MATHEMATICS MATTERS

Keeping an eye on diabetes

Diabetes is on the rise in the UK, but current methods of directly measuring patients' blood sugar levels have their drawbacks. Mathematics is playing a crucial role in finding a new, non-invasive, way to monitor the disease.

It costs the NHS £1 million an hour to treat the UK's 2.8 million diabetics. It is estimated a further 850,000 people are unaware they are living with the condition. With the number of UK diabetics expected to smash the four million mark by 2025, mathematics is underpinning a new technique which might help to monitor patients using something unexpected: their eyes.

Diabetes, of which there are two types, is caused by the body's inability to absorb glucose (sugar) into cells. In non-diabetics a hormone called insulin - produced in the pancreas - acts like a key, unlocking cells and allowing the glucose used in energy production to enter. The two types of diabetes occur when either the key or the lock is faulty. In both cases glucose can't enter cells, remaining in the bloodstream with potentially dangerous effects.

Existing techniques monitor glucose levels by pricking the finger to draw a small amount of blood before testing it. However, this is an invasive method – the skin is broken – and so there is always a risk of infection. The repeated action of the needle entering the finger can also cause nerve ending damage and the needles themselves need to be carefully disposed of. With this in mind, a team of researchers at Lein Applied Diagnostics, based in Reading, wants to replace finger prick testing with non-invasive scans of the eye. Estimates suggest that replacing conventional finger prick testing could save the NHS £30 million a year.

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The link between diabetes and the eye is well established: it can cause blurred vision, cataracts, damage to the retina and, in extreme circumstances, total blindness.

However, there are more subtle effects that can help to betray the amount of glucose in the blood. Rising glucose levels cause changes within the eye, which in turn affect its optical properties and therefore the way light passes through it.

The team at Lein Applied Diagnostics has invented a device which scans the eye thirty times a second. Light is shone through the eye and is reflected back into the device where it is recorded. The reflected light shines brightest at a number of points across the detector, corresponding to where the light enters the front and back surfaces of sections of the eye. The distance between these 'peaks' is related to distances within the eye, which in turn can help provide a measure of blood glucose levels. However, to accurately infer those levels these changes have to be known to thousandths of a millimetre.

Several mathematical techniques are required to reach this level of precision. Firstly, small movements of the patient during the scanning procedure mean that not every scan is of sufficient quality. To overcome this, the shape of the peaks is analysed using what is called an "active curve selection algorithm" and those of the wrong shape are weeded out. The scans continue until 90 measurements of high enough quality have been recorded. This typically takes 1-2 minutes to complete.

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There is also natural 'noise' in the system. Noise is the result of random fluctuations that occur in the system over the course of many measurements. These fluctuations are not associated with the eye itself but with imperfections in the optical equipment or signals from the mains electricity. This noise 'blurs' the measurements and makes it difficult to accurately determine the exact location of the peaks in the detector. If the location of the peaks isn't known precisely it has a profound knock on effect on the end reading. To deal with this another mathematical algorithm is applied which removes the noise and 'smooths out' the signal.

Once the readings have been filtered for quality, and the noise reduced, the remaining valid measurements are averaged to give the most accurate figure for the changes within the eye. The challenge then is to accurately calibrate these changes with blood glucose levels, and mathematicians at Lein Applied Diagnostics, aided by the National Physical Laboratory, have been doing just that by producing a statistical model. Trials have already been conducted where finger prick tests and eye scans have been run side-by-side in an attempt to get their mathematical model to give the same results as conventional finger prick testing.

As future tests bring the two methods into further agreement, the aim is to reduce the technology from a large static device to truly portable hand-held technology – about the size of a mobile phone. Such a cheap, lightweight and non-invasive diabetes test would move the technology into the home, allowing patients to non-invasively monitor their blood glucose levels for themselves. The invention could also have a profound effect in poorer countries, with aid agencies taking the device from village to village, testing for diabetes without drawing blood.

With 1 in 16 British people set to suffer from diabetes by the year 2025, it is increasingly vital to measure patients' blood glucose to help keep the condition under control. The pioneering mathematical work at Lein Applied Diagnostics is paving the way for a new age of non-invasive diabetes testing both at home and abroad.

TECHNICAL SUPPLEMENT

Active curve selection

As changes within the eye have to be known to thousandths of a millimetre it is imperative that the eye is scanned accurately. The shape of the peaks detected depends on the angle at which the light hits the eye. The team at Lein measured the way the shape of the peaks changed as the angle of incidence was varied. For example, if the scan was out of alignment by five degrees then the amplitude of the peak halved. Combining this empirical information with further modelling they developed an algorithm which only selects curves that exhibit the same shape as a peak with an angle of incidence of zero.

Noise reduction

The unwanted noise within the detector is reduced using a signal processing technique called a Butterworth filter which was invented by British engineer Stephen Butterworth in the 1930s.

A filter lets certain frequencies through (the passband) and stops certain frequencies (the stopband). So, ideally, with the scanner you only want to allow frequencies related to the scans into the passband and dump all external frequencies (eg mains) into the stopband.

However, no filter is perfect and so the filtering can never be done with 100% efficiency. A Butterworth filter offers a good compromise because it is 'maximally flat' in the passband - it has the same response across that region. There are also no ripples in the passband and so Butterworth filter is most sensitive to the frequencies you want.

References

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