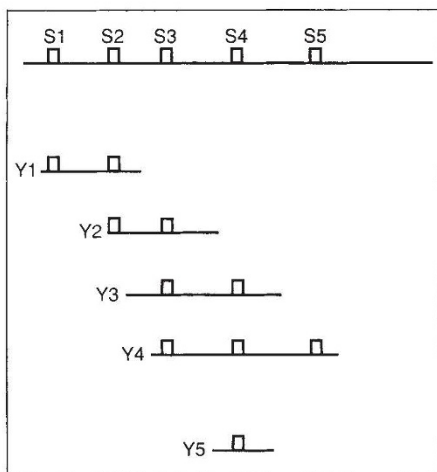


the genome — this is the cloned DNA map. What Page's and Cohen's groups have done is to apply this on a grand scale.

The chromosome 21 project required 198 STS to be placed on over 70,000 YACs. To avoid the impossible task of carrying out $198 \times 70,000$ PCRs, the YACs were grouped into 92 pools. If a pool was positive, 28 sub-pools were screened that allowed the clone to be identified uniquely and the individual clone to be finally checked directly. In all, 810 YACs were isolated by this procedure, and they were then arranged into overlapping sets of clones by the



Identification of overlapping YACs using STS mapping. YACs Y1–5 are tested for STS markers S1–5, organized in the human genome as shown in the top line. Y1 and Y2 can be aligned because they both contain S2, Y2 and Y3 both contain S3, Y4 is positioned because it contains S3–5 and Y5 is placed because it only contains S4.

process detailed in the figure. The STS were all located on the long arm of the almost acrocentric chromosome and cover some 40–50 megabases.

The Y chromosome analysis required 160 STS to be analysed on 10,368 YACs. The YACs were pooled into 18 groups: each positive pool was itself divided up into further sub-pools, allowing, on average, just 26 rounds of PCR to identify the YAC. This process allowed Foote *et al.*² to isolate 234 YACs which were then assembled into a complete map by STS alignment. The STS were all located in the euchromatic region of the Y and so the 30-megabase map does not contain the highly repetitive DNA and centromeric portions of the 60-megabase chromosome.

Despite the global efforts put into genome mapping, STS densities on both of these chromosomes were not high enough for the laboratories concerned to use published STS alone. Considerable time and energy had to be put into generating new STS markers: the chromosome 21 project required 85 new

ones and Page's laboratory, as the group reports in a beautiful companion paper⁴, required 104.

What is the use of the YAC map? Clearly, it has established a definitive STS map of two chromosomes but its primary role is as a resource for at least three areas of biology. Researchers using positional cloning approaches to isolate genes can go directly from flanking marker to YACs, eliminating the laborious, time-consuming (and often ineffective) approach of chromosome walking. DNA sequencers can now tackle whole chromosomes, opening up huge areas of study in evolutionary biology and the natural history of DNA sequences. Finally, the relationship of chromosome structure and DNA sequence can become technically addressable.

At the risk of belittling a substantial achievement, there are still some serious drawbacks to these YAC maps. Some 40% (chromosome 21) and not more than 50–60% (Y chromosome) of the YACs contains artefactual hybrids of 21 or Y DNA with DNA from some other chromosome. These 'chimaeric' clones are very problematic to work with — how do you know which piece of DNA comes from the correct genomic region? YACs are also generally awkward to isolate in pure form.

The *Caenorhabditis elegans* genome analysis project has always been a paradigm for the human genome project, and that team use cosmids (containing 40,000 base pairs of foreign DNA) as their primary resource. There is no doubt that, given the choice, the resource user would rather be given DNA fragments in a more tractable form than YACs. Cosmids are perhaps not the ideal cloning vector either, but it would be wrong to assume that YAC maps are the final solution to the problem; they clearly are not, but it is not so obvious as to what the next step should be.

That being said, it would be quite wrong to give the impression that these papers are not landmarks within the Human Genome Project. They represent a massive body of work and the important message is that it can be done and it is now only a matter of time (and money) before all human chromosomes are completed: we can be sure that the work will not stop at humans, and a full mouse map will be a marvellously powerful adjunct to the genetic analysis of this organism which is central to much of research in biology. □

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Light fantastic

ARTIFICIAL light is one of the few really important inventions. It is still imperfect. Fluorescent lamps flicker and have an odd, spiky colour spectrum; the tungsten-filament lamp runs so cool that most of its output is invisible infrared. Ideally, it should run at about 5,700 K, the temperature of the Sun's surface. It would then emit mainly in the visible spectrum, giving a clear, bright light indistinguishable from daylight.

The snag is that tungsten melts at 3,700 K, and begins to evaporate at a mere 2,800 K. The tungsten-halogen lamp cunningly counters this by running its filament in an atmosphere of volatile halogen. Evaporating tungsten atoms react with the halogen to form halide vapour. The halide molecules decompose again when they hit the hot filament, thus depositing the metal back in place. The old carbon-filament lamps were 'conditioned' in the same way, by running the filaments in an atmosphere of hydrocarbon vapour. Thin weak spots, with a higher local resistance, got hot enough to decompose the vapour, thus depositing carbon to thicken and reinforce the weak spot.

In this connection, Daedalus recalls the new technique of chemical vapour deposition of diamond. A mixture of hydrogen and a hydrocarbon gas such as methane can deposit a thin coherent coating of diamond on a suitable heated substrate. Diamond has the highest melting point of any substance, probably greater than 5,000 K. So, says Daedalus, a tungsten or graphite filament, operated in a suitable hydrogen-hydrocarbon atmosphere, should rapidly acquire a diamond coating. It could then be run at up to 5,000 K or even higher. Encapsulated in diamond, the conductor could not evaporate even if it melted (tungsten would, graphite probably would not). And although the diamond would steadily evaporate, its hot vapour would react with the surrounding hydrogen to give a hydrocarbon which would deposit it back on the filament.

At a stroke, the humble light bulb will be transformed. It will give at least ten times as much light per watt, and that light will be pure natural sunlight. The harsh, head-aching fluorescent office environment, with its stroboscopic flicker and weird off-colours, will be banished. Indoor workers will regain that long lost instinctive outdoor cheer, and will even slowly acquire a slight but becoming natural tan. Indoor plants will flourish as never before. Daedalus was worried that a special ozone layer might be needed around the new bulbs to absorb damaging far ultraviolet, but he soon realized that the glass envelope could be designed to absorb that part of the solar spectrum. David Jones