

Ya Gotta Believe!

It's not that I like being a naysayer; it just comes over me sometimes. I do my best to fight it: When I catch myself singing "It Ain't Necessarily So" in the shower, I force myself to switch to "AX-centuate the positive!" But, truth to tell, I can't quite "EE-liminate the negative!" completely. It's a problem. Our optimistic "can do" culture, including our science, puts tremendous emphasis on the positive. We prefer cockeyed optimists to wet blankets and irrational exuberance to pessimistic prudence. Affirmation smacks of youth, confidence, success, and hypomania. Negation smacks of age, timidity, failure, and depression.

Rationally, it's not supposed to be that way, at least not in science. We're supposed to be equally open to affirmation and negation of hypotheses. Charles Darwin said, "To kill an error is as good a service as, and sometimes even better than, the establishing of a new truth or fact." Nonetheless, negation reliably evokes more resistance than does (nonheretical) affirmation.

There are several reasons for this. One is the cultural bias alluded to above. I think it derives from a tendency toward dichotomous thinking (a theme Stephen Jay Gould has emphasized): light versus darkness, good versus evil, success versus failure, building up versus tearing down. This contrasts with a more dynamic, organic view: renewal and decay depend on each other—both osteoblasts and osteoclasts are important for shaping and strengthening bone.

Other reasons are more closely linked to how science works. A well-designed and executed set of experiments should be as believable in negating as in affirming a hypothesis. In practice, however, it feels easier to affirm a hypothesis. Positive results seem to need fewer, mostly negative, controls. "Failure to find" is a notoriously dangerous basis for conclusions, and we are all leery of it. But appropriate controls (mostly positive—eliciting the effect another way and showing that the perturbation in question does change some other meaningful measure) can provide confidence in negative results. It is also important not to confuse negative results and negative conclusions.

Once on the table for a while, findings and conclusions tend to receive support. Papers appear to confirm a hypothesis by piling on more evidence of the same kind as that which generated the hypothesis in

the first place. Consider, for example, the finding that A, known to increase C, first increases B, and the inference that B mediates A's effect on C. It ain't necessarily so. Then come papers that say it happens elsewhere too, under other conditions and in other systems, "strengthening" the conclusion that B mediates C. Such papers don't really strengthen the conclusion, just the original findings, and leave in place whatever inadequacies there were in going from the result to the conclusion. Finding that B can go up without an increase in C, for example, and that C can go up without an increase in B would, together, be positive results that negate the hypothesis more strongly than the original results affirmed it.

Another problem for negation is its derivative value. There's not much point in negating propositions that no one believes anyway. Once a proposition is put forth, however, its negation should be as valuable as its affirmation. The more plausible, widely believed, or well established the idea, the more valuable its negation. Overturning an entrenched idea therefore justly garners more credit than nipping a nascent one in the bud. Affirmation also has derivative value but gains more credit when an idea is still new.

Which raises, finally, career considerations. New positive claims give you something to sell in the scientific marketplace, something to work on, new paths to follow. Affirmation follows and extends such claims. Alfred Gilman (author of the original "Blue Bible" of pharmacology) advised, "In your research, try to use a drug after it's been shown to be specific and before it's shown to be nonspecific." The same can be said for genes. With luck, you'll get tenure before the story collapses. Negating a hypothesis is like putting up a "NO THRU STREET" sign. Career-wise, it's usually best to put things on the communal list, or at least underline things recently added, but they also serve who cross them off.

I still hope to become a visionary someday. Meanwhile, maybe I can turn my naysaying to good use—by being an editor or something.

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