

Physics Department Newsletter

Volume 1, Issue 01











Multi-Photon Microscopy Lasers

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A New Tool For 3D Microrheology FPGA Boards For Laser Pulsing



Physics Newsletter

Welcome to Your Physics Department Newsletter

Vol. 1 Issue 01

Dr. Paul Dalgarno, Senior Program Director of Physics

It gives me great pleasure to introduce everyone to this first issue of our new Department Newsletter. Communication and sharing of good stories, news and experiences is especially important in these difficult times. I really want to thank Sean Keenan for not only formulating the idea of this newsletter, but for his monumental efforts as editor. I really look forward to seeing future editions and contributions from both staff and students alike.

In all the chaos and disruption, it is important to remember that – not only are we working hard to continue our commitment to teaching and education – but that world class research and innovation continues through the discipline. It's been a difficult academic year and to be honest we envisage this semester will be equally, if not more challenging. It great to hear about some of the positive work still going on through the department and some of the science coming out form that extensive hard work: all done in a safe and socially distanced way, of course.

Developing Cost-Effective High-Energy Lasers for Multi-Photon Microscopy

Dr. R. McCracken (Group Lead), Dr. D. Bajek (Research Associate) and Mr. E. Allen (PhD Student)

Multi-photon microscopy has been a ubiquitous tool in life sciences research for many years and, has the advantage of being able to image more deeply into tissue than traditional confocal microscopy, making it a popular choice for brain studies because it allows imaging of individual synapses and can also be performed in live animals. Today, the majority of multi-photon research employs two-photon techniques, where fluorescent dyes that emit light upon excitation are used in a specimen. A focused laser beam emitting long-wavelength photons excites an electron in the dye to a higher energy state when two photons are simultaneously absorbed. The advantage of this technique over single photon imaging is that it allows generation of twophoton signals in very small volumes, which provides highresolution images as the laser beam is scanned over the sample of choice. Additionally, the long wavelengths used to generate two-photon signals also permit cellular imaging deeper into tissue via non-invasive penetration at depths of \sim 500-700 μ m.

In 2013, Cornell University physicist Professor Chris Xu demonstrated in vivo three-photon microscopy (3PM) for the first time. In 3PM three low-energy photons have to be simultaneously absorbed to achieve the excitation of a fluorescent molecule. In addition, a longer wavelength is used, meaning the light scatters less and enables even deeper penetration into tissue, with imaging possible at depths of greater than 1mm. Non-invasive high-resolution imaging of cells at such depths would be highly beneficial for research in areas including regenerative medicine and leukemia, but 3PM is not without its challenges.

Currently, the technique has to make use of femtosecond

sources that operate with low pulse repetition frequencies (1 - 10 MHz), so that they deliver the high pulse energies (>250nJ) required to create the three-photon interaction. These sources operate across the nearinfrared (1200-1800 nm) and have to be limited to sub-2 W average power levels to avoid tissue heating. Commercial three-photon excitation systems based on optical parametric amplifiers (OPAs) are available, however these are highly inefficient and prohibitively expensive for the majority of research facilities. In addition, the need for a ~40 W pump laser, combined with the OPA, makes the footprint of the system prohibitive in labs where space is at a premium.



3PM at longer wavelengths enables deeper imaging than 2PM.

Our new research project, carried out in collaboration with microscopy equipment manufacturer Scientifica and laser manufacturer Chromacity, is working to develop cost-efficient lasers for 3PM by exploring novel laser architectures and low-MHz optical parametric oscillators (OPOs), pumped by Chromacity's ultrafast fiber laser technology. In contrast to single-pass OPAs, OPOs are four to five times more efficient, can provide shorter pulses with increased wavelength tuneability, and are significantly more cost effective. However, the OPO cavity length usually must match that of its pump laser, limiting outputs to >80MHz due to space constraints. Our project aims to combine patented IP in the generation of low-MHz high-energy

OPO pulses with know-how in the construction of dispersioncontrolled compact cavities to develop a commercially viable alternative that is compatible with existing microscopy platforms.

Physicists Build New Tool to Explore the Microscopic World

Dr. P. Dalgarno, Dr. L. Paterson and Dr. A. Matheson.

Drs. Paul Dalgarno, Lynn Paterson and Andrew Matheson from the Physics department at Heriot Watt University are working on building and using a new type of microscope used to "feel" the mechanical environment within a tiny sample.

They are closely collaborating with engineers from the Universities of Nottingham and Glasgow, plus chemists and cancer biologists from Nottingham with a collective vision to explore the microscopic world from a biological cell's perspective. What does a cell or tissue 'feel' when it is part of a living organism or if it is grown in a dish in a lab, and how does the cell respond to nearby hard or soft structures. How does it respond to pushing, pulling or twisting forces? These questions are key to understanding how cancer cells become invasive. For example, what triggers cancer cells to be able to push their way through structures they shouldn't be pushing through.

The work combines the skills of Dr Paterson (optical trapping), Dr Dalgarno (multiplane imaging) and Dr Matheson (soft matter and rheology) and they have named the bespoke instrument "OpTiMuM"; Optical Tweezers with Integrated Multiplane Microscopy – a new tool for 3D microrheology.

The technique involves tracking the 3D motion of an optically trapped microscopic sphere at the location of interest within the



"OpTiMuM" enables the tracking of trapped particles in 3 dimensions – the group hopes this new tool will enable more in-depth analysis of complex biomechanical processes.

sample. 3D positions are acquired by simultaneously capturing images of the microsphere from multiple planes. Using the position data and statistical analyses, the viscosity and elasticity in the microscopic volume around the microsphere can be determined. Ultimately, they hope the tool will enable experiments where the micromechanical properties of a cells' *Editor – S. Keenan; Graphics / Assistant Editor – M. Damyanov*

surroundings may be controllably manipulated and quantified, and the biochemical reaction of the cells to this change can be observed, so the unknow links between what a cell feels and how it reacts can be discovered.

The project (<u>nusense</u>) is being supported by Technology Touching Lives through EPSRC/BBSRC/MRC (Engineering and Physical Sciences Research Council/Biotechnology and Biological Sciences Research Council/Medical Research Council) joint grants EP/R035563/1, EP/R035156/1 and EP/R035067/1.

Fabio's "Tricky Question"

Dr. F. Biancalana

One of the basic operations that we learn when studying math is the addition of integer numbers. Summing up numbers is something we are used to in everyday life and it comes quite naturally to most of us. However, we typically sum up a finite amount of numbers at any one time - for instance, 1 + 1 =2 or 10 + 20 + 30 = 60, etc...

But what about infinite sums of integers? What if I were to ask you to sum up all of the integers from 1 to infinity (1 + 2 + 3 + 4 + 5 + 6 + ... and so on) what is the final result? Is the answer infinity - since the partial sum grows indefinitely? Or is it something different? Obviously, it must be an integer, right? Or is it really?

The answer to this question is by no means trivial – and may surprise you! If you can work it out on your own then you definitely have huge talent. So, think about it, use your brain without searching stuff on Google and I'll give the solution in the next issue of the Newsletter!

Kalmo Branco

Design and Implementation of an FPGA-based Direct Digital Synthesizer for Laser Diode Pulsing

M. Damyanov, 3rd Year MPhys Mathematical Physics

During the summer of 2020 I worked as an undergraduate intern on a research project supervised by Dr. Ross Donaldson and his PhD Student Alfonso Tello Castillo. The aim was to develop a new, more flexible and convenient method for pulsing laser diodes that can be used in the place of the traditional pulsing technologies. The ability to generate a wide range of frequencies was a substantial part of the desired operational flexibility. That

For discussion of the solution please contact <u>Dr. Biancalana</u>. If you would like to contribute your own "tricky question" then please email <u>the team</u>.

is why the attention was directed towards frequency synthesis technology.

Frequency synthesizers are electronic circuits that use a single reference frequency to generate a range of frequencies. These

circuits are used in many modern devices such as radio and satellite receivers. mobile telephones, GPS systems and more. The frequency synthesis technique used in the project



Oscilloscope trace of the experimental results.

was Direct Digital Synthesis (DDS). DDS constructs the signal digitally from "scratch" by generating the phase, frequency and amplitude. Consequently, signals of arbitrary waveform can be created using this technique. This is big - since we wanted to generate signals with normalized gaussian shape. The DDS system was implemented using an FPGA board.

FPGA stands for field-programmable gate array. It is an integrated circuit that contains an array of programmable logic blocks which can be "wired" together in different configurations. The configurations are generally specified by using a hardware description language (HDL). FPGA boards are characterized with high run speed, parallel processing capabilities, physical size convenience and more. These features make them attractive as a base for the implementation of direct digital synthesizers.

The DDS system was developed over the course of eight weeks. First the high-level and low-level configuration designs were created.

Then, the code for the FPGA board was written using VHDLwhich took the bulk of the project time. A



BASYS 3 FGPA board used for this experiment.

precise scientific approach was adopted along the way which allowed us to deal with the encountered challenges effectively. After the labs were reopened the system was tested with astonishing success.

This was the first time I worked as an intern on a research project. Due to the coronavirus lockdown we were working remotely from our homes and from different countries. Therefore, good communication was essential. Every week I presented a report in front of the research team, providing detail on how the project is progressing. This sharpened my communication skills. Although it wasn't a typical research internship where everyone is working in a lab and can meet face to face it gave me invaluable experience and insight. Moreover, I had never heard of FPGA boards and hardware programming languages before, not to mention frequency synthesis technology. I read several books on these topics in preparation for the project and, as a result of that, gained new skills which I have come to find out are of exceptional demand both in industry and academia. My advice to all undergraduate students is to make use of their free time and gather important knowledge and skills that will provide them with an advantage on their future path.

A Note From The Editor

S. Keenan, 5th Year MPhys Physics

First of all, I want to wish everyone a Happy New Year! I think we all needed that break over Christmas and to "recharge" in time for this new academic year – I certainly did!

I have been slowly working away at this newsletter over the past few months and it is nice to finally have a finished product to send out. With that, I wanted to take the time to pay special thanks to the contributing authors – without you this first issue wouldn't be possible! A special mention to Dr. E. Gauger for giving us the handwritten material for the front cover.

Thank you for taking the time to read this far, a lot of work has gone into producing this and I hope that it has been of interest and worthwhile in some way. I am always looking for new content and ideas to keep things fresh – once we get underway there is plenty of room to add opinion pieces or comments if there is interest to do so. This is YOUR newsletter – something to keep everyone up-to-date and in the loop with our department – whether you are an undergraduate, postgraduate, PhD student, academic or otherwise. For undergraduates our time at university plays a huge part in our future paths – I do hope that this newsletter could even be a way of keeping alumni in touch with the department and each other.

If you can spare 5 minutes then please fill in the following survey.

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