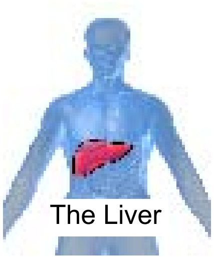
Winter 2018 RICHMOND SCIENTIFIC SOCIETY NEWSLETTER No. 102

LECTURE SUMMARIES by Dave Williams

12/09/18 ***Applying Maths in Medical Imaging*** Dr Gordon Hunter, Kingston University

Assisting the diagnosis of liver cancers from contrast-enhanced ultrasound videos



The liver is the largest organ by volume in the human body. After lung cancer, it is the second most common cause of world deaths from cancer (746,000 per year).

Most are due to a single growth called a Focal Liver Lesion (FLL). Diagnosis is normally via a conventional ('B-mode') ultrasound scan, but this is often inconclusive. Contrast Enhanced Ultrasound (CEUS) gives much improvement, but has further complications.

Other modes of imaging such as CT or MRI are better, but are expensive and require non-portable equipment. However they are often used if the initial ultrasound diagnosis indicates a positive identification.

In CEUS, a contrast agent, usually a suspension of stabilised microbubbles of an inert chemical, is intravenously injected. This improves the contrast between different body tissues to transmission, reflection and refraction of ultrasonic waves.

The agent takes time to reach the tissues and organs of interest, which gradually become enriched with the agent, and then depleted. Different tissues get enriched and depleted at different rates - but this feature can also be useful. A video recording of the ultrasonic image is started by the radiographer when the agent is injected, resulting in variations in reflected brightness over time. An expert hepatic radiologist then assesses the recording to see whether any lesions are present.

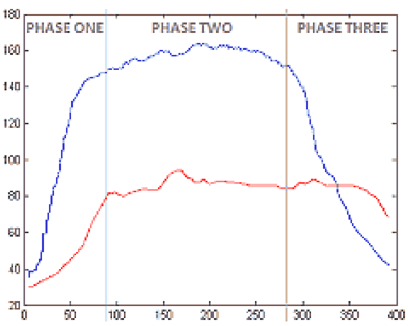
The radiologist has to find a suitable video frame in which there is good contrast between the healthy and potentially cancerous areas of the liver. The healthy tissues (parenchyma) and the boundaries of any lesions are marked on the image using an annotation tool. The differing increase and decay in brightness of the lesions compared with healthy tissue helps identification, but this is made difficult by the movement of the patient and of the hand held ultrasonic transducer.

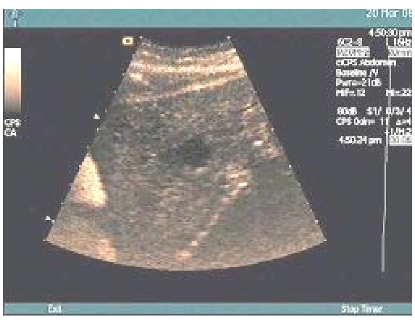
This analysis can be very time consuming, and the expert's time is expensive, so can some or all of it be automated to any degree?

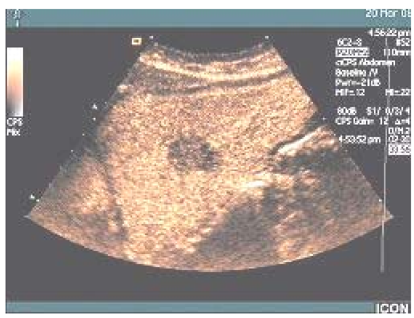
If so, the aim is for correct, reproducible results, not subject to human error, and creation of standardised criteria for the quantification of liver lesions. It is important to assess the repeatability and reproducibility for different people/days/centres.

Dr Hunter was involved in a study using 60 videos of CEUS examinations, each with a single FLL, of various types. The videos ranged from 30sec to several minutes.

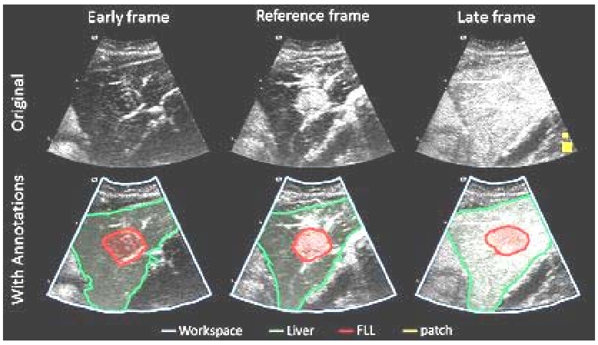
Each video had a copy with manually-annotated regions as described above, and also an expert's choice of the 'best' reference frame to initialise the above annotations: the 'Gold Standard' frame.







The graph shows concentration of contrast agent over time. The X-axis shows seconds. The agent builds up in phase 1, stays constant in phase 2 and flows out in phase three. The first scan during phase 1 shows a lesion as very dark against a brighter healthy ground.



The second scan was taken 6 minutes later in phase 3, and shows improved contrast between the lesion and the background, owing to the differing rates of flow in the lesion and healthy tissue.

The top row is three scans converted to greyscale. The bottom row has markings from the expert - healthy tissue in green and lesion in red.

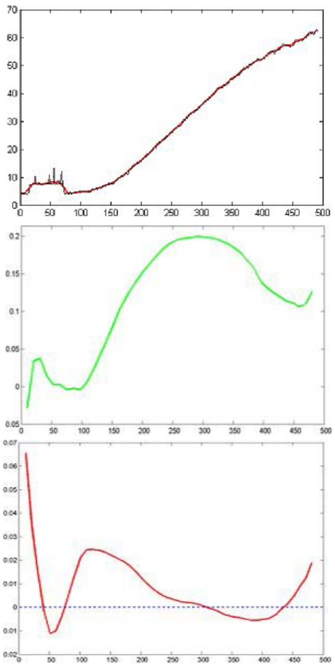
The best contrast between the two is in the middle phase-2 Gold Standard frame.

It was found that the response from benign FLL's can be a) always brighter than the surroundings, b) always darker, or c) first darker then lighter. But malignant FLL's were first lighter then darker.

Challenges in image analysis include low quality noisy images with poor edge definition, irregular patterns due to patient's and clinician's movements, out-of-plane motion, and dispersion in depth.

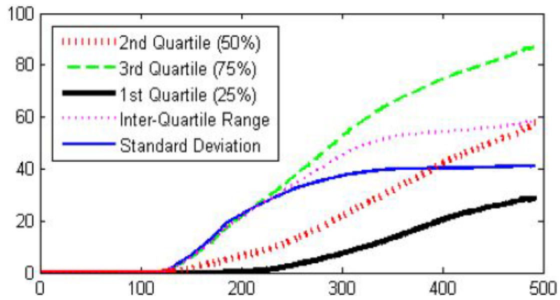
To find the optimal reference frame, three methods were described for analysing the brown-scale image intended for human analysis converted to greyscale.

1. Gradient Based: maximum contrast will occur when the rate of change of brightness is maximal.
2. Positional Spread of Brightness v Time.
3. Neighbourhood Spread of Average Brightness v Time: the image is divided into local areas, small compared to the overall image size. This reduces the influence of grainy 'noise' in the image.



For method 1, graphs (left) show a) brightness v time over 500 frames, b) the time derivative of it, showing a maximum rate of change at frame 300, and c) the time derivative of that, becoming zero at frame 300, indicating it as the optimal one. The initial zeros are ignored by only considering slow changes around zero.

For method 2, instead of taking the full range of brightness, we take the Standard Deviation of it, to eliminate random peaks. The plots (right) show no obvious indication of best frame so this method was abandoned.



For method 3, the standard deviation in the image of the small area averages v time is investigated, and the frame giving the maximum value will be the one with the greatest contrast between patches and considered the optimum. This method performed the best of the three.

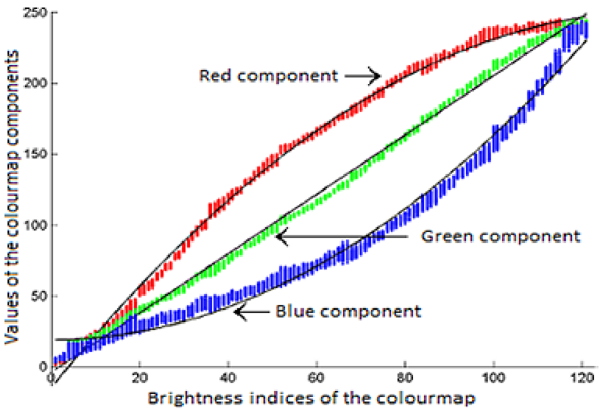
In practice, experts often tended to select a later frame than this one.

When the expert had indicated a random point inside a lesion, automated methods were used to draw an accurate outline round the lesion. The lecturer spent some time describing the details of these methods and how closely the results agreed with outlines drawn by the experts.

Another study was in contrast optimisation. Each video uses 121 brownscale levels rather than normal colour or greyscale. These pixel values are encoded by the equipment manufacturer as RGB triplets using a secret algorithm, yet most processing is done using brightness not colour.

Conventional RGB to grey transformation using the American NTSC standard is optimised for TV viewing, rather than for "quantitative contrast" for false colour. The formula is:
Brightness Y = 0.299 x Red + 0.587 x Green + 0.114 x Blue
This is dominated by green to match the human eye, but may not be best for auto-processing.
The first method tried was to rescale linearly the 121 brownscale levels to 256 greyscale levels, but only producing 121 unique values. This is simple to do, but may not optimise contrast.

The next method was to plot RGB values of colour-map pixels as functions of colour-map row, which is supposed to represent brightness.



As the green channel is linear, a quick method is to use this for brightness and ignore the others.

In a third method, a 3D scatter plot of RGB values showed that the greatest range of values lie along one particular vector, and brightness along it was:

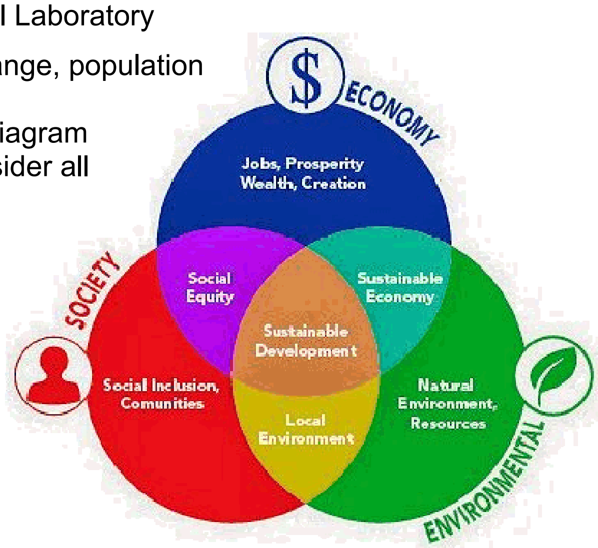
Y = 0.48 x R + 0.32 x G + 0.30 x B

This is dominated by the red component owing to the image being in brownscale. Results for this method were only slightly better than for the simple green channel, but processing time was long.

Finally, Dr Hunter said that significant advances had been made in automating the final prognosis from the behaviour of the lesion to ease the expert's task, but it was still a work in progress.

17/10/18 ***Measuring the Earth from Space (and being a woman in science)***
Dr Emma Woolliams, National Physical Laboratory

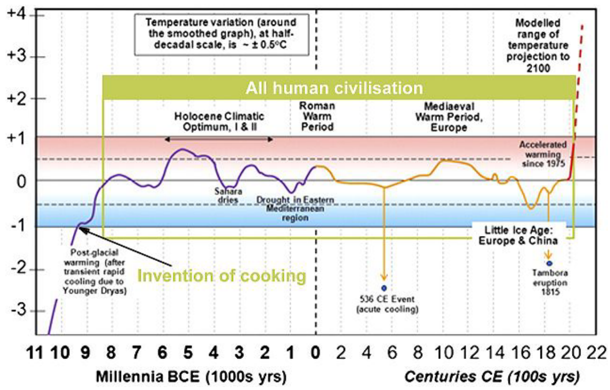
The Earth is subject to pressures such as climate change, population and wealth increase, biodiversity loss and pollution.
In the old days, the three outer factors on this Venn diagram were considered in isolation, Now we all have to consider all three together for total sustainable development.
Dr Woolliams showed a 2015 UN poster depicting 17 "Sustainable Development Goals" consisting of:



1. No poverty
2. Zero hunger
3. Good health and well-being
4. Quality education
5. Gender equality
6. Clean water and sanitation
7. Affordable and clean energy
8. Decent work and economic growth
9. Industry innovation and infrastructure
10. Reduced inequalities
11. Sustainable cities and communities
12. Responsible consumption and production
13. Climate action
14. Life below water
15. Life on land
16. Peace, justice and strong institutions
17. Partnerships for the goals

Every country has to respond to the UN every year with 240 indicators of the progress they are making towards these goals.

Dr Woolliams is mainly concerned with goal 13 and to a lesser extent 2, 11, 14 and 15.

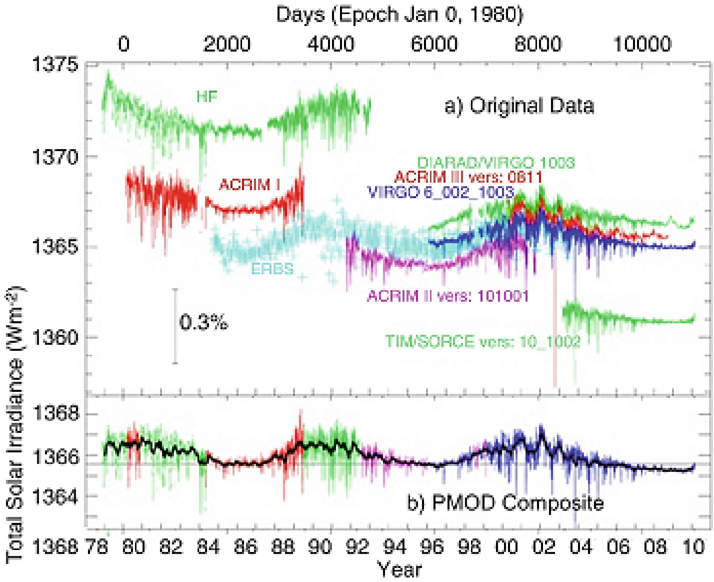


The graph (right) shows that temperature has been within ±0.5 degrees since the invention of cooking until now, whereupon temperature starts to rise rapidly, probably caused by Man.

Climate scientists use a global atmospheric model in which the atmosphere and oceans are divided into three-dimensional cells covering the earth, linked by differential equations. Past climate in each cell is entered into the world's biggest computers to predict future climate.

The Global Climate Observing System (GCOS) is responsible for collating measurements that go into such climate models. GCOS has defined ~54 Essential Climate Variables (ECVs), of which climate modellers need reliable measurements for their models. These include Leaf Cover, Fractional Absorbed Photosynthetically Active Radiation (FAPAR), Lakes, Ocean Colour, Ocean Acidity, Sea Level, Carbon Dioxide, Ozone, Glaciers, Sea Ice Extent, Phytoplankton.

In addition to thousands of instruments recording local variables, there are now many satellites monitoring large areas. To try to ensure that results from these are in agreement, the satellites are calibrated before launch. However the calibration is not maintained after launch, owing to vibration and solar radiation.



Here are some plots of solar irradiance from different satellites covering various overlapping time periods. The lower plot is a composite made by manipulating the offsets between the input plots. The variations in this plot are due to sunspot activity.

As there is no calibration reference in space (at least at the moment), some Earth based references have been set up. Dr Woolliams's team set up one in a Namibian desert that monitors the appearance of the sand, and provides results to be sent to satellites to calibrate their own views of the spot, and hence their views of other locations.

The light from the moon can also be used as a cross-reference for all satellites that see it.

It has been possible to apply complex mathematical analysis to the observed differences in output between satellites, in order to correct their data.

Raw satellite data in the form of voltages from cameras is converted into irradiances from prior calibration. These are converted into climate data from mathematical models from prior knowledge. Then compared with 'Gridded Climate Data Records'. After further analysis, the results are published and future action on them can ideally be agreed worldwide.

It is difficult to relate conditions on the ground to conditions derived from satellite data. One study involved producing a 3D computer model of the trees in Wytham Woods, Oxfordshire, from many laser scans. Dr Woolliams showed a video fly-through of the model. By comparing the summer and winter versions with the appearance of the woods from above by drones and satellites, it was found that there is a lot more carbon in the trees than previously thought.

In summary, all climate models require more detail before they can be used to determine action.

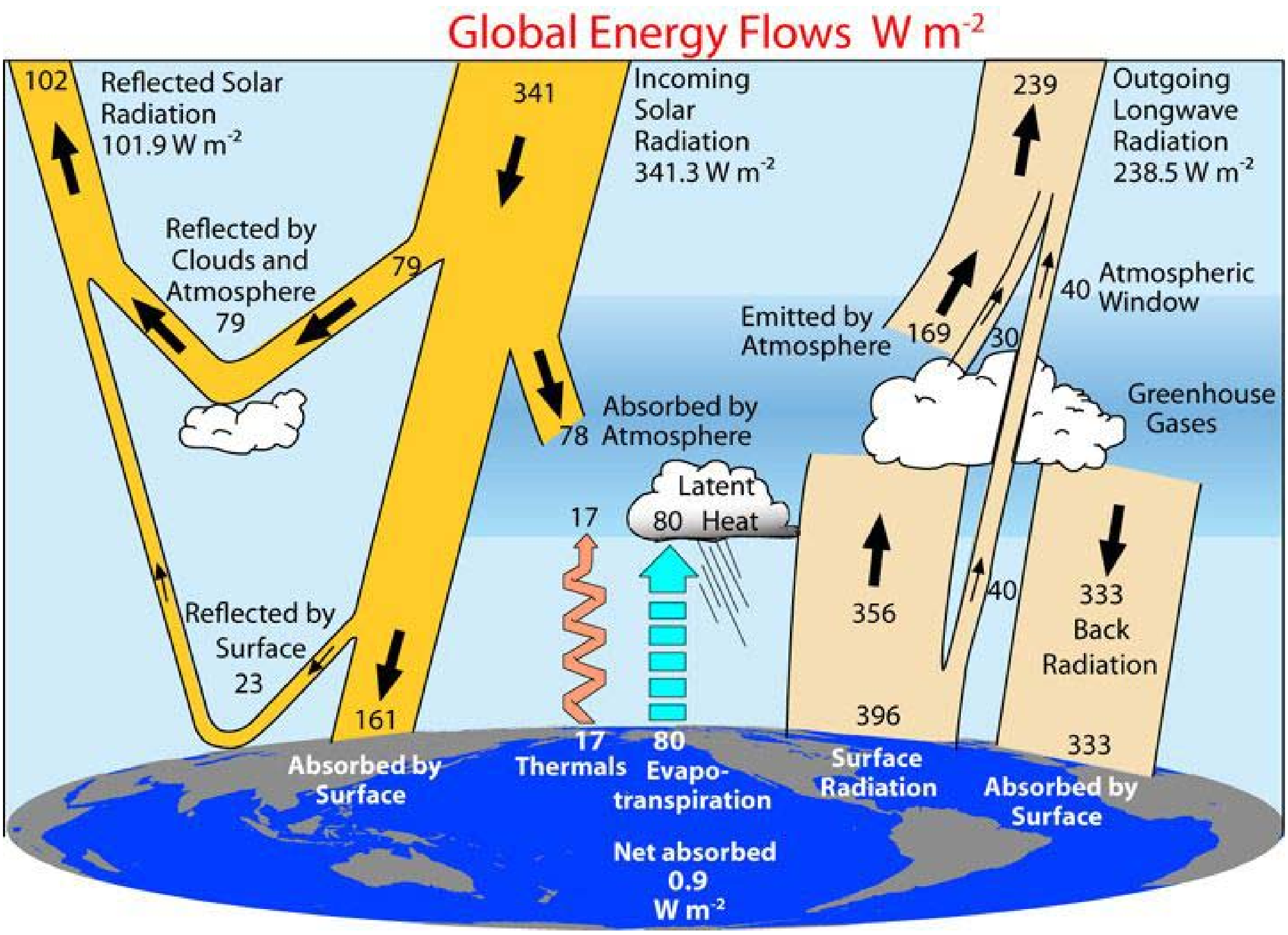
Changing the subject to 'Women in science', Dr Woolliams sketched out her career, which included presenting a paper about a temperature standard at the Royal Society, but noted that there were few women in science. She described a computer simulation of a company in which the results of annual assessments were biased by only 1% towards men over women, which resulted in a gross inequality in numbers at the top end of the management scale.

Finally she said that if humanity is going to make progress on climate change - and the other UN sustainable development goals - it is important that we use all of our combined intelligence irrespective of sex, race or affluence.

24/10/18 ***Climate Change: Science, Policy and Opinion***

David Warrilow, Royal Meteorological Society

Climate change can be caused by changes to the sun's output, changes to the earth's orbit (long term), meteorites (very intermittent), volcanic eruptions (intermittent), geological changes (long term) and composition of the atmosphere - especially greenhouse gases, the main topic here.



From Trenberth, Fasullo, and Kiehl - published in the Bulletin of the America Meteorological Society (2009)

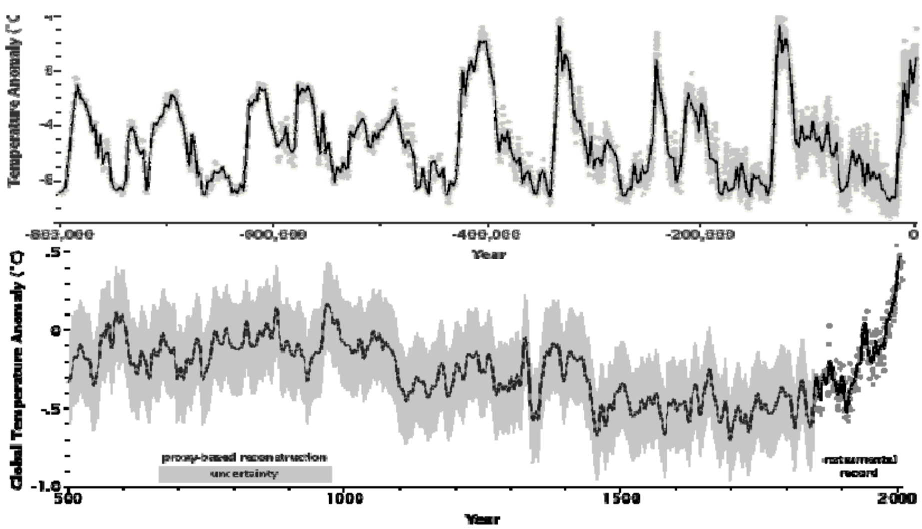
The greenhouse effect is so called from the way greenhouse glass lets in the sun's rays but prevents the resulting heat from readily getting out. This diagram shows the balance sheet of total equal energy entering and leaving the Earth. About half (161/341) of the incoming solar radiation heats up the surface and the rest is reflected back to space.

Most of the heat radiated by the surface gets absorbed and re-radiated back to the surface by greenhouse gases. This actually helps to support life because of the resulting warmer surface temperature. However this will become a problem if the temperature rises too much.

Greenhouse gases include water vapour (short lifetime in the atmosphere), carbon dioxide (long lifetime), methane, nitrous oxide and industrial gases (e.g. HFCs, CFCs, CF_4 and SF_6).

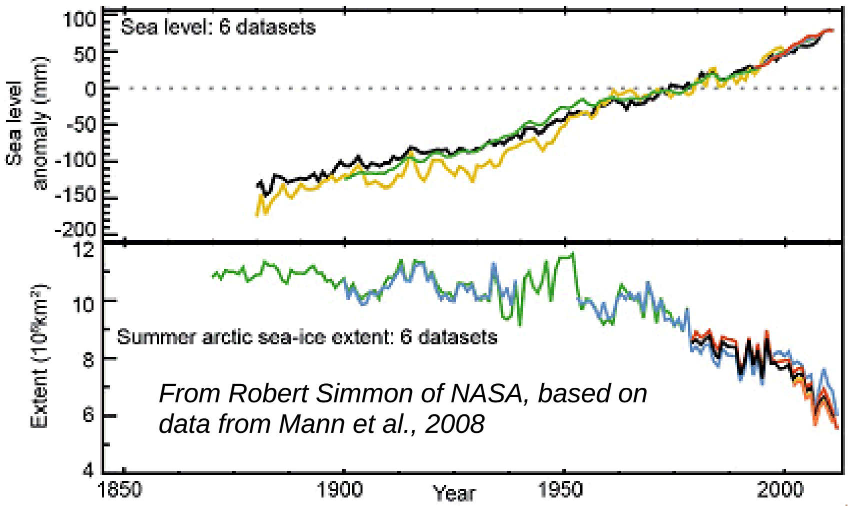
The temperature over the last 800,000 years deduced from ice cores is shown on this NASA graph. The peaks and troughs correspond to waxing and waning of ice sheets in response to slow changes to the shape of the Earth's orbit and the tilt of its axis of rotation.

However, the last 1,500 years shows a steep rise over the last 100 years.

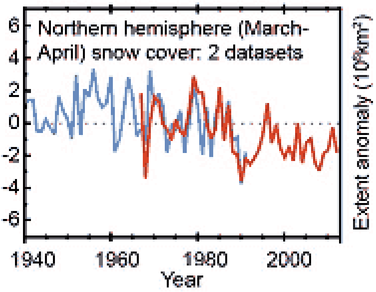


Charts from Robert Simmon of NASA, based on data from Jouzel et al 2007 and Mann et al 2008. (see https://earthobservatory.nasa.gov/features/GlobalWarming/page3.php)

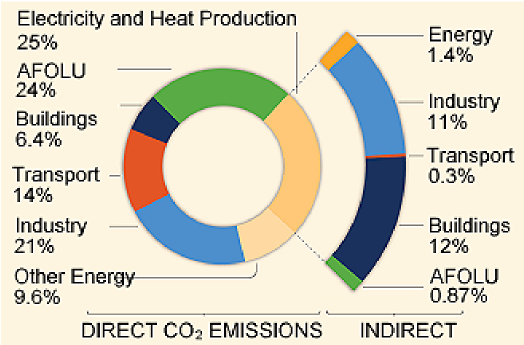
In addition to temperature rise, sea level is rising, and extents of arctic sea ice and land snow cover are falling as shown in the following graphs.



From Robert Simmon of NASA, based on data from Mann et al., 2008

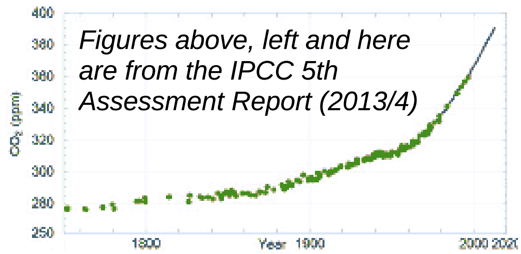


The main factor is the rise in CO_2 levels since the industrial period, as shown below, with similar rises in methane and nitrous oxide.



CO_2 arises from many human activities which are fundamental to modern life.

Doing nothing about these emissions could mean a rise of almost 4^{O}C by 2100 and about 75cm sea level rise, with a longer term rise in the order of metres.



Figures above, left and here are from the IPCC 5th Assessment Report (2013/4)

In July 1988 a major international conference in Toronto considered possible actions regarding climate change. The UK position at the time was that it is a serious threat to society but is uncertain in scale and timing. Therefore we should undertake actions to reduce it which are of wider benefit, and should enhance research over the next 10 years to reduce uncertainty.

The speaker joined the Dept of the Environment in August 1988, and found that few in the government were particularly aware of the risks of climate change, until Mrs Thatcher brought it to the fore in a speech to the Royal Society that September. This raised the public profile of the issue considerably, helped by other environmental concerns, including destruction of the ozone layer, air pollution from one country affecting others, acid rain and photochemical smog.

Challenges of responding to climate change were listed by the speaker as:

- Need for authoritative and widely accepted evidence - IPCC formed in late 1988; first report 1990
- The basis for world's economy was driving climate change e.g. use of fossil fuels
  - so fundamental change needed in technology and behaviour
- Strong resistance from vested interests who stood to lose.
- Global response needed involving all nations. UNFCCC was formed in 1992.
- Benefits may not be fully apparent for several decades
- Adaptation required to cope with residual climate change.

The top four CO_2 emitters are India (7%, increasing), EU (10%, decreasing), USA (15%. decreasing) and China, which has doubled its emission in the last 10 years (28%),

The aim of the UN Framework Convention on Climate Change (UNFCCC) was stated in 1992 as: *...to achieve, in accordance with the relevant provisions of the Convention, stabilization of greenhouse gas concentrations in the atmosphere at a level that would prevent dangerous anthropogenic interference with the climate system. Such a level should be achieved within a time frame sufficient to allow ecosystems to adapt naturally to climate change, to ensure that food production is not threatened and to enable economic development to proceed sustainably.*

But it did not define "dangerous" and "sufficient time frame". In 1997 the EU proposed a 550ppm CO_2 limit and a 2^{O}C temperature rise limit. but small island states later proposed a 1.5^{O}C limit. A Paris agreement in 2015 agreed a 2^{O}C limit and an aspiration to 1.5^{O}C. It was predicted that to achieve this, global CO_2 production would need to be zero by about the middle of the century.

Such reductions in emissions will require political will, substantial investment, innovation and concerted action.

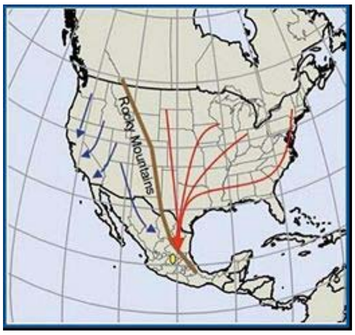
28/11/18 ***Quantum Biology - from animal migration to future cell therapies***

Alex Jones, Principal Research Scientist, National Physical Laboratory

Apparently, some animals can sense the Earth's magnetic field and take action on it. How do they do it? Can we make use of their methods in medicine?

All the physical universe including your biological self is quantum mechanical. Quantum biology is the manifestation of non-trivial effects. Quantum things like entanglement or tunnelling require a property called coherence: different parts of the system vibrating in the same phase. In noisy, badly behaved macroscopic environments like biology, random vibrations tend to drown out these small quantum vibrations.

In 2011, Philip Ball, writing in Nature, coined the phrase 'the Dawn of Quantum Biology' because some things such as photosynthesis, enzyme catalysis and animal magneto-reception are showing increasing evidence of dependence on quantum effects.



Stephen Reppert studied the autumn migration of Monarch butterflies. They start off in their millions from all over southern Canada and fly to one tiny area.

Stephen experimented on a tethered Monarch, and found it always tried to fly in one direction, governed at least in part by the Earth's magnetic field.

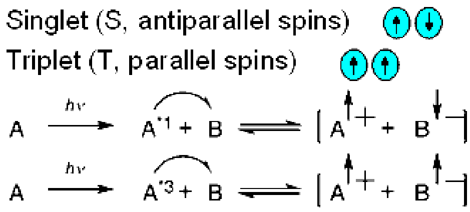
A scientific husband & wife team by the name of Wiltschko measured the take-off directions of birds under different conditions. They found that the colour of light falling on them affected their magnetic sense. Under pure red light, they were completely disoriented.

The speaker introduced the idea of photochemistry, in which one of two molecules A or B can absorb light energy. If they were bonded together they might split into two free radicals A & B, a 'radical pair'. If they were separate an electron might be transferred from A to B, producing two free radicals of opposite charge. If molecule A was bonded with hydrogen (H), then H might get bonded to B.

In electromagnetic fields, the electric and magnetic wave components are inextricably linked at right angles. A moving electric charge generates a magnetic field. An electron has negative charge and an intrinsic quantum mechanical spin, producing a magnetic field. If the electron is subjected to an external field the two fields will interact, making the spin axis of the electron precess in a conical motion with a frequency proportional to the external field.

According to the rules of thermodynamics, to perturb a (bio)chemical system the input of energy E has to be greater than the internal energy of the system, which is proportional to Boltzmann's constant k_B x temperature. A strong magnetic field of 1 Tesla, typical of an MRI scanner, produces about 11.2 Joules/mol. The energy of a biological system at 37^{O}C is about 2500 Joules/mol. So to affect it, a field of 230T would be needed, but the Earth's field is only 50μT.

However, a system in a very unstable state after absorbing light might be tipped over the edge into different outcomes by such a weak field.

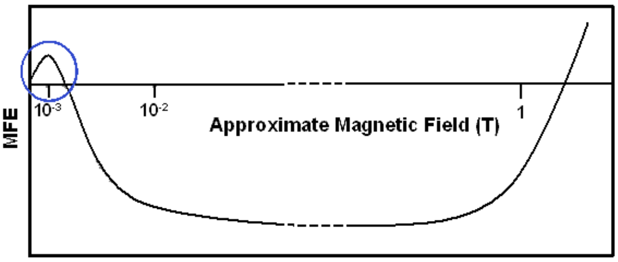


The previously mentioned radical pairs consist of two radicals with individual spins. The pair can be a 'singlet' having antiparallel spins, or a 'triplet' having parallel spins.

Protons also have spins producing magnetic fields. If radical A has more protons than radical B its electrons will be in a bigger field and so precess more quickly.

Singlet states can then interconvert with triplet states. Although the singlet and triplet states are the same chemical composition, they have different reactivities; singlets can recombine, triplets cannot. The addition of the Earth's magnetic field will change the relative proportions of singlet and triplet components in a composite material, and so change the reactivity of the whole.

The chemical outcome of its reactions is a highly non-linear function of field strength, with an opposite outcome at very small fields compared with that at greater fields, as illustrated by this graph of Magnetic Field Effect versus field strength. The circle denotes the region of similar magnitudes to the Earth's magnetic field. The speaker went on to describe experiments with fruit flies and rats involving light-sensitive proteins, and the possibility of using a combination of light and magnetic fields in novel gene therapies.



CALENDAR OF SCIENTIFIC LECTURES

Day	Date	Time	Host	Title
Tue	22/01/19	19:00	IET1	Debugging the Human Brain
Wed	30/01/19	13:00	GC1	50 Years of Lunar Exploration
Thu	31/01/19	18:30	IET2	Lighting Up the Underground
Wed	06/02/19	19:15	IET3	Power from Poo
Tue	12/02/19	18:00	GC1	Computer Vision: machines that see
Wed	13/02/19	15:00, 18:00	GS	Geological disposal of radioactive waste in the UK
Wed	13/02/19	18:00	GC1	Infections of the Lung and Heart
Wed	**13/02/19**	**20:00**	**RSS**	**Things we have measured at the NPL**
Wed	20/02/19	18:00	GC1	Volcanoes and Society
Tue	26/02/19	18:00	GC1	Zombie Ants and Fearless Mice: what parasites can tell us about the brain
Wed	**13/03/19**	**20:00**	**RSS**	**Women in Zoology**
Tue	19/03/19	18:00	GC1	Deep Learning: miracle or snake oil?
Thu	21/03/19	13:10	UCL	If self-driving cars are the answer, what’s the question?
Wed	27/03/19	15:00, 18:00	GS	Diamond windows into the deep Earth.
Wed	27/03/19	18:00	GC1	Infections of the Abdominal Organs
Tue	07/04/19	18:00	GC2	The Unacclaimed Accompanist
Wed	**10/04/19**	**20:00**	**RSS**	**Forensic Science - DNA Evidence**
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
Wed	**15/05/19**	**20:00**	**RSS**	**The Heart, Ancient and Modern**
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 slip to earthquakes

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

IET1: Institution of Engineering and Technology, 2 Savoy Place, London WC2R 0BL
IET2: Queen Mary University, Preston Room, 404 Bancroft Road, London E14DH
IET3: The Adelaide, 57 Park Road, Teddington, TW11 0AU
All IET events: http://www.theiet.org/events/search/allevents.cfm

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

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

RSS: Richmond Scientific Society, Vestry Hall, 21 Paradise Rd, Richmond TW9 1SA
http://www.rss.btck.co.uk/lectureprogramme