, decoherence *should* occur. This is a problem many physicists face when trying to build quantum computers and so this technology currently only exists at temperatures very close to absolute zero and also devices must be shielded to suppress molecular noise.[3] Research, therefore, on how these fragile quantum states are maintained at such temperatures in this biological environment and how to avoid the 'washing away' of these quantum states by the turbulent thermodynamic interiors of big objects i.e. decoherence, could help the physical world to build practical quantum computers or inspire a new generation of solar cells. Solar panels are already competing for a share in the energy industry and the power generated by them is expected to increase in the future, as shown by Figure 1. Solar PV generation increased by 22% in 2019 and was the second-largest absolute generation growth of all renewable technologies. It is on track to achieve the levels envisioned by the Sustainable Development Scenario.[7] Current panels, however, are limited by losses during energy transport, and at best only achieve a 70% efficiency. Applying biology-inspired quantum coherence to solar cells therefore has the potential to greatly increase the efficiency of solar cells and thereby create a blueprint to delivering a cleaner world. Dorfman et al[8] analysed photosynthesis as a quantum heat engine, thereby proposing that quantum coherence could boost the photocurrent of a photocell by at least 27% compared to a classical photocell. A team from the University of Cambridge produced a model of an artificial photocell that could work as a quantum heat engine, acting as a reaction centre. It was shown that that it could deliver an energetic electron to an acceptor molecule, with a similar Carnot limit-busting efficiency enhancement to natural photosynthesis.[9] Therefore, a quantum solar cell could use this artificial reaction centre to capture energetic electrons, via the absorption of photons, and convert them to stable chemical energy.[3] Other factors to consider would be the ability to produce the actual energy for these reactions (similar to ATP) or the harnessing of molecular noise (in the manner that photosynthetic organisms do) to maintain quantum coherence. However, the knowledge on how this is achieved is currently too limited. Overall, this research could teach scientists how to engineer the molecular structure of a chromophore, using earth-abundant materials to introduce into solar energy technologies.[10] Although this is an extremely simplified overview of how quantum biology may be utilised, such an advance could be revolutionary.

A Different Perspective – How can Physics help Biology?

There are many ways in which physics can be applied to biology e.g. the development of technology such as electron microscopy or NMR spectroscopy are crucial in gaining insight into biological function for both therapeutic and diagnostic applications. Or, physics may seek to break down complex and messy systems found in biology into their fundamentals constituents to explain them through known universal laws. For example, Boyle’s law, which describes the relationship between pressure and volume of a gas, has been vital to understanding the principles of gas exchange. Overall, combining the two fields opens up new opportunities for innovation and scientific progress to be made.

X-ray Crystallography

Perhaps, one of the most famous contributions of physics to biology is X-ray crystallography. This tool uses the diffraction phenomena of X-rays by crystals which can be attributed to the phase relationships between two or more waves, thereby producing a diffraction pattern, to help deduce the structure of complex molecules. It looks at three mathematical and physical properties to provide a better understanding for the biological sciences: geometry of diffraction, symmetry observed in the pattern and the variation of intensity in the discrete diffraction measurements.[11]

Nowhere has this tool benefitted society more than in health and medicine – it has pioneered groundbreaking studies within the field of biology, such as the structure of penicillin which inspired the creation of antibiotic treatment and the structure of insulin which helped with the understanding of diabetes, both discovered by Dorothy Hodgkin. Furthermore, through the crystallographs produced by Rosalind Franklin, Watson and Crick were able to discover the double helix of DNA which allowed scientists to understand how it replicates.[12] X-ray crystallography remains a vital technique to understanding complex biological molecules and finding new ways of treating disease. A more recent achievement using crystallography, is the discovery of the structure of a ribosome, and the way antibiotics disrupt it, which will provide major insight on how to tackle the growing resistance of bacteria to antibiotics,[12] which Dorothy Hodgkin helped make possible. And therefore, from just a few examples, it can be seen that crystallography will continue to be a central tool in the future for scientists globally, showing how crucial a multidisciplinary approach, which integrates the fields of biology and physics is to advancing further.

Medical Physics

There are many ways in which physics can be applied to medicine and is involved at the frontiers of research. Developing new equipment such as imaging modalities ranging from PET to SPECT or MRI to optical is just one of the basic necessities that physics can provide to help the scientific field of medicine to grow and evolve so that new treatments can be discovered.

Radiation therapy is a form of cancer treatment where malignant cells are controlled or killed. It aims to maximise the damage to tumour cells whilst maintaining the surrounding healthy tissue. Currently, photon or electron beams are the most conventional types of radiation used however, new treatments such as proton therapy have been introduced as alternatives. The principles of conventional cancer treatments and proton therapy are very similar. When energised protons pass near orbiting electrons, they ionise atoms, consequently changing the characteristics of the molecule within which the atom is. This damages molecules such as DNA, thereby destroying specific cell functions such as replication.[13]

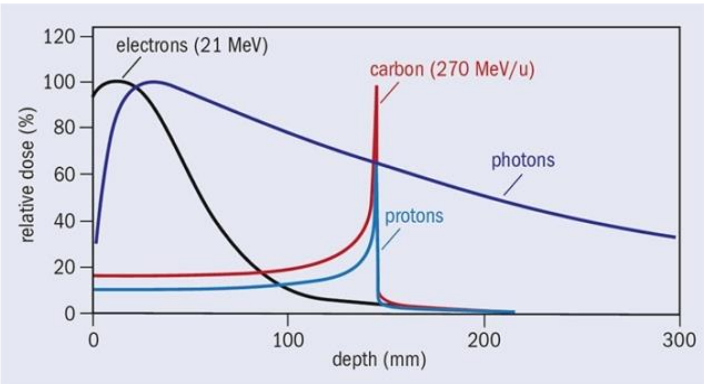

Figure 3: The Bragg peak of protons and several other ions.[15]

The main advantage of proton therapy is shown by Figure 3. Protons (and carbon ions) slowly deposit their energy as they migrate towards a cancerous tumour, and then deposit a significant amount of their energy near the endpoint of the trajectory, in a very concentrated manner known as the Bragg Peak, beyond which very little energy is deposited, which contrasts that of X-ray therapies.[15] This Bragg-peak effect provoked the discovery of using hadrons for cancer treatment. This also offers the advantage of shaping particle beams with greater precision, thereby providing a more accurate treatment of the tumour and minimalising damage to the surrounding tissue. Currently, approximately 450 individuals die everyday in the UK due to cancer[14] and so further research on how to optimise this therapy may help to save many lives.

Along with technologies and research facilities, such as the cyclotron, being provided by the physics community, the culture of multidisciplinary collaboration at the heart of organisations such as CERN is navigating towards a range of different fields,[15] promoting the growth of hadron therapy which integrates both physics and biology.

Bionanotechnology

This particular field is a rapidly emerging one that sits at the convergence of nanotechnology and biology. It applies the tools of nanotechnology to biological problems, creating specialised applications.

In the UK, up to one in every 1000 people are affected by deep vein thrombosis (DVT) annually.[16] However, current thrombolytic agents can greatly increase risk of intracranial hemorrhage which can lead to stroke or death and more targeted treatments such as thrombectomies can often lead to a pulmonary embolism and so a better form of treatment with more optimistic outcomes is required.

A recent emerging therapy, which, although is still in its infancy, has great potential is a type of sonothrombolysis, which uses ultrasound waves to remove blood clots. However, this new possible form of treatment combines the use of an ultrasound drill with specially engineered nanodroplets to break apart blood clots.[17] They have a low boiling point so that a small amount of energy delivered by an ultrasonic drill can vaporise them, forming microbubbles that rapidly expand and contract to break down a clot via cavitation which is where microscopic streams weaken the mechanical structure of the clot.[18] Due to their small size, nanodroplets can penetrate retracted clots with low porosity and so the vibrations can open up holes in the clot that enable the entry of enzyme-enhancing drugs to encourage further breakdown. Over a period of 30 minutes, clots were found to have reduced by 40%, an increase of 23% for treatments that combine ultrasound, microbubbles and enzyme-activating drugs.[18] However, a peak negative pressure of 3-5mPa, provided by the ultrasound waves, is still needed to activate the nanodroplets and this exceeds the safety limit for ultrasound imaging and therefore will hinder their clinical translation.[17] Nonetheless, the development of this prospective treatment for DVT provides an insight into how physics and cutting-edge technology are entangled with medicine in such a manner where the two disciplines compliment one another, helping each to progress into the future.

Conclusion

From physics-inspired biology to biologically-inspired physics, this multidisciplinary approach opens up an extraordinarily wide field, from encompassing the behaviour of systems at a molecular level to working with the nature of whole ecosystems. It seeks to solve complex problems in physics through biological mechanisms and problems in biology by considering these mechanisms as physical systems. From quantum phenomena observed in such a fundamental and crucial process for life, to the study of the physical properties of biological molecules via X-ray diffraction, it is clear that there are lessons that can be taken from both disciplines, to provide new perspectives into the two scientific realms.

One might regard the two scientific fields as complete opposites – where theoretical physics searches for simple and universal mathematical laws that act as the underlying principles of the natural world, whereas biology explores the complexity and diversity of life. One of the barriers to incorporating multidisciplinary approaches is the protective nature of many highly focused scientists on their area of expertise. However, working at the interface between these disciplines has already shown to and will also continue to help promote future revolutionary breakthroughs in medicine and healthcare, as well as the biological and physical sciences and industry.

Almira Sohail

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