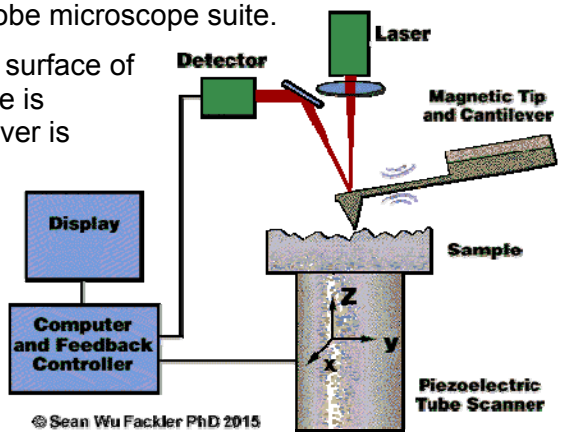
Spring 2019 RICHMOND SCIENTIFIC SOCIETY NEWSLETTER No. 103

LECTURE SUMMARIES by Dave Williams

19/12/18 ***Scanning Probe Microscopy: measurements in the nanoscale***
Andrés Muñiz-Piniella Director of C4AD CIC

When Andrés worked at the National Physical Laboratory he started by designing experimental setups to fit inside a scanning electron microscope. He moved on to atomic force microscopy and ended up managing the clean room and the scanning probe microscope suite.

The probe on the end of a flexible cantilever rests on the surface of the sample being scanned. The XY position of the sample is controlled by the machine, and the bending of the cantilever is monitored by a laser and detector. There is feedback to adjust its mounting so that the cantilever is maintained unbent, thus signalling the height Z of the probe.



This is Atomic Force Microscopy (AFM), but there is another technique used on electrically conductive samples, called Scanning Tunnelling Microscopy (STM). In this the tungsten probe is very close to the sample and a voltage is applied between the probe and the sample. A small tunnelling current flows dependent on the gap, and positional feedback maintains the current and hence the gap.

Atomic Force Microscopy does not have to have the probe in contact with the material as described above; there is a non-contact method using sensing of Van der Waals forces that tie atoms together. At a first scan the cantilever oscillates at its resonant frequency; as it gets close to the surface the Van der Waals forces cause a shift of the resonant frequency. After an optimal height is chosen the change is what is used as feedback which generates the output signal.

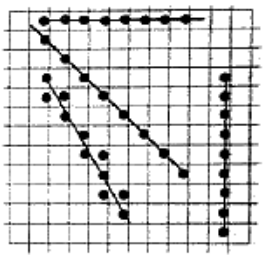
Other methods: Kelvin probe microscopy involves vibrating the probe around its various resonant frequencies, at the same time adding a high carrier frequency, producing sideband frequencies that vary in the same way as the resonant frequencies. Scanning Thermal Microscopy (SThM) has a tiny thermocouple that detects how much heat is being absorbed by the sample. Current AFM (I-AFM) senses current. Piezo Force AFM uses tiny vibrations caused by the sample to generate voltages across a piezo crystal.

While scanning the sample, the environment can be changed. For example heating/cooling, high/ultra-high vacuum to reduce damping on the probe and also reduce surface water, nitrogen atmosphere to stop oxidation in air, high humidity for testing corrosion.

A sample has to be stored with considerations regarding vacuum, exposure to light, dessicator, and labelling. It has to be prepared with considerations of cleanroom, polishing, cleaving, and not breathing on it. A database is kept of tests done and relevant ISO standards. Quality procedures are important, and tests must be reproducible.

Probes are normally made of silicon. They can be coated, tilted, pyramidal, long form factor, coated with carbon nanotube, or DNA to match DNA in the sample. They can suffer erosion. Assembly can involve glue, alignment, silver paste, silver glue, check/measurement of conductivity. The right type must be chosen for the job.

The feedback loops and speed of scanning must be adjusted so that the probe position settles within each pixel examined. Some machines average out the initial oscillations in output; others just give an output after oscillations have died out, but take much longer to do the full scan.



Data section plots should be along the X or Y axis or at 45°, otherwise erratic results may arise from off-course pixels as in the lowest plot here.

16/01/19 ***NMR Spectroscopy: a miscellany of molecular microscopy***

Paul Driscoll Francis Crick Institute

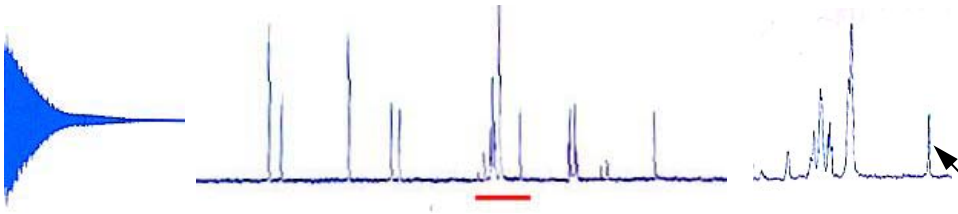
The concept of NMR (Nuclear Magnetic Resonance) takes advantage of something called quantum mechanical nuclear spin, which can be described mathematically in terms of certain nuclei's 'spin'. They don't actually spin but have angular momentum, which is quantised into specific amplitudes and can be positive or negative.

Unlike medical NMR scans, the speaker works on small biological samples, usually in aqueous solution in a thin-walled glass tube. *left*

It would be put into an NMR machine such as this one, "the most powerful machine in the country" at the Crick Institute. *right*

There are several other NMR machines at the Institute.

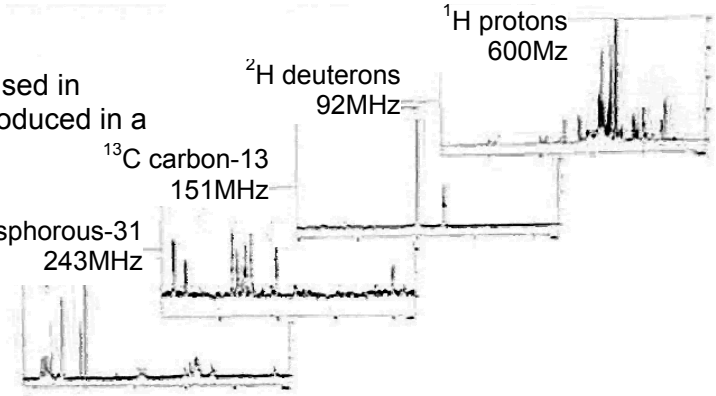
The field from nuclei in response to a radio pulse in the ambient strong magnetic field looks like damped ringing. The waveform is then subjected to Fourier analysis to give a frequency spectrum which shows peaks characteristic of individual molecules.

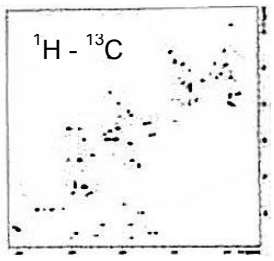


Output Wide range Fourier transform Expanded section CH_3 methyl group

The magnetic field in the machine is produced by superconducting coils in liquid helium inside a vacuum space inside a liquid nitrogen tank to limit helium boil-off. The radio signal coils are also held at low temperature by liquid helium to minimise thermal noise in the response.

Here are plots from four substances often used in biological samples, showing frequencies produced in a 14 Tesla magnetic field.





This is a 2D plot correlating the carbon atom to the proton atom in an individual CH bond.

This technique has been extended to 3D and 4D plots in certain applications.

After sketching out how NMR research is being used to determine the structure of proteins, the speaker ended by describing three particular projects he's been involved with.

Jeremy Brockes FRS did a study of the perfect regeneration of severed limbs in salamanders. The limbs were cut off beyond the blastema, a sort of elbow. The blastema has 'positional identity' and 'knows' what should grow there. If the blastema is transplanted elsewhere, a limb will grow from the new position. Using DNA sequencing, he concluded that a protein structure like CD59 in humans held the information, but it seems that salamanders have special genes that allow regeneration.

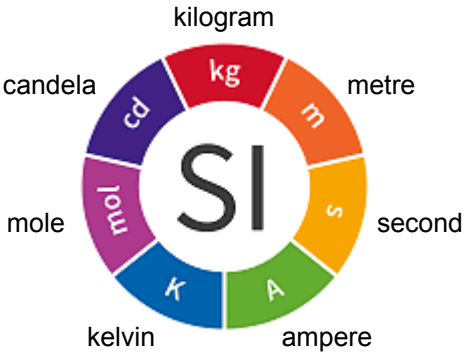
Alex Gould studied how nutrition leads to development in Drosophila fruit-flies. He showed that a particular gene ARK controls it. Humans also have it; starvation during pregnancy produces a baby with a normal size head but a small body. The field of research is called metabolomics technology and both NMR and mass spectrometry have their parts to play.

Dimitrios Anastasio, a colleague at the Crick Institute, is interested in cancer, liver regeneration and the fundamental metabolism involved in most processes. He studied glycolysis, the exploitation of glucose in both normal and tumour cells, which lead to different outcomes. A protein called PKM2 was thought to be responsible for the difference, and he had the idea to fuse a light-sensitive protein called LOV2 to the PKM2 to modify its action using light.

The speaker suggested using NMR to analyse experimental chemical reactions, and it was found that the spectra gave quick and clear indications of what was happening. Exposure of the mix to light showed how to control the production of pyrolase, a substance that was produced from normal cells but not tumour cells. It was even found possible to inject LED light into the NMR machine sample via an optical fibre, giving instant results.

13/02/19 ***Things we have measured at the NPL*** Fiona Auty, National Physical Laboratory

Measurement is the quantitative comparison of an unknown quantity with a standard quantity. The quality of the standard used depends on the importance of the measurement; hospital scanners are directly calibrated at NPL, but kitchen scales are calibrated via a chain of intermediate copies of standards involving time and distance from NPL.



Some things are brought to NPL by the manufacturers because they don't know how to measure them themselves.

There is one thing the whole world agrees on: the seven units shown here. They have grown up in history in the way they were measured, but this year, the kilogram will be redefined.

At time of writing it is the only unit still based on a physical thing, a lump of platinum in a safe in a vault in BIPM, the World Bureau of Measures near Paris. Every few years, the ceremony of opening it to the view of officials from around the world is performed to prove its existence!

On 20th May, World Metrology Day, it will be redefined by an experiment using Planck's constant.

Now to more mundane topics. A biscuit manufacturer used the sound they make on breaking to decide whether they were fresh enough, and asked NPL if it was possible to make a machine to do it in a reproducible manner not requiring a human expert. NPL investigated and told them yes.

NPL was asked to design a ventilation system for the House of Commons debating chamber, so to do the design they built a scale model with an air vent representing each person.

In 1980 Concorde was accurately weighed by load cells placed under each wheel in turn, like every new aircraft, to determine fuel consumption with various passenger loadings.

In 1942 the sounds of car horns were measured to see if they were loud enough to warn pedestrians.

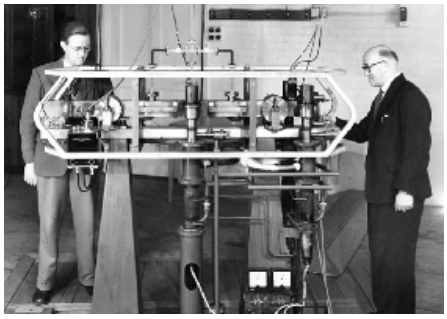
The speaker showed a photo of herself when she first joined NPL, with a prototype of a hand-held chip-&-pin machine that had been designed in-house.

When the National Lottery first started, they asked NPL to devise a method of measuring the lottery balls for consistency.

In 1976 NPL were asked to come and mend Big Ben clock when it broke in the hot weather.

When mobile phones first came out there was worry that the radio waves might harm the user's brain, so NPL made a rig in the shape of a human head filled with gel and a temperature probe. As an outcome, standards of permissible RF radiation were eventually decided.

In 1910 NPL had tanks for testing models of new ships (nowadays computer simulation is used). One of them was used to test the wartime bouncing bomb, and appeared in the film *Dambusters*.



In 1955 NPL built the world's first caesium atomic clock, designed by Louis Essen here on the right. It's now in the London Science Museum. The modern versions still use the same concept but are far more accurate, to the tune of one second in millions of years. Clocks based on optical principles are now being developed that promise one second in the lifetime of the universe, whatever that might be.

NPL runs air quality networks for the UK. Large vans take air samples, methane from refuse and smoke from chimneys.

In 2017 NPL started working with Cancer Research UK to develop means to observe cancer cells under a wide range of views in real time, without delays that could have serious implications.

NPL did a lot of work in standardising the output of the new low-energy CFL and LED lightbulbs.

A travel company wanted to know where in the world was the bluest sky. NPL designed the equipment and the company sent someone on a three-month measurement trip. It was a matter of luck what the weather was like each day, but the final verdict was Brazil.

Cauliflowers in the ground are covered by their leaves, making it difficult for picking machines to tell if they're ripe. NPL created a sensor that uses terahertz technology to see through the leaves.

Alan Turing designed the first electronic computer at NPL. In the 1940's NPL tested all taximeters.

Finally a quote from Lord Kelvin: *When you can measure what you are speaking about and you express it in numbers you know something about it; but when you cannot measure it, when you cannot express it in numbers, your knowledge of it is a meagre and unsatisfactory kind.*

CALENDAR OF SOME SCIENTIFIC LECTURES

Day	Date	Time	Host	Title
Tue	07/04/19	18:00	GC2	The Unacclaimed Accompanist
Tue	16/04/19	18:00	GC1	Text Mining: A Test of Character
Tue	23/04/19	13:10	UCL	Perception in the brain: what can EEG tell us?
Tue	30/04/19	13:00	GC1	500 Years of Maths: are we living in a new golden age?
Wed	01/05/19	12:15	LS	Putting Flesh on Ancient Bones
	07/05/19	18:00	RSC	Sodium and lithium ion battery manufacturing
Tue	21/05/19	18:00	GC1	Exploring Earth from Space
Wed	12/06/19	15:00, 18:00	GS	Did the Earth move for you? From slips to earthquakes
	1-7/7/19	See website	RS	Summer Science Exhibition 1st-7th July

All events are free but booking may be required. Some can also be viewed online live and later.

Host Venues:

GS: Geological Society, Burlington House, Piccadilly, London W1J 0BG
https://www.geolsoc.org.uk/events

GC1: Museum of London, 150 London Wall, EC2Y 5HN

GC2: Mercers' Hall, Ironmonger Lane, London EC2V 8HE
All Gresham College events: http://www.gresham.ac.uk/lectures-and-events

LS: Linnean Society, Burlington House, Piccadilly, London W1J 0BF
https://www.linnean.org/meetings-and-events/events

RS: Royal Society, 6-9 Carlton House Terrace, London SW1Y 5AG, (020) 7451 2500
https://royalsociety.org

RSC: Royal Society of Chemistry, Burlington House, Piccadilly, W1J 0BA http://www.rsc.org

UCL: Darwin Lecture Theatre, Darwin Building, access via Malet Place, London WC1E 6BT
http://events.ucl.ac.uk/calendar