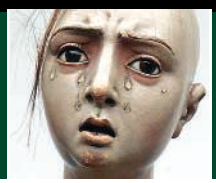
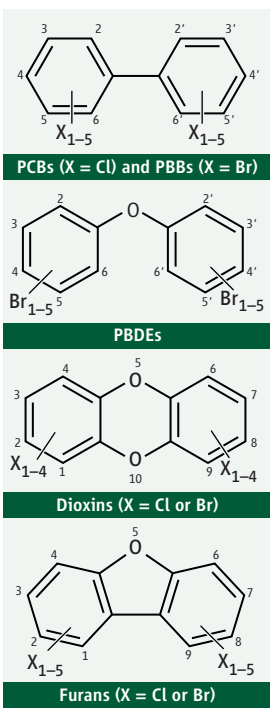


LETTERS

edited by Jennifer Sills

The Fire Retardant Dilemma

ALTHOUGH SMOKING AND FIRE DEATHS ARE RAPIDLY DECREASING IN THE United States (*1*), proposed new flammability regulations could add tens of millions of additional pounds of potentially toxic fire-retardant chemicals to bed clothing, pillows, and foam within upholstered furniture (*2*). In the 1970s, the flame retardants brominated tris [tris (2,3-dibromopropyl) phosphate] and chlorinated tris [tris (1,3-dichloro-2-propyl) phosphate] were removed from use in children's sleepwear after being found to be mutagens (*3*, *4*) that could be absorbed into children's bodies (*5*). They are also probable human carcinogens (*6*, *7*). Today, chlorinated tris is the second most used fire retardant in furniture, found in amounts up to 5% of the foam's weight. How did this happen?



Related structures. PBDEs, used as fire retardants in furniture, are structurally similar to the known human toxicants PBBs, PCBs, dioxins, and furans. In addition to having similar mechanisms of toxicity in animal studies, they also bioaccumulate and persist in both humans and animals.

In the 1980s, the fire retardant pentabromodiphenyl ether (pentaBDE) was added to polyurethane foam to meet California's Technical Bulletin 117; to date, no other states have similar regulations. PentaBDE disassociates from foam and migrates into the indoor environment [especially household dust (*8*)]; studies show that pentaBDE is bioaccumulating and has the potential to adversely affect health (*9*) and the environment. In 2003, California banned pentaBDE; eight other states and the European Union (EU) followed suit. In 2004, the U.S. manufacturer voluntarily ceased production.

PentaBDE was replaced by chlorinated tris and unknown proprietary mixtures containing chemicals such as chloroalkyl phosphates, halogenated aryl esters, and tetrabromophthalate diol diester, which may be no safer. An EPA study of these chemicals shows areas of concern, as well as large data gaps for human health and environmental safety information for all of them (*10*).

While we continue to risk our health through exposure to these retardants, they do not appear to provide measurable fire protection. From 1980 to 1999, states that did not regulate furniture flammability experienced declines in fire death rates similar to that seen in California (*1*). Other causes of fire death reductions nationwide include a 50% decrease in per capita cigarette consumption since 1980; enforcement of improved building, fire, and electrical code; and increased use of smoke detectors and sprinklers. Recent legislation mandating fire-safe cigarettes in 22 states, including California, should bring further reductions in deaths due to fire, without adding questionable chemicals to home furnishings.

Detection. Biophysical chemist Arlene Blum, using an x-ray fluorescence analyzer, measures 5% bromine from the fire retardant in her couch foam.

New European regulations for the Registration, Evaluation, and Authorization of Chemicals (REACH) require industry to provide data to establish the safety of new and existing chemicals. The United States should follow suit. In California, Assemblyman Mark Leno introduced AB 706, a bill that authorizes the state to consider human health and environmental impacts, as well as fire safety, when regulating flammability. This bill would prohibit the most toxic classes of chemicals in furniture, mattresses, and bed clothing (unless the manufacturer can establish their safety) and stop the cycle of replacing one toxic fire retardant with another.

Fire-retardant chemicals in our homes should not pose a greater hazard to our health and environment than the risk of the fires they are supposed to prevent. Equivalent or greater fire safety can be achieved with new technologies and materials, furniture design, and green chemistry.

ARLENE BLUM

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References and Notes

1. J. R. Hall Jr., "U.S. unintentional fire death rates by state" (Fire Analysis and Research Division, National Fire Protection Association, Quincy, MA, 2006).
2. There are four types of new regulations and legislation under consideration: (i) federal regulation by the CPSC ("CPSC staff draft standard for upholstered furniture flammability, May 2005"); (ii) U.S. Senate CPSC Reform Act of 2007 (S.2045) (U.S. Senate Bill 3616); (iii) pending California state regulation 604 to require bedding and pillows to be fire retardant [*Tech. Bull. 604* (State of California, Department of Consumer Affairs, DRAFT, 2005)]; and (iv) bills in four states (Illinois House Bill 1610, New Jersey Assembly Bill 2299, New York Assembly Bill 1417, and Pennsylvania Senate Bill SB 173) to adopt California TB117 for furniture flammability.
3. A. Blum, B. N. Ames, *Science* **195**, 17 (1977).
4. M. D. Gold, A. Blum, B. N. Ames, *Science* **200**, 785 (1978).
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6. *Report on Carcinogens, Eleventh Edition* (U.S. Department of Health and Human Services, National Toxicology Program, Research Triangle Park, NC, 2005); http://ntp.niehs.nih.gov/ntp/roc/eleventh/profiles/s061tris.pdf.
7. M. Babich, "CPSC staff preliminary risk assessment of flame retardant (FR) chemicals in upholstered furniture foam" (U.S. Consumer Product Safety Commission, Bethesda, MD,

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2006), p. 5; available at www.cpsc.gov/library/foia/foia07/brief/ufurn2.pdf.
8. M. Lorber, *J. Exposure Sci. Environ. Epidemiol.*, published online 11 April 2007 (PMID: 17426733).
9. T. A. McDonald, *Integrated Environ. Assess. Manage.* **1**, 343 (2005).
10. EPA, *Furniture Flame Retardancy Partnership: Environmental Profiles of Chemical Flame-Retardant Alternatives for Low-Density Polyurethane Foam* (EPA 742-R-05-002A, September, 2005), pp. 4-2 to 4-5.

Addressing Cumulative Selection

IN HIS UNFAVORABLE REVIEW ("GOD AS GENETIC engineer," Books *et al.*, 8 June, p. 1427) of my book, *The Edge of Evolution* (*1*), Sean Carroll writes that "Behe's chief error is minimizing the power of natural selection to act cumulatively," and implies that I fail to discuss "pyrimethamine resistance in malarial parasites … —a notable omission given Behe's extensive discussion of malarial drug resistance." The insinuation is that I included only what fit my purposes. Yet I explicitly discuss multiple mutations of pyrimethamine resistance: "Although the first mutation (at position 108 of the protein, as it happens) grants some resistance to the drug, the malaria is still vulnerable to larger doses. Adding more mutations (at positions 51, 59, and a few others) can increase the level of resistance" [(*1*), p. 79]. In the same section, I also discuss the development of insecticide resistance in mosquitoes by "tiny, incremental steps—amino acid by amino acid—leading from one biological level to another." Furthermore, in other sections, I describe a cumulative Darwinian route to antifreeze proteins and extensively address hemoglobin C-Harlem to illustrate the crucial difference between beneficial intermediate mutations and deleterious intermediate ones.

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Reference
1. M. J. Behe, *The Edge of Evolution: The Search for the Limits of Darwinism* (Free Press, New York, 2007).

Response

BEHE DID INDEED DISCUSS PYRIMETHAMINE resistance on pages 75 and 76 of his book (*1*). My criticism is that Behe omitted the clear evidence for the cumulative selection of multiple changes in the drug target protein in nature and that he invoked an altogether different and unsupported explanation in an attempt to bolster his main premise. In his Letter, Behe has misrepresented the thrust of the actual text of his book.

With respect to the latter, the passage he quotes in his Letter about how "[a]dding more mutations … can increase the level of resistance" is immediately followed in his book by the disclaimer that "[h]owever, as usual there's a hitch. Some of those extra mutations (but not the first one) seem to interfere with the normal work of the protein" (p. 75). Behe is clearly seeking to convey the message that there is some impediment to Darwinian evolution via multiple intermediates, both in this specific case and in general (hence the phrase "as usual").

However, this is not the case. Careful inspection of the data in the reference I cited (*2*) reveals that, in fact, certain mutations (e.g., $Cys^{59} \rightarrow Arg$) increase specific parameters of the enzyme's performance. Structural studies suggest that this mutation, found at very high frequency in drug-resistant parasites in nature, improves enzyme binding to substrates in the context of otherwise adverse mutations (*3*). Furthermore, pyrimethamine-resistant dihydrofolate reductase enzymes actually have activities equal to or better than the wild-type enzyme (*4*). Behe also neglects to note the fact that such triple and quadruple mutant enzymes have been found in isolates from India, Southeast Asia, Eastern Africa, and South America, including areas where pyrimethamine use has been limited. The latter suggests that mutant parasites may be as fit as wild-type parasites.

Instead of enlightening his readers with an explanation of how sequential mutation and cumulative selection has operated in this example, Behe changes the direction of the discussion back to the main (and erroneous) argument of his book—the necessity for two or more simultaneous mutations for changes in function. He speculates that "two further, simultaneous mutations seem to be necessary" for the evolution of pyrimethamine resistance, despite the fact that the authors I cited (*2*) explicitly demonstrated two different pathways to triple and quadruple mutants via stepwise processes. Behe does not cite this work and he obfuscates the clear but inconvenient message in this body of data.

If, as Behe now seems to imply in his Letter, he is a greater proponent of cumulative selection than I gave him credit for, why would he, with so many available examples, characterize it as "rare"? It is because cumulative selection is fully capable of producing what he claims Darwinian evolution cannot do. The minimization of cumulative selection and the complete disregard of a massive literature surrounding protein interactions are crucial to Behe's entirely unfounded conclusion that "complex interactive machinery … can't be put together gradually" (p. 81) and must therefore be designed. **SEAN B. CARROLL**

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3. J. Yuvaniyama *et al.*, *Nat. Struct. Biol.* **10**, 357 (2003).
4. C. I. Sandefur, J. M. Wooden, I. K. Quaye, W. Sirawaraporn, C. H. Sibley, *Mol. Biochem. Parasitol.* **154**, 1 (2007).

TECHNICAL COMMENT ABSTRACTS

COMMENT ON "Emergence of Novel Color Vision in Mice Engineered to Express a Human Cone Photopigment"

Walter Makous

Jacobs *et al.* (Reports, 23 March 2007, p. 1723) reported that plasticity in the mammalian visual system permitted the emergence of "a new dimension of sensory experience" in mice genetically engineered to express a human long-wavelength–sensitive cone photopigment. However, neither neural plasticity nor a new dimension of sensory experience is required to explain their results.

Full text at www.sciencemag.org/cgi/content/full/318/5848/196b

RESPONSE TO COMMENT ON "Emergence of Novel Color Vision in Mice Engineered to Express a Human Cone Photopigment"

Gerald H. Jacobs and Jeremy Nathans

Makous suggests that the novel color vision documented in knock-in mice neither requires visual system plasticity nor implies the emergence of a new dimension of sensory experience. We explain why we disagree.

Full text at www.sciencemag.org/cgi/content/full/318/5848/196c

Letters to the Editor

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