400–550 cm^{-1} for films produced with an ion energy of 30 eV (the energy that produced the maximum endohedral signal in the laser-desorption mass-spectrometry results). The double maximum that we observe shows close similarities with the predicted P and R branches but is shifted by about 50–75 cm^{-1} to the blue, indicating that the endohedral potential is slightly deeper and narrower than predicted theoretically.

As our method produces films that contain only the particular fullerene deposited and its endohedral version in a ratio of around 3:1 (for Li), we can investigate the properties of the endohedral material without further purification. Similar results using Na^+, K^+ and Rb^+ ion beams show that the method can be extended to larger ions and might also be applicable to non-alkali-metal systems.

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Genome analysis

SIR — The recent commentary from Venter, Smith and Hood[1] proposed a simplified approach to sequencing the human genome. Many parts of this proposal are very attractive and make good use of the dispersed facilities that exist internationally for small, large and massive scale DNA sequence determination.

The ultimate use of the "sequence-tagged connector" (STC) approach depends very much on the quality of the library that is to act as a shared public resource; the authors do not discuss this problem in detail. They cite two studies[2,3] to argue that bacterial artificial chromosome (BAC) clones "seem to represent human DNA far more faithfully than their YAC (yeast artificial chromosome) or cosmid counterparts". Both refs 2 and 3 show that DNA is stable in BAC clones that are subject to serial propagation. The basis of instability of cosmids under these circumstances has been discussed by several workers[4] but this misses a key point: the technical problem has been that regions of DNA simply do not appear in properly grown cosmid (and YAC) libraries, not that a high proportion of deleted cosmids are found in such cases (although this is sometimes found in badly handled libraries). This suggests that the difficulty is not simply in the intrinsic instability of high-copy cosmid-replication systems. It is still unclear that BACs are any more successful with the problematic regions because, by definition, these regions have not been isolated from human DNA.

A second issue that also needs to be addressed is the actual distribution of ends of DNA molecules generated by random shear (or partial digestion) of total genomic DNA. Very little is known about the detailed distribution of end-sequences under these experimental conditions, particularly after the necessarily gentle procedures for isolation of large DNAs have been used. In most library constructions this is not normally a problem but in the STC proposal it becomes a significant issue: clustering of end points or under-representation of regions would generate gaps in STC coverage. Of course, these can be identified by the developing physical mapping reagents, which is precisely the role that these maps have always occupied in 'traditional' descriptions of the genome project.

When they first appeared, YAC libraries were widely held to overcome many of the difficulties associated with cosmids: it is only now that we have a clear understanding of their deficiencies. Indeed, Venter *et al.* point out that in the T-cell receptor region, 1 BAC clone in 17 has a deletion, suggesting 5–6% of BAC clones could be rearranged.

The reliance of the STC proposal on a single library has obvious advantages, but does require that the properties of the target library be very well understood. It is not clear that any single cloning vector is yet understood in these terms. As a consequence, the undeniable cost effectiveness, ready availability and ease of resource sharing of the library underpinning the STC proposal, should not be allowed to obscure the heavy reliance of this approach on an untested quantity, that of clone distribution and stability in a rigorous sense. It would be a mistake to assume, once again, that technical advances can be frozen by selection of exclusive approaches. In genome analysis, flexibility of resources as well as approach must remain a key strategy.

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Colour-blind camouflage

SIR — Cuttlefish are remarkable for their powers of camouflage, which is in part due to their ability to generate disruptive patterns in the skin, using neurally controlled chromatophores. We show here, however, that cuttlefish produce patterns on variegated backgrounds only if these contain appreciable differences in intensity: differences in wavelength are not responded to. This result may seem counterintuitive, but it supports other evidence that cuttlefish (like octopuses) are colour blind.

Although it is well known that cephalopods that live on the bottom of the sea use chromatophores to camouflage themselves on various backgrounds, it is not generally realized that like most cephalopods (with the notable exception of the firefly squid, *Watasenia*[1,2]) they are almost certainly colour-blind[3–5]. How do such animals match their background so well? One theory[6,7] has emphasized that they achieve a degree of "general colour resemblance"[8] with iridophores and leucophores, which can reflect the predominant wavelengths in the immediate environment. Yet effective camouflage does not depend on general colour resemblance alone. One powerful and widespread technique used by animals for crypsis is patterning, especially the various forms of "disruptive" patterns[8] that break up the overall form of the body. Patterning in cephalopods is effected by the chromatophores, and because these are neurally controlled the animal can use them to generate, as appropriate, a range of finely graded patterns in its skin, from uniform, through stipples and mottles to bolds and disruptives[9].

Cuttlefish (*Sepia officinalis*) have numerous, small chromatophores containing either yellow, orange-red or dark brown pigment granules[9], and they have large eyes with a single visual pigment (λ_{max} 492 nm; ref. 10). We tested their patterning responses to a series of specially designed backgrounds. We placed individuals in small tanks containing a gravel substrate, and once they had settled we