bury's subgenera as genera, thereby creating unnecessary havoc in the literature and language. Had they created subgenera, as Pilsbury did, their work would have been valuable and unexceptionable.

Darwin once argued strongly against the rule of priority, claiming that the best description, not the first, should create the species name[5]. But he conceded defeat when it was put to him that the law of priority alone would stand as an objective criterion which all would accept, whereas a rule based on opinion would be unenforceable. Exactly the same argument can be used against the present freedom to invent new genera or to move species from one to another at will, as it can only be a matter of opinion as to which species need or need not be separated generically.

When Darwin was faced with new and unfamiliar names for his broad genus *Scalpellum* he rejected them[6], commenting that such changes undermined the basis of classification — by which we believe he meant convenience to the body of naturalists. How inconvenient indeed has the system become when the current half life of many generic names is only about 30 years.

D. J. CRISP
School of Animal Biology,
G. E. FOGG
School of Ocean Sciences,
University College of North Wales,
Bangor, Gwynedd, LL57 2UW, UK

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Molecular biology running into a cul-de-sac?

SIR—The answer to your question whether molecular biology is running into a dead end (*Nature* **335**, 11; 1988) is yes, if its purpose is to help understand the uniqueness of life and its functions. Your parallel with the quandaries of spectroscopy in the 1920s before their resolution by quantum mechanics is apt, you could have added the quandary of the Michelson–Morley effect: that was resolved by the advent of special relativity. In both cases revolutionary insights were needed, inspired by Mach's positivist principles.

Biology is faced by two similar quandaries, both of which question whether DNA is the exclusive bearer of heritable information or whether all heritable information is structurally engraved in macromolecules. The first arises from the disparity between molecular and organismal evolution, exemplified by the sibling species of *Tetrahymena*, which do not interbreed, but are morphologically indistinguishable[1,2]. Despite the similarity, there is remarkable variation between these sibling species at the molecular level and there seems to be almost a complete dissociation between the molecular and the morphological levels.

A complementary dissociation, but on a much shorter timescale, arises in differentiation. Somatic cells maintain their unique identities throughout a lifetime, although all (except lymphocytes) have the same DNA. The 'modern' view is that stable interactions arise between the genome and its microenvironment during development. But when the cells of a tissue are grown in monolayer culture, they sequentially lose differentiated functions[3]. Stable inheritance of the differentiated state therefore depends on the organized state of the tissue rather than the DNA and its immediate environment. The predictable behaviour of the whole — organism, tissue — and the unpredictability of the parts — the isolated cell — has an uncanny resemblance to the predictability of the ensemble in quantum mechanics and the unpredictability of individual atoms and subatomic particles.

The epigenetic dilemma of Lederberg[4] questions the adequacy of molecular reductionism for the transmission of biological information. This was recognized by Niels Bohr, who believed that life must be considered an elementary fact that cannot be explained, just as the quantum of action, along with elementary particles, forms the foundation of atomic physics[5]. He also observed that "only by renouncing an explanation about life in the ordinary sense do we gain the possibility of accounting for its characteristics"[6]. Similarly, the geneticist Sewall Wright suggested we treat the whole cell as a single gene at a higher level of integration than the chromosomal genes[7]. But the DNA revolution led a generation of biologists to believe that the secret of life lay entirely in the structure and function of DNA.

This faith is misplaced and the reductionist programme must be supplemented with a new conceptual framework. This will develop if we learn to think and work at the level of the cell and higher, as Bohr and Wright suggested. An example of how this might be done builds from the observation that the multiplication rates of individual cells in a cell culture population are heterogeneous. The reason why the fastest growing clone does not take over the population lies at the cellular, rather than the molecular, level. The fastest growing clones tend to throw off slower growing subclones, and the slowest growing ones tend to throw off faster growing subclones[8]. So although we cannot predict the behaviour of any individual cell, the population as a whole maintains a constant growth rate. There is a resemblance to the methodology of quantum mechanics here in substituting a probabilistic for a deterministic description.

A second example is the study of the neoplastic transformation of cells in culture which has recently focused on the activation of oncogenes, and on chromosomal rearrangements. Oncogenes are demonstrated in tumours by transfecting NIH 3T3 cells with tumour DNA and getting them to transform. But NIH 3T3 cultures undergo spontaneous transformation if left undisturbed long enough. This transformation occurs only under specified conditions, requires competent cells, and most — but not all — of recently transformed cells revert to the normal state when transferred[9]. This operational analysis of the spontaneous transformation shows it to be an epigenetic rather than a genetic process; that is, one highly dependent on specific environmental conditions and at first partly, but not fully, reversible at the cell population level[10]. This does not exclude the possibility that mutations in DNA occur at some stage during the development of a tumour, and even contribute to that development. But it emphasizes that the driving force is a process of continuous interaction between cell and environment which can be attacked only at that level.

Experimental results must be viewed in a new theoretical framework. Walter Elsasser proposes the existence of two tiers for maintenance and transmission of heritable information in organisms[11]. The first is the familiar replication-readout of DNA, and is the province of reductionism. The second — the "holistic memory" — is related to epigenesis and accounts for the unique characteristics of life. He states that "causal chains cannot be traced beyond a terminal point because they are lost in the unfathomable complexity of the organism." Therefore, we are required to work with the living state, be it cell or organism. We must now develop a robust model system which will give epigenetic studies at the cell and population levels the convenience and quantitation that phage and bacterial systems provided for molecular genetics.

HARRY RUBIN
Department of Molecular Biology,
University of California,
Berkeley,
California 94720, USA

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