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LETTERS

Space Station, a.k.a. "Project Vampire"?

It is becoming increasingly evident that a large space station—U.S. or international—has taken on a political life of its own without any substantive purpose remotely commensurate with its cost. Within the prevailing budgetary climate, it is virtually certain that continuation of the development of a space station will diminish our progress in space science, space applications, and aeronautics.

Faced with this expectation, a colleague has suggested a descriptive name for the space station program—Project Vampire—a term with at least three appropriate meanings. First, it refers to the mythical creature that sucks the blood from innocent victims (the scientific community) while they sleep. Second, the short form "vamp" means a seductive female who victimizes gullible males (members of the Congress and the general public without distinction as to gender). Third, the word "vampire" might be considered an acronym for the Van Allen Memorial Permanently Inhabited Research Emporium, in honor of this writer's persistent and, thus far, unheeded criticism of the space station development.

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Ordering Organisms

How curious that Ernst Mayr (Letters, 10 June, p. 1519) should taxonomize the systems for ordering organisms into "Darwinian" (Linnean) and "Hennigian" (cladistic). Darwin had no use for Linnaeus' method, as his letters to G. Waterhouse in 1843 clearly show (*1*).

Most authors say it is an endeavour to discover the laws according to which the Creator has willed to produce organized beings—But what empty high-sounding sentences these are—it does not mean order in time of creation, nor propinquity to any one type, as man.—in fact it means just nothing. According to my opinion, (which I give everyone leave to hoot at . . .) classification consists in grouping beings according to their actual relationship, ie their consanguinity, or descent from common stocks. . . . *All rules for a natural classification are futile until you can clearly explain, what you are aiming at.* (Italics in the original)

Hennig's system (cladistics) is concerned with order of time in "creation" as well as strict propinquity of descent, which the Linnean system is not. The Linnean system has no underlying philosophy, as Linnaeus' contemporary critics pointed out (*2*). Darwin did not invent cladistics, but these and other documents show that he would have been more sympathetic to Hennig's views than to Linnaeus' vapid formalization of Aristotelian taxonomy.

The occasion for Mayr's letter was a Random Samples item (25 Mar., p. 1688) that appeared to group the Permian synapsid *Cotylorhynchus* among the mammals. It is not a mammal and not a mammalian ancestor, and this question has nothing to do with cladistics or Linnaeus. Most of the mammalian characteristics Mayr discusses in this respect cannot even be determined in fossils. Contrary to what Mayr says, *Cotylorhynchus* is not (and never was) a reptile, but a synapsid; it does not belong to the "Pelycosauria," which Mayr italicizes as if it were a genus or species; "Pelycosauria," unless rigidly circumscribed to *Dimetrodon* and a few other forms, is not even a monophyletic taxon.

If Mayr thinks that "both systems of classifying are legitimate," he might try to get a National Science Foundation grant to taxonomize using the Linnean system. Meanwhile, Darwin's name should not be invoked to endorse a system that he regarded as an abhorrent convention.

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■

Gap Junctions and Intercellular Communications

In their report "Unidirectional coupling of gap junctions between neuroglia" (12 Nov. 1993, p. 1072), Stephen R. Robinson *et al.* report that the low molecular weight dyes Lucifer yellow and biocytin pass readily from astrocytes to oligodendrocytes (in the myelinated band of rabbit retina), but rarely pass in the other direction. As a possible

explanation for this observation, the authors propose that this could result from a difference in pore diameter at either side of the gap junction (p. 1074).

A "[m]odel of the unidirectional diffusion of dye between coupled oligodendrocytes and astrocytes" likened to "a fish in a fish trap" is offered in figure 3 of their report (p. 1073). This explanation cannot be correct, for by this mechanism, starting with equal concentrations of Lucifer yellow in both cells, the dye would presumably diffuse preferentially from the astrocyte to the oligodendrocyte, spontaneously creating a concentration gradient—a clear violation of the Second Law of Thermodynamics. One could preserve the model by assuming that convective flow occurs through the junction, in which case the dye would be preferentially dragged in one direction.

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It is amusing to find Maxwell's demon in the pages of *Science* again, more than a century after its exorcism, and in plain view of the ever-watchful reviewers of your magazine. Robinson *et al.* suggest that gap junction channels might sustain a gradient of permeant molecules between the two compartments simply by being asymmetrically shaped, like "fish traps," so that molecules on the thin end of the junction have a harder time getting into the channel. For the reasons why fish traps don't work on the molecular scale one may consult any college physics text; a particularly nice description is given by Richard Feynman (*1*).

Robinson *et al.* derive their speculations from the observation that dye injected into a cell type A spreads readily through gap junctions into cell type B, whereas dye injected into B does not spread to A. A simple explanation might be that cell B contains a mobile buffer that binds most of the dye molecules, such that they are no longer permeant. After injecting that cell, only a small fraction of the total dye is free and thus available for diffusion into cell A. By contrast, injection of cell A, which does not contain the impermeant buffer, is followed by free passage of the dye into cell B.

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The observations of Robinson *et al.* suggest that chemical rectification in gap junctions, which was experimentally shown in vitro by Flagg-Newton and Loewenstein (*1*), may indeed be of physiological relevance in vivo. Flagg-Newton and Loewenstein modeled the mechanism of chemical rectification through a postulation of "asymmetric free-energy barriers" that might exist in heterotypic gap junctions. The suggested revision of Loewenstein's model based on pore size is inappropriate for explaining unidirectional dye coupling.

Aside from theoretical questions about the validity of some aspects of the model proposed by Robinson *et al.*, it is inconsistent with the following observations. First, Lucifer yellow readily passes through gap junctions in cells that express connexin 32 channels (*2*), and it is not clear why it would not do so in oligodendrocytes that express connexin 32. Second, electrophysiological studies (*3*) give evidence against the prediction that one should expect a larger ion conductance for connexin 43 than for connexin 32. Contrary to the expectation of Robinson *et al*, single-channel conductances range from 60 to 90 picosiemens for connexin 43 and from 120 to 150 picosiemens for connexin 32.

The model proposed by Flagg-Newton and Loewenstein gives the most plausible mechanistic interpretation yet of chemical rectification on the basis of asymmetric energy barriers. It takes into account electrochemical interactions of permeants with the pore wall (binding sites) and thus addressses substrate specificity, an important channel property with regard to functional differences within the ever-growing connexin gene family. Robinson *et al.* base their model on arguments of pore sizes. However, this is too simplistic an approach to understanding chemical rectification, because pore size and single-channel conductance are not simply related. A helpful analogy when characterizing gap junctions as ion channels can be found from studies with porins (*4*), which are outer membrane proteins from gram-negative bacteria. Both gap junctions and porins form large, nonselective ion channels in artificial membranes. Maltoporin, the *lamB* gene product of *Escherichia coli*, facilitates the flux of maltodextrines through the bacterial outer membrane. Maltodextrines are too large for outer membrane protein F porin channels which, compared with maltoporin, show a five- to tenfold higher ion conductance for small electrolytes (*5*).

The key to understanding these differences in ion conductance, permeability, and pore size lies in the substrate specificity and in a putative induced-fit channel-gating mechanism. Enzymes use induced-fit mechanisms to maximize their catalytic activity by lowering activation barriers that appear along a reaction coordinate (*6*). Ion

channels can be regarded as enzymes that provide such a reaction coordinate for ions to cross biological membranes. There is no doubt that chemical rectification in gap junctions is critically dependent on heterotypic junction formation, but rectification must be based on dynamic processes involving gating mechanisms that affect channel open probabilities (electrical rectification) or asymmetric changes in activation barriers (chemical rectification).

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Response: We thank the correspondents for allowing us the opportunity to revise our viewpoint. As noted by Buehler, Finkelstein, and Meister, a model based solely on pore diameter is untenable. We accept their arguments and agree that an adequate model for our observations already is on hand (*1*). We must emphasize, however, that the fish-trap model was not the centerpiece of our report. A much more important feature is the demonstration that unidirectional dye coupling occurs in intact neural tissue. This observation has not been challenged. Our finding that oligodendrocytes in rabbit retina are only occasionally coupled to other cells when injected with Lucifer yellow (*2*) has been confirmed (*3*). Furthermore, a recent in vitro study found that Ca^{2+} waves propagate from astrocytes to neurons, but not back in the other direction (*4*). The passage of these waves was blocked by the application of octanol, which suggests that they were mediated by gap junctions.

The key question raised by Nedergaard (*4*) and us is whether unidirectional coupling has any functional significance. One of the challenges now facing cell biologists is to find out if heterologous gap junctions in vivo do indeed mediate the directional flow of intercellular signals.

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■

Overlapping Dissertation Topics

The practice of assigning graduate students overlapping dissertation topics comes to my attention with increasing frequency. This practice puts great pressure on a student to finish before the student or students with overlapping topics, because finishing in any other position means starting over. The practice has been hypothesized as an explanation of patterns of sabotage of graduate students' experiments by other graduate students and as a strategy embraced by some researchers to put pressure on graduate students to help them stay ahead of competing labs. I find the spectrum of opinion expressed about this practice, to range from shock to matter-of-fact acceptance.

One department had addressed the problem by changing its policy regarding thesis proposals. The graduate students there are still threatened by postdocs moving in on their research, however.

I welcome comment from others about the extent to which this practice has caught on, especially in hot areas of scientific research. What are morally relevant factors that may influence its effect? Is the course of research in some areas so unpredictable that researchers are forced to err on the side of assigning potentially overlapping topics lest they leave gaps in the lab's research program? Is there evidence that under this sort of pressure some students falsify results? How does this practice affect the dropout rates (or hospitalization or suicide rates) in a field? How does it affect the trust and trustworthiness of a researcher who is trained in a place where it was used?

Informal standards and sanctions need to be established that are the substance of a functioning moral community.

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Corrections and Clarifications

A table accompanying Christopher Anderson's article "Fusion research at the crossroads" (29 Apr., p. 648) incorrectly stated the length of time the JT-60-U machine at the Naka Fusion Research Establishment in Japan was closed for an upgrade. The reactor was shut down for 14 months between November 1989 and January 1991, not for a 4-year period between 1989 and 1993. The information in the table was supplied by the U.S. Department of Energy.