tween haploid and tetraploid yeast strains, they unearthed 10 genes that were ploidy induced and 7 genes that were ploidy repressed. For example, comparing gene expression in tetraploids versus haploids (see the figure), mRNA levels for *CLN1* (a cell cycle protein, G_1 cyclin) were about a factor of 10 lower whereas those for *CTS1* (a protein involved in the separation of mother and daughter cells) were about a factor of 10 higher. These 17 genes are at the top of a large group of genes, most of which are less dramatically up- or down-regulated in response to increased ploidy.

Polyploid cells and tissues are usually larger and more metabolically active than their diploid counterparts. These differences increase with increasing ploidy, yet there is no theory to explain the functional significance of polyploidy (*6*). It is known from yeast genetics that yeast cells expressing low levels of G_1 cyclins delay "START" (the entry point into the cell cycle) and, therefore, achieve a greater cell size during G_1 phase. The ploidy-dependent repression of G_1 cyclins observed by Galitski and colleagues may explain the greater cell size associated with higher ploidy. As most polyploid cells are bigger than their diploid brethren, the insights provided by yeast may be applicable to other organisms. The authors made similar satisfying correlations for phenotypes associated with ploidy-dependent induction of *CTS1* (cell adhesion), and repression of *GIC2* (cell shape) and *FLO11* (invasiveness). In comparison to haploids, which invade an agar substrate efficiently, tetraploids are poorly invasive. By introducing *FLO11* on a multicopy plasmid into tetraploid yeast and restoring their invasiveness, Galitski and co-workers elegantly established a direct connection between loss of the invasive phenotype in tetraploids and the repressive effect of increased ploidy on *FLO11* expression.

The ability of the yeast gene expression data to explain these biological phenomena is gratifying and lends support to the biological importance of ploidy-dependent gene regulation. How gene transcription responds to ploidy is unclear, but a variety of mechanisms can be envisioned. An increase in total cellular DNA results in a corresponding increase in nuclear size and a reduction in the ratio of nuclear surface area to nuclear volume. Galitski *et al.* suggest that these physical changes may affect the import and final concentration of transcription factors and regulatory proteins within the nucleus, thus accounting for global changes in gene transcription profiles. Whatever the molecular explanation might be, the existence of a ploidy-dependent mode of gene regulation has been firmly established, and one can predict with certainty that biological systems will take advantage of this novel mode of gene regulation wherever possible.

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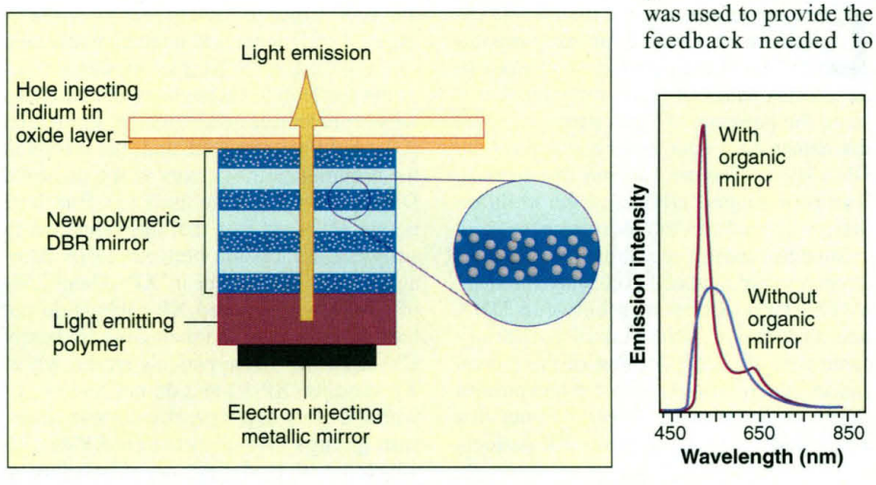
PERSPECTIVES: OPTOELECTRONICS

Reflections on Polymers

William L. Barnes and Ifor D. W. Samuel

A decade ago, it was discovered that semiconducting organic polymeric materials could be made into light-emitting diodes (LEDs) (*1*). When electrons and holes injected into a suitable polymer capture each other, they form an exciton, which can then decay to produce a photon—light. Despite continuing controversy over some of the details of exciton generation and recombination, so much progress has been made that Philips Components now has a pilot-scale production plant aiming for polymers to take part of the estimated $40 billion per year displays market. The properties of the emitted light can be controlled by placing the polymer layer between two mirrors to form a tiny cavity, known as a microcavity. To date, inorganic materials have been used to make these mirrors (*2*). Now, Ho and colleagues (*3*) show on page 233 of this issue that control of the emitted light can be achieved using layered structures of semiconducting organic polymers .

The attraction of these semiconducting organic materials is twofold. First, at the molecular level their composition may be readily controlled to adjust their charge-transport properties (*4*) and the color of their emission (*5*), both of which are vital for commercially viable display devices. Second, these tunable polymers can be processed in solution. It has recently been shown that organic LEDs can be produced by ink-jet printing (*6*) and spin cast onto flexible substrates (*7*), emphasizing the potential their easy processing confers. Many of the organic LEDs studied to date are composite optical microcavity structures (*8*).The light-emitting polymer is confined to a thin (~100-nm) layer sandwiched between two inorganic mirrors that often also serve as the charge-injecting contacts (see the figure). Microcavities enable control over the optical properties of the emitted light. Recently, a layered inorganic dielectric mirror was used to provide the feedback needed to



Polymer mirrors. By sequentially spinning polymer layers that are alternately doped with and free of 5-nm silica beads, a charge-transporting microcavity mirror is formed; DBR, distributed Bragg reflector (**left**). Injection of electrons and holes results in the emission of light, the spectrum of which is modified by the polymeric mirror [**right**, modified from (*2*)].

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demonstrate laser light emission from conjugated polymer microcavities (*9*). Ho and colleagues show how such mirrors can now be made from the same type of organic polymer layers that form the emissive part of the microcavity structure. Their work will pave the way for new polymer optoelectronic devices.

By making a periodic stack of layers that have alternating high and low refractive indices, one can produce an optical mirror whose high reflectivity arises from the constructive interference between reflections from the individual layer interfaces. By adjusting the periodicity, one can control the wavelength at which reflection occurs (see the figure). That this can be done with polymers is no surprise, because polymers have a range of different refractive indices. The use of such a structure in an LED, however, requires the mirror to also have appropriate charge-transporting properties. The work of Ho *et al.* now shows how this can be achieved.

To control the refractive index of the emissive polymer material, the authors doped it with small silica beads about 5 nm in diameter. The refractive index of silica is typically 1.46, compared with those of many light-emitting conjugated polymers, which are often greater than 2. This feature allowed them to produce refractive indices in the range 1.6 to 2.7 by using doping levels of up to 50% by volume. One might have expected that such a procedure would result in strong optical scattering, a mechanism used for making white paint (*10*). However, the size of beads used by Ho *et al.* is only a small fraction of the wavelength, and therefore the films exhibit minimal extra scattering and have a well-defined refractive index. The new functionality comes not simply from controlling this refractive index, but in combining layers of different refractive indices. Ho and colleagues made their high-reflectivity mirrors by sequentially depositing two polymers, one doped with silica beads, the other not. The resulting microcavity effect of the new organic mirror is perhaps best shown by the reduced-width spectrum that emerges from the device (see the figure).

To overcome problems of reduced electrical conductivity associated with adding the silica beads, the authors adopted a chemical doping strategy. This allowed operational LEDs to be made, however, they require operating voltages 10 times those required by normal organic LEDs and thus have a rather poor power efficiency. Although further studies are clearly needed to make practical microcavity LED devices, this work shows much potential.

Ho and colleagues have shown that the optical and electrical properties of conjugated polymers may be controlled by making use of design at several different length scales. This is the essence of their advance. If the problems of poor electrical conductivity can be overcome, then this approach may lead to a competitive microcavity LED design. Ultimately one might hope that this approach would help to demonstrate electrically pumped lasing, although the issue of charge transport is even more critical here. Ho *et al.*'s use of form to control function is complemented by studies of periodic structuring in the plane of the microcavity that have been successfully used to demonstrate optically pumped lasing in various solid-state organic systems (*11*). With an increasing number of aspects of functionality now under our control, we should be better placed to take full advantage of these fascinating materials.

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PERSPECTIVES: BIOMEDICINE

Stopping DNA Replication in Its Tracks

James E. Cleaver

Living organisms have a remarkable capacity to be prepared for every eventuality. All of the genomes sequenced so far contain suites of fascinating genes that sense the presence of DNA damage, signal that things have gone awry, and correct the DNA lesion. The mechanisms that serve to restore damaged DNA and get cells on their way include nucleotide, base, and mismatch repair, recombinational repair, direct reversal, and cell cycle checkpoints.

The first connection between DNA damage, repair, and human pathology came with the identification of the human cancer syndrome xeroderma pigmentosum (XP) (*1*). Relative to people without this autosomal recessive disease, XP patients are 1000 times as susceptible to sunlight-induced melanoma and nonmelanoma skin cancers. Cells from XP patients cannot carry out nucleotide excision repair (NER), in which nucleotides damaged by ultraviolet (UV) light are removed, and this results in the accumulation of errors as the damaged DNA tries to replicate itself (*2*). But there is one awkward fact that has remained to sully the association between DNA damage, repair, and cancer in XP: About 25% of clinically diagnosed XP patients do not have NER defects and their cells are barely UV sensitive. These patients are known as XP variants (XP-V) and do not seem to fit with the other seven genetic complementation groups (XP-A through XP-G), in which the affected genes are all involved in NER (*3*). Many laboratories have hunted for the XP-V gene without success, and the reason for the susceptibility of XP-V patients to UV-induced skin cancers has remained unclear. A defect in replication of damaged DNA was suspected, but the mechanism was unknown (*4*). Now Johnson *et al.* reporting on page 263 of this issue (*5*), and Masutani *et al.*, reporting in a recent issue of *Nature* (*6*), reveal the identity of the XP-V gene.

XP-V cells are unable to replicate the leading strand of their DNA past pyrimidine dimers, which are formed as photoproducts after UV exposure (see the figure, top panel) (*7*). Photoproducts located on the lagging strand only interrupt formation of very small DNA fragments (Okazaki fragments, about 100 nucleotides in length) such that DNA replication is able to proceed. Continued synthesis of the lagging strand induces an asymmetrical replication fork that results in extended single-stranded regions of the leading strand parental DNA. These regions resemble the DNA structures formed by degradation and resynthesis during correction of DNA mismatches, and this is reminiscent of the connection between NER of transcribed strands and mismatch repair. These single-strand gaps have long been recognized, and kinetic experiments show that they are eventually filled in (even in the UV-exposed XP-V cells) by mechanisms that involve either bypass of

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