Engaging the Reader in the Story of Science

Systematic approaches to writing—or maybe more explicitly, systems engineering approaches to writing—hold promise for helping inexperienced writers describe their discoveries in a form that is acceptable to readers. Perhaps more important, they hold promise for helping inexperienced writers produce something sufficiently well organized to give their mentors a good enough framework from which a more polished presentation may be achieved.

Blind use of these systems can, however, have a debilitating effect on the life of science. For many, the primary assumption underlying these systems is that all that really matters is that the discovery is added to the world's database of scientific knowledge and that the citation is added to the author's CV. They assume that the reader's interest in the paper is "just the facts, ma'am," and that the most efficient way to get to them is preferred. Furthermore, with the proliferation of journals, a decent discovery, no matter how mechanically written, can find a publisher eventually.

One too-frequent consequence of using the systems approach is that only enough attention is given to a paper's introduction to make sure that it is entered in the correct place in the worldwide database. The methods and results are described with such machine-like precision that it is easy to imagine that the tabs dividing the database fields are already in place. The discussion gives little attention to the context of the discovery, closing with a suggestion for future work that promises little more than another rung in the database, one step down from this entry.

Although these papers may well find a willing publisher, I think such mechanical papers do harm to science and medicine by emphasizing its drudgery and hiding its creativity. I cannot imagine that they would attract creative people to careers in science or that the best physicians would take up a life in academic medicine after they read typical reports of clinical trials.

I believe, even so, that good papers can come from the systems approach to writing, as long as the author recognizes that facts are not enough to carry an effective article. If we expect to engage the readers of science and medicine, then we should give the story just as much attention as the feature writer does. We should allow the reader to walk along with us as we set out to prove a hypothesis or determine which treatment is most effective.

The contrast between a good story and drudgery requires a brief glimpse of the systems engineering model. Journal editors see examples of this model day after day.

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> [Name of disease] strikes [number] people in the US annually, killing [number] victims every year. In spite of [some advance or other], the annual [incidence/mortality/cost/morbidity] continues to rise, reaching [number of people/dollars/victims] in [year]. Clearly, a new approach to treatment is needed. In this article, we describe a phase III randomized trial of treatment Z versus Y in a cohort of 23 patients with [name of disease].
>
> [Collections of tables listing patient characteristics, regimens, side effects, and treatment outcomes follow.]
>
> In conclusion, treatment Z showed only a minor trend toward prolonged survival (P = 0.0213). A larger and longer trial of treatment Z is needed to demonstrate its effectiveness.

As is typical, there is little or no attempt to relate the need for new treatments to a specific failure of past treatments. The author does not set the study in context or show an understanding of how we got here. The consequence is a weak conclusion that asks others to extend the author's present results without sufficient rationale for doing so. I suspect most such studies simply end with the first report, their best hope for a long life being inclusion in a meta-analysis.

A Grant Application That Tells the Tale

Engaging stories in journal articles are, in contrast, rich in detail and reflect the creativity of their authors rather than well-established scripts. For example, in a rationale for a clinical protocol from a 1998 Radiation Therapy Oncology Group core grant application, directed by James Cox, the writers first state the hypothesis: "Nonconventional methods of delivering substantially higher radiotherapy doses will prolong survival for glioblastoma multiforme patients." They then give the background:

> "No survival benefit was observed among the malignant glioma patients in RTOG 90-06 receiving a total dose of hyperfractionated radiotherapy 20% higher than standard. A modest prolongation of median survival time was observed among patients randomized to receive a 50.0-Gy brachytherapy boost in addition to standard chemoradiation in BTCG 87-01. These recent observations as well as the pilot experiences with SRS boost therapy support the hypothesis that any radiotherapy-related survival

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improvement for glioblastoma multiforme patients must come with doses at least 50% higher biologically than standard. It is likely that 50% higher radiotherapy doses delivered conventionally would have unacceptable toxicity, so new methods of dose delivery must be tested. Which method is best will be influenced by the histology, geometry, and location of a particular tumor. The committee proposes to test the hypothesis [in clinical trials of four new treatments: stereotactic radiosurgery, accelerated hyperfractionation, three-dimensional conformal radiation, and fractionated stereotactic radiation]."

Unlike the systems engineering model, this introduction ascribes the need for additional exploration of "new methods" to specific failures of previous attempts to improve survival. Furthermore, it proposes a series of specific solutions whose relation to previous work is clear. It is much more satisfying to the reader (in this case, the grant reviewer) to learn just how and why previous attempts failed and to see proposed solutions that are related to those failures. And the reviewer can easily imagine that the articles published as a result of this work will show the same insight into the problems and potential of radiotherapy.

Some Journal Articles That Engage

In a journal article I admire,[1] the story begins as follows:

"The nature of the genetic code was established initially by experiments in vitro, but its verification in vivo by mutational studies followed rapidly. . . . Such evidence is not available, however, concerning the nature of codon recognition by individual isoaccepting tRNAs in vivo.

"Specific codon responses that are expected from a given anticodon sequence in accordance with Crick's hypothesis . . . have generally been supported. . . . Nevertheless, there are exceptions. . . . A 'two out of three' method for codon recognition was suggested some years ago . . . and has since been extended and proposed in a formal hypothesis by Lagerkvist . . . namely that the code is read operationally on a two-letter basis for certain codon families. . . . No clear-cut evidence has been presented concerning the precise nature of synonymous codon recognition by isoaccepting tRNAs in intact cells. . . . We describe genetic experiments . . . and present evidence concerning the question of whether, in vivo, glyT tRNA is the only GGA-reading glycine tRNA."

The paper reveals the excitement in the ebb and flow of scientific knowledge.

The authors go on to show that in fact Lagerkvist's hypothesis is not supported by in vivo experiments.

Notice how the authors place this work in the context of efforts to establish the nature of the genetic code, taking its origins back to a paper by Francis Crick published 25 years earlier. The authors could have chosen simply to disagree with the preceding work, but instead they chose to relate their studies to this broader context.

Furthermore, we see scientists at work, examining a current hypothesis, doubting its validity, devising experiments to prove or disprove it, and concluding that the generalization of a hypothesis based on in vitro work with one tRNA was not borne out by in vivo work with another. The paper reveals the excitement in the ebb and flow of scientific knowledge.

My next example[2] typifies a response to a challenge posed in the literature and a dogma disassembled. It begins as follows:

"Hematologic remission in acute lymphoblastic leukemia (ALL) is defined as fewer than 5% lymphoblasts. . . . However, leukemia cells could persist even when no lymphoblasts are visible. . . . The detection of residual ALL by PCR led Nizet to pose four questions. . . .

"To answer those questions, and in so doing establish the relation between treatment outcome and submicroscopic evidence of residual disease, we initiated a prospective study. . . . We found evidence of residual leukemia in 15 of 17 patients who remained in prolonged remission. . . ."

The authors then give four paragraphs in answers to Nizet's questions and sum up as follows:

"Taken together, our results challenge the dogma about the nature of cure . . . implying that more than 10,000 leukemia cells may persist in a patient who remains in long-term remission . . . and the cure of ALL may not require the elimination of all leukemia cells."

Although the discovery that leukemia cells may persist even when the patient is cured is exciting in itself, the authors heighten interest by structuring the story of the discovery around a set of basic questions posed by a leading researcher in the field.

In my next example,[3] the authors offered to extend a hypothesis:

"No studies have been reported that examined the susceptibility of cells from these mice to the effects of carcinogens in vitro, and thus removed from the systemic influences. . . . We report the results of transformation experiments of skin-derived fibroblasts from black mice and yellow mice."

But their results contradicted the hypothesis:

"The consistent and significantly increased transformation rates of the [black mice] when compared to cells from [the yellow mice] were unexpected. . . . The results suggest the unexpected conclusion that in primary cultures the

Engaging the Reader *continued*

> [yellow] gene inhibits spontaneous and chemically induced transformation."

Furthermore, they admit that they missed some clues in the literature—"two reports in the literature suggest that this in vitro finding . . . might have been expected"—but go on to say that they have given the yellow gene a heretofore unappreciated significance:

> "Because the yellow gene actually suppressed transformation, we can consider the yellow gene to have strikingly disparate effects on the tumorigenic process."

How much more interesting this story is than the pretense of inventing a new hypothesis after the results prove the original one invalid!

Toward Telling the Story

Anyone who edits, writes, or reviews manuscripts can cite examples of articles written to engage the reader in a story. Perhaps these and other similar examples will help author's editors and peer reviewers consider more than mechanical correctness in regard to writing and to question authors in the search for the story behind the facts. I hope they will help give authors the courage to tell their story as it happened, knowing that readers bring the same hope to scientific papers that they bring to the daily paper or *The New Yorker*: that the writer will intrigue them with a well-written story.

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