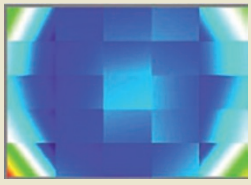
Adaptive optics in microscopy



Light microscopy of whole tissues is often complicated by distortions caused by the optical inhomogeneities in the biological specimen. By borrowing and adapting approaches from astronomy, Ji *et al.* develop adaptive optics to correct aberrations. The correction is achieved using a 'spatial light modulator', an active optical element that permits adjustment of the tilt and phase of the light passing through more than 100 individual segments at the rear pupil of the objective lens. The extent of the modulation for each of the segments is determined by an algorithm that first measures and corrects the spatial deflections caused by the sample inhomogeneities and then corrects errors in the phase for each of the segments. The improvements in signal strength, image fidelity and resolution that can be achieved using adaptive optics are demonstrated by imaging fluorescent beads and neurons in 300- to 500-μm thick brain slices. The technique can be used to improve the performance of many wide-field and point scanning microscopy technologies, including the latest super resolution techniques that are especially sensitive to optical aberrations. (*Nat. Methods* advance online publication, December 27, 2009, doi:10.1038/nmeth.1411) *ME*

Digestible plant walls

Rigid cell walls give plants strength, but they also confound attempts by plant genetic engineers to convert woody plants to biofuels. Creating rigid cell walls requires intermolecular cross-linking of pectins, facilitated by de-methyl-esterified homogalacturonans (HGA). Releasing fermentable sugars from plant cell walls, on the other hand, requires environmentally unfriendly chemicals or high temperatures. Now Lionetti *et al.* show that plants transformed with enzymes that inhibit the de-esterification of HGA polymers are more accessible to enzymatic degradation. Twice as much sugar was released from the leaves of transgenic *Arabidopsis thaliana* plants overexpressing fungal polygalacturonase, 60% more when plants were transformed with a pectin methylesterase inhibitor (PMEI). To show that pectin architecture was being modified, the researchers reacted the transgenic leaves with an antibody that binds to blocks of de-esterified HGA and found reduced binding to the transgenic plants. They were able to replicate these findings in wheat (*Triticum durum*), an industrially important plant. Finally, they found that *Arabidopsis* expressing PMEI had more biomass than the control plants (due to cell expansion). This contrasts with polygalacturonase-expressing transgenic plants that generally have less biomass. The group suggests that regulating polygalacturonase expression in time and space might prevent the loss of biomass. (*Proc. Natl. Acad. Sci. USA* **107**, 616–621, 2010) *LD*

Microarray SNP detection heats up

Gresham *et al.* have discovered new rules to enhance the accuracy of DNA microarrays. These rules substantially improve the ability of probes on the array to bind the correct sequence when similar sequences are present in a sample, which is particularly useful when identifying variation at the level of single nucleotide polymorphisms (SNPs). The authors varied different experimental parameters and discovered that a probe is best able to discriminate SNPs when its melting temperature (T_m) is ~2–5 °C below the temperature used to hybridize samples to the array. This knowledge was used to design microarrays with probes between 16 and 35 nt in length—in contrast to the common practice of making uniform-length probes—such that all probes have the same melting temperature, and thus all achieve optimal performance at the same hybridization temperature, ~2–5 °C above the T_m. These so called isothermal microarrays outperformed conventional arrays at identifying heterozygous SNPs. The use of an optimum hybridization temperature in tandem with uniform T_m probes (varying in length) may be useful for designing arrays for other applications. (*Proc. Nat. Acad. Sci. USA*, published online January 8, 2010, doi:10.1073/pnas.0913883107) *CM*

Co-workers in transcription factories

Chromosome conformation capture on a chip (4C) is capable of detecting remote chromatin interactions on a genome-wide scale. Schoenfelder *et al.* use a modification of this method to analyze the genome-wide repertoire of transcriptional interactions associated with globin genes in erythroid tissues. Their technique, dubbed enhanced ChIP-4C, first cross-links proteins and DNA to generate a snapshot of the spatial organization of the nucleus. However, the 4C assay is then modified to incorporate an RNA polymerase–recognizing antibody that identifies DNA that is near to, but not necessarily on the same chromosome as, actively transcribed copies of the 'bait' gene (that is, globin). Subsequently, a biotinylated bait-specific DNA probe is used to enrich for 'prey' sequences, which are cross-linked to the bait. The DNA in the enriched sample is then identified by microarray analysis. Analysis of the promoters of actively transcribed globin genes in mouse cells reveals a transcription factor, Klf1, required for regulating genes in globin-containing 'transcription factories' in the nucleus. The approach should facilitate understanding of how genes are brought together in the nucleus to regulate their expression. (*Nat. Genet.* **42**, 53–61, 2010) *CM*

Platelet ally

Biotech has no shortage of new ideas on how to staunch bleeding. Where traditional therapy amounts to little more than the application of pressure or absorbent material, research in the past decade has sought to enhance the body's intrinsic mechanisms of coagulation. Allogeneic platelets, recombinant clotting factors, red blood cells displaying the cell-adhesive RGD sequence, self-assembling peptides, liposomes and a block copolymer of hemoglobin and fibrinogen are some of the strategies that have been tried, but none has demonstrated adequate safety and efficacy. Now Bertram *et al.* have proposed to control bleeding with "synthetic platelets," or nanoparticles consisting of poly(lactic-co-glycolic acid)-poly-L-lysine block copolymer cores carrying polyethylene glycol chains that are capped with RGD sequences. Working with a rat model of major injury to the femoral artery, the authors found that the nanoparticles bind to platelets and boost clot formation more effectively than existing therapies. Moreover, the nanoparticles were rapidly cleared from the circulation, and no adverse effects were observed. (*Sci. Transl. Med.*, published online December 16, 2009, doi:10.1126/scitranslmed.3000397) *KA*

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