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DALTON CUMBRIAN FACILITY NEWSLETTER

SEPTMBER 2020

User access | Accelerator Systems Development | New Equipment | Staff Profile | DCF goes viral | Project Spotlight

WELCOME

Dear friends, colleagues and collaborators,

A lot has happened since our last newsletter and, like many of you, our normal operations have been drastically altered by the pandemic. Staff at DCF have adapted marvellously to the situation and, after a somewhat abrupt hiatus, we are now accepting users again. You can read more about our access arrangements below.

We continue to expand our capability and this edition of our newsletter describes the development of new end stations for the accelerator, plus new equipment for particle size analysis. In terms of research challenges, we've taken the opportunity to showcase some work in the life sciences: our project spotlight focusses on biological scaffolds and we're also excited to share some very new work in virology.

We're pleased to welcome two new staff members to our team. Paul Kenny is now our Health, Safety & Compliance Advisor, having joined us in the middle of lockdown while Lian Murdoch joins us as Executive Assistant to Kevin and me. You might be wondering just what the directors of DCF get up to so you can read more about Kevin on pages 4 & 5.

In future editions you can expect to hear more about developments in automated sample handling, our experiences of hosting the GREEN Centre for Doctoral Training, and more. Watch this space and in the meantime, stay safe.

Fred Currell
Director of DCF

Laura Leay
Editor

USER ACCESS

We have recently started to open for experimental work and our resident researchers have been quick to get back into the lab. Some of our external users have also been able to use to the gamma irradiator with more bookings made for the coming months, meanwhile the accelerator team will be operating a mail-in service.

We are doing things slightly differently now to comply with social distancing guidelines and operations are restricted to 9 am – 5 pm. To maintain social distancing, only researchers and technical staff with a need to be on-site have returned and work patterns have been scheduled to minimise occupancy. Please talk to the relevant person to make appropriate arrangement for your research.

THE GAMMA IRRADIATOR

Anyone wishing to use the gamma irradiator should contact ruth.edge@manchester.ac.uk and explain how often they will need to access the facility. Since we have reduced the number of building occupants, we ask visitors to limit the number of people on the experimental team and to be flexible when requesting dates.

THE PARTICLE ACELERATOR SYSTEMS

For the particle accelerator systems, our current priority is to carry out those irradiations which were already scheduled prior to lockdown and which had to be cancelled at short notice. A call for proposals has also recently been issued which will cover the period up to Christmas.

The accelerator team will run experiments on your behalf. To assist this, we are equipping data acquisition and control room computers with Zoom video-conference capabilities. We expect a key researcher from each team to be available during any allocated beamtime for video, telephone or email contact to facilitate any experimental issues which may arise during an irradiation.

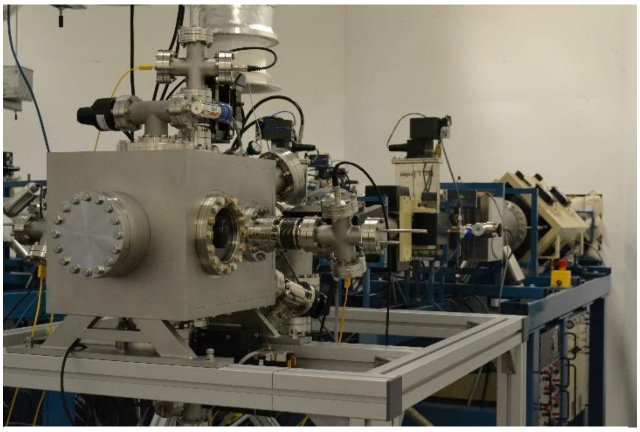
The maximum duration for continuous irradiation using a particle accelerator must fit in to the working day and so will be less than 8 hours long to allow time for accelerator start-up and shutdown, sample mounting, calibration and other necessary operations.

A FINAL NOTE

We will continue to operate as required by the University and Government Covid-19 guidance during the ongoing pandemic which means that the above restrictions may change.

ACCELERATOR SYSTEMS DEVELOPMENT

For radiation damage experiments we are commissioning a new experimental end chamber and have taken delivery of two new nickel endstages. The end chamber is currently being installed on beamline L5 (which has also received an upgrade to produce better ion beam focussing & steering) on the 5 MV tandem - DAFNE. The new chamber is an enhancement of the existing one on beamline LB on the 2.5 MV single ended accelerator, which it will ultimately replace. In the meantime it will improve the accessibility of heavy ion irradiations using DAFNE.



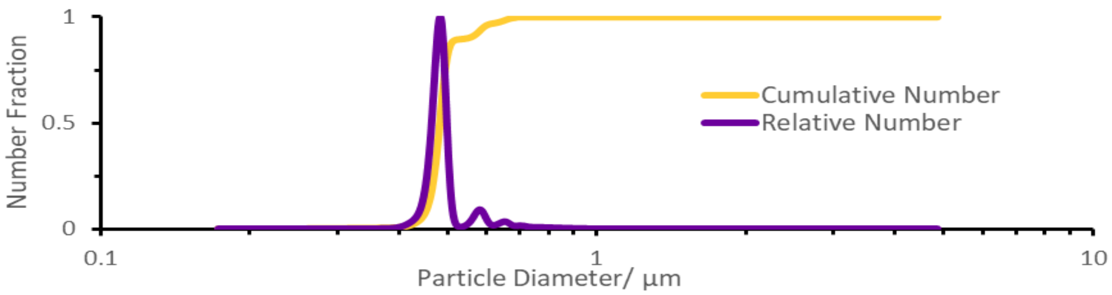
The new radiation damage end station, now installed on L5 of the 5 MV tandem ion accelerator

The nickel endstages will provide more flexibility in sample changes and allow us to finally retire the old nimonic stage.

In other developments, we are beginning a programme to develop a pulsed proton capability using a surplus magnetic kicker donated by STFC's Daresbury Laboratory. The kicker was originally developed to inject electron pulses into the EMMA accelerator and will now be used to kick short proton pulses onto samples for pulsed radiolysis type experiments at DCF. The pulse duration will be around 70 ns in length, with a frequency of 15 to 17 pulses per second; the short pulse length will also be of interest in ToF neutron spectroscopy measurements. Significant effort is ahead for the DCF team to integrate this equipment into an ion beam beamline, including the design of purpose built high vacuum enclosures and recommissioning the high voltage electronics and systems controls. To find out more, please contact Andy Smith or Fred Currell.

NEW EQUIPMENT

Particle size analysis can now be performed using our new model DC24000 CPS Disc Centrifuge from Analytik. The instrument provides ultrahigh resolution, high accuracy measurement in the size range 3 nm to 60 μm and can also be used for determining the thickness of nanoparticle coatings.



Particle size data collected from 0.483 micron PVC in deionised water

STAFF PROFILE

Kevin Warren
Director of Operations and Sustainability

Q: How did you come to be working at DCF?
I worked for BNFL until 2008 before moving on to become Nuclear Development Manager for the Northwest Regional Development Agency, managing public sector and EU investments made in support of nuclear projects across the region. Through this I worked on occasions with the University and, in 2010, was offered a role to help set up and operate its new centre for radiation science, which it had just started constructing.

My journey through BNFL began, after my 'A' Levels, in their Analytical Chemistry department before moving to Calder Hall nuclear power station. I was part of a team looking after the primary gas coolant and secondary water coolant systems, environmental monitoring and process engineering of chemical treatment at the power station. I loved working at an operating power station and eventually the Station Manager became so fed up of me hanging around he made me Head of Chemistry.

My one minor claim to fame is being the last Head of Chemistry at the world's first commercial nuclear power station in 2003, when Calder Hall reached the end of its operating life. I changed roles to lead development of the first detailed decommissioning plan for Calder Hall, working at Berkeley with other Magnox Generation colleagues. My final role for BNFL was to lead development of the decommissioning planning for various facilities at Sellafield, a plan costing £15 billion and lasting >100 years (so at least I wouldn't be around if it proved to be horribly inaccurate).

Q: How did it feel to see DCF grow from a plot of land to the thriving facility it is now?
Looking back, it was very mixed experience. Initially frustrating, as I wanted to get started, but also exciting as it started to form. For me the best part was when the big pieces of equipment, such as the gamma irradiator and the first ion accelerator, were installed. DCF then turned from a shiny new building into a research facility able to support experiments that couldn't be done anywhere else in the country.

Q: What is most rewarding and most challenging about directing operations at DCF?
To me at least, it doesn't (and nor should it) feel that there are differentiated groups of academics, professional staff, research associates, PhD students, external researchers...etc. working at DCF. It just feels like one fluid group of people who work incredibly hard and take pride in what they do. I also really enjoy the way that people always come up with new ideas and new ways of doing things.

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Perhaps more frustrating than challenging is sometimes not getting funding for things that you know would allow DCF to thrive, grow and contribute even more. You just have to accept it though and not get disheartened, as there are always other opportunities just around the corner. For example, I've been trying to secure funding to expand the footprint of DCF since just after it opened and have a special filing cabinet just for my collection of rejection letters. However, one day soon…!

Q: What do you like to do to relax?
It may not classify under this heading for most people, but cycling is my favourite pastime and I find a 100 km ride into the Lake District very relaxing. Walking our two dogs, Archie & Bobby, is also something I enjoy. Jillian (Mrs W) and I own a lodge in Scotland, where I like to mix the cycling, dog walking and other general outdoorsy stuff with sitting on the balcony with a wee dram or two and the odd game of golf!

Q: Apart from Liverpool FC's league position, what has been the biggest positive for you in the last 12 months?
As I can't talk about football, then it would be the continued dedication of everyone here. There are always challenges presented when operating and simultaneously carrying out multiple experiments in a highly complex research facility. Sometimes challenges are relatively minor and easily overcome, but still frustrating. Other times challenges may appear daunting and all consuming. However, I have the privilege of working with a group of people who always 'find a way'. And not just a way to get by, but a way to make things better. I'm aware this may come over as a sounding a bit corny, but without the people here DCF is just a store for very expensive scientific equipment.

Q: Where do you see DCF five years from now?
My desire has always been to see DCF firmly established on the international stage as a highly regarded research centre delivering consistently excellent radiation science. We have unique facilities here and great people. Match that with the ever growing opportunities for radiation science to make huge contributions to improving our world, whether it is through its essential contribution to providing clean, safe energy or its use in detecting and treating illness, and I firmly believe we will achieve even greater things in the years ahead.

DCF GOES VIRAL

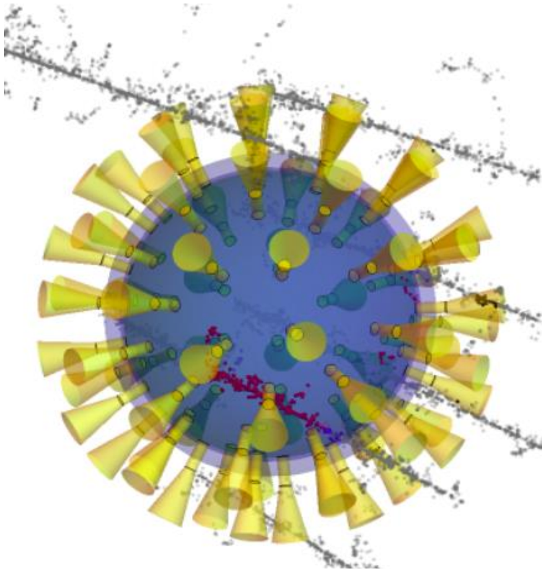
Fred Currell
For the Virion Inactivation and RNA's Underlying Structures (VIRUS) project

Lockdown came rapidly and after the dust settled the residential DCF community met in the zoomiverse for *DCF-vs-Covid-19* idea-sharing sessions. The goal: think about research directions DCF could embark on that were relevant to the crisis. Broadly we found two categories of ideas: radiation modification/synthesis of drugs or PPE; radiation inactivation of viruses. The later was inspired by a really exciting project taking place at GSI in Germany[*] under the leadership of Marco Durante, a world-renowned biophysicist.

Wanting to contribute to the understanding of ion-irradiated vaccine development, we embarked on planning, permission processes, grant writing and simulation. The basic idea is very simple – high-energy ions form long thin tracks which can pass right through a virion, the technical name for the particle which invades a host to become an active virus. An ion passing through a virion typically damages only one or two of the 70-plus spike proteins required to mediate cell entry. However, on passing through the virion's core there is a good chance it will break the RNA in a process very similar to the one used in cancer therapy to break DNA strands. This should render the virion inactive – it would enter the cell in the usual manner, provoke the same immune response but be unable to reproduce. The product is a ***Structurally Intact Radiation Inactivated Virion (SIRI-V)***. Our modelling suggests 3 MeV He^{2+} ions will be well suited to this. Interestingly but slightly disappointingly, the same modelling and that of the GSI group suggest protons are not suited to this application due to their lower ionisation density.

Of course, handling live viruses is not something to be undertaken lightly and we have been working very closely with University of Manchester biosafety staff to determine how to achieve this. Safety procedures have been drafted, University permissions for the first steps have been granted while grant applications and papers are being submitted[†]. Once DCF's backlog of beamtime commitments is cleared, we are planning the first experiments that will involve just RNA strands.

The path is a long one but one of the value of this approach is that it is universal; it can be applied to pretty much any RNA virus. We probably won't deliver a vaccine for this pandemic, but we certainly plan to be ready for the next one!



Modelling of tracks from a 3 MeV He^{2+} ion passing through a SARS-CoV virion. Dots show ionisation events: grey outside virion, black inside a spike protein, red inside the nucleocapsid containing the RNA.

[*] https://www.research-in-germany.org/news/2020/4/2020-04-17_Inactivated_viruses_for_vaccine_development.html
[†] https://www.biorxiv.org/content/10.1101/2020.08.24.265553v2

PROJECT SPOTLIGHT

Radiation Sterilisation of Decellularised Biological Scaffolds
Helen Berry, Leeds

THE BACKGROUND
Decellularisation has emerged as an auspicious strategy for generation of functional biological scaffolds that have near-native properties, reduced immunogenicity and tissue growth potential, for clinical applications such as heart valve replacement. Currently, decellularised biological scaffold production relies on donor tissue screening, antibiotic mixtures, liquid chemical sterilants, and aseptic techniques to achieve sterility. This method provides a suboptimal sterility assurance level (the probability that a single unit remains nonsterile), and thus a higher than desirable risk of a product causing infection upon implantation. Additionally, it increases the complexity of commercial manufacturing processes due to the environmental control and process validation requirements.

THE CHALLENGE
Traditional product sterilisation methods damage the integrity of natural biological structures. Steam, dry heat, and ethylene oxide degrade proteinaceous materials. Ionising radiation can cause changes in the primary structure of collagen, including free radical induced crosslinking between individual collagen fibres and polypeptide chain scission.

The research challenge is therefore to identify an optimal approach for sterilising novel implantable biological scaffolds that delivers a high level of sterility assurance, which can meet microbial inactivation validation criteria without compromising on the material's structure and functional performance. In the case of regenerative scaffolds, this includes preservation of desirable cell-biomaterial interactions and tissue integration.

THE SOLUTION
Introduction of novel radioprotective compounds and modification of gamma radiation dose delivery are being explored to overcome the detrimental consequences of radiation sterilisation processes. A balance between protection of the scaffold functional properties and capacity for inactivation of microbial contamination will be established, to allow implementation of terminal sterilisation and conformance with relevant medical device and human tissue product regulations.

THE BENEFITS
A research team from the University of Leeds is working closely with The University of Manchester's Dalton Cumbrian Facility to overcome the challenges of realising terminal sterilisation of novel functional biological scaffolds. Access to the unique irradiation equipment at the Dalton Cumbrian Facility is providing the researchers with enhanced flexibility to explore the effects of both cumulative radiation dose and dose rate.