to cause human retinal diseases is increased (enriched) in rod photoreceptors compared with other tissues[1,3]. The reason that such a high number of genes (71) causing retinal diseases have been identified is because photoreceptor function has an unusually direct and measurable relationship to the clinical 'phenotype' — visual disability. So it is relatively easy to detect even subtle clinical problems and the genes responsible for them.

This close link between genotype and phenotype made photoreceptors a good model system for Cepko and colleagues[1]. There are several techniques for profiling the gene-expression pattern of a cell or tissue. The authors used 'serial analysis of gene expression' (SAGE)[4,5] to quantify the mRNAs isolated from developing and mature mouse retinas (Fig. 1). Each SAGE 'library' contains large numbers of 'tags' — short sequences from the so-called 3′ end of an mRNA, most of which are unique to that mRNA. A relatively unbiased estimate of the abundance of the mRNA type is obtained by simply counting tags. The authors counted over 50,000 tags per library, and identified 70–80% of the different mRNAs expressed at each retinal stage[6]. Using four criteria, they then picked out those mRNAs that are both moderately abundant and enriched in rods.

The authors examined 1,119 different tags that are abundant in the retina, and found that about half satisfied at least two of the criteria for rod enrichment[1] (although two-thirds were also expressed outside the retina). Next, they looked back at 22 retinal-disease genes that had been mapped and identified, and showed that 11 fell into the 'increased expression in the rod' class. Extending this to all identified retinal-disease genes gave a similar result, with 33 of 71 showing rod-enriched expression. However, many of these disease genes were identified by the more traditional map–search approach precisely because they are highly expressed in the retina or affect vision-specific processes.

Cepko and colleagues therefore looked in detail at 237 uncharacterized, moderately abundant genes that show increased expression in rod cells, and identified their human counterparts and map positions. They found that 86 of these genes map to 37 regions containing unidentified retinal-disease genes, suggesting that they are excellent candidates. Subsequent work has already confirmed that mutations in at least one of these genes underlie a retinal disorder (S. Daiger, personal communication). If the same approach holds for other diseases, the advantage is considerable — a 30–100-fold reduction in the number of genes to be screened.

One interesting feature of the authors' results is that these 237 more abundant genes represent a minority (perhaps 10%) of the total number enriched in rods[6,7]. The majority of mRNAs showing tissue-enriched expression are generally found at much lower abundance. Yet a large proportion of the abundant class is implicated in retinal diseases. Why should a high absolute abundance correlate with involvement in disease? The answer may lie in the genetic mechanism at work. It could be that strongly expressed genes are associated with 'dominant' diseases, where a 50% loss of normal product or 50% gain of aberrant product has a substantial effect on the phenotype of the tissue in question. In contrast, recessive phenotypes are by definition insensitive to a 50% change in a gene product that is typically less abundant and less likely to gain an abnormal function. In line with this hypothesis, one photoreceptor SAGE library[1] showed median values of roughly 300 and 60 mRNA copies per cell for genes associated with dominant and recessive diseases, respectively.

It also seems probable that a higher proportion of dominant than recessive disease genes have been identified so far, because they are easier to map. But there are clearly many retinal-disease genes still to be mapped; the total number is almost certainly two or three times the present figure of 124 mapped genes (versus the 71 that have been identified; ref. 3). So the apparent excess of abundant mRNAs among disease genes could wane as more recessive mutations are identified. Eventually the low-abundance class of genes may turn out to be numerically more important in disease.

Will the new approach[1] be useful in identifying other disease genes? In genetically complex disorders, the relationship between genetic abnormality and disease is far less direct[8], and the processes that lead to disease are more diverse and less clear, than in the retina. Yet, in many cases, particular cells and tissues are still strongly implicated. So, because the genomic regions to be searched are often much larger than in simpler disorders, the new approach offers a substantial short cut. The new findings are also of considerable biological interest: the discovery of hundreds of photoreceptor-enriched genes will keep biologists busy for years. More generally, the paper clearly shows the need for more in-depth gene-expression profiles, to help researchers in their quest for the genetic basis of inherited diseases. ■

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Daedalus

Reduced bandwidth

World culture is dominated by film and television. The alleged need for streaming video and video-on-demand drives many technical efforts, typically to boost computer transmission. But the resulting increase in bandwidth chokes the 'last mile' of old telephone wire to each viewer. And all this technology still relies on the century-old discovery that repeated still pictures, presented at 24 frames a second or more, give most people the illusion of motion. Meanwhile, sensory psychology has moved on.

Daedalus points out that the human eye slides around a scene, and makes several jumps per second (saccades) in the process. With each jump, large changes go unnoticed. This 'change blindness' allows a watching computer to change the hair colour of a human figure during a saccade, or even to remove it entirely, without detection. A convincing moving image could be presented at only a few frames a second if the frames were made to coincide with the shifts of attention of the human visual system itself.

Cinema and digital cameras, of course, register 24 or more complete frames a second; but they are not the problem. DREADCO physiologists are discovering just how few frames, if chosen to change during a saccade or an eye movement, will be sufficient to give the illusion of continuous movement on a video screen. They are studying viewers' eyes to spot the moments of change blindness. With luck, everybody will react alike. If they do, a few well-chosen frames, certainly fewer than 24, should give the illusion of perfect movement.

But even if we are all different, the technique will still work. Each video screen will have a small camera that detects optical cues from the viewer. Such 'interactive systems' are already being tested. Instead of 24 or more complete frames a second, far fewer will do a much better job. Personal data will be relayed back to the junction where broadband video meets the 'last mile' of telephone wire. Final bandwidth, the bugbear of all video systems, will be minimized.

The new DREADCO technology will only work for computer-transmitted video; the old cinema will still need 24 frames a second. But even if audience members all make different saccade choices, we may have some in common. A computer-controlled projector could select its frames, or show only parts of them, saving wear on the film and enhancing the pleasure of the audience. David Jones