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## Time for the one year hold to go?

Should structural biologists be allowed to withhold data that support published results for up to a year after publication? As structural data become of more importance to those working in other fields, the justification for this unusual practice are beginning to come under close scrutiny, both from those within and outside the field.

With the rest of biology looking over their shoulders, structural biologists are once again opening the question up for debate. Joel Sussman, the head of the Brookhaven Protein Data Bank (PDB) — the main repository for coordinates — raises the question in a recent editorial of the PDB newsletter. At the same time several luminaries in the field, including Sussman and Alex Wlodawer, of the National Cancer Institute in the US, have just published a letter in *Science*<sup>1</sup> raising the issue. Furthermore, Wlodawer is looking for co-sponsors of a petition to the International Union of Crystallographers (IUCr), whose recommendation of a one year hold for coordinates has been widely adopted by journals and funding agencies, asking that they reconsider their position\*.

Sussman is quite blunt about the matter, "I think the situation is ridiculous." Richard Roberts, from New England Biolabs, agrees, "I don't think there should be any hold whatsoever; I find it quite appalling that there is." As does Andy McMahon, a mouse developmental geneticist at Harvard Medical School, "It's completely unreasonable. Nobody is forced to publish a paper. But once a paper is published I regard that as a promise to the scientific community to supply others with the reagents that are mentioned in the paper." Why did structural biologists break with scientific tradition? Guy Dodson, at the University of York and the Medical Research Council, London, was the chairman of the committee on Biological Macromolecules set up by the IUCr to look into the matter a decade ago. "The one year hold policy for coordinates and four year hold policy for structure factors was what the community, as a whole, regarded as the fairest resolution of the conflict of interest between their own research investments and proper publication."

What makes the data from three-dimensional structures special? Paul Sigler, at Yale and the Howard Hughes Medical Institute, elaborates: "Coordinates are quite different from other 'bits' of scientific information for two reasons. The first is that a structure is an enormous harvest of information which is extremely valuable. The second is that structural analysis is highly risky. You may not know for a year and a half whether a project will succeed. Such a long investment is worthwhile only because the person who does the research reaps a significant reward at the end of the period of research, often after a dry spell of three or more years. Thus, I think structural biologists are entitled to a little bit of free time to analyze their data."

Brian Matthews, at the University of Oregon, provides further clarification, "Supporting grant applications, especially for younger faculty members who are pursuing tenure, requires that they publish rapidly—they are under tremendous pressure. They don't have the option of using the coordinates to extend the study prior to publication." Dodson adds that "competition between some structure labs is ferocious: the G protein field, for example. Those labs would not have published their results if they had not been able to hold their coordinates for a year."

Another reason for the importance of the hold period, some structural biologists claim, is the increasing role that the pharmaceutical industry plays in structural biology, both as a source of funds and new structures. Sigler notes that the collaboration of academics with industry is contingent on the academic scientists being able to publish in a timely manner, while the companies maintain a degree of secrecy so that they may taken full advantage of the structural data.

\*The text of Alex Wlodawer's petition to the International Union of Crystallographers (IUCr) asking that they reconsider their position regarding the one year hold, and his request for co-sponsors can be found at <http://structbio.nature.com> — where it is also possible to vote anonymously on the matter.

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Wayne Hendrickson, at Columbia University, New York, adds, "My prejudice at the moment is to maintain the one year hold. I hold this position on completely pragmatic grounds, as those of us who collaborate with industry are more likely to get things published if we can put coordinates on hold than if we have to deposit them immediately. With transgenic mice, for example, you can have your cake and eat it too, because you can patent a mouse — you cannot patent a coordinate set. Thus you can give the mouse to your colleagues for free and still sell it to a pharmaceutical company for several million dollars. You don't have that option with coordinates."

Dodson notes that "putting the coordinates in the PDB forces researchers and companies who want to collaborate to approach us." Robert Huber, at the Max Plank Institut fur Biochemie, Martinsried, Germany, adds that "when the coordinates are deposited and released they are used anonymously and the original authors are rarely contacted." Sussman does not agree, "My experience has been that when we release coordinates, in some cases before publication, we get many enquiries from people wanting to collaborate, and, as a consequence of this, much more mileage out of the research."

How do those who want the one year hold abolished counter these arguments? Sussman says that the time and investment arguments now have little force, "Nowadays determining a structure doesn't take that much time. And I don't agree with the argument that the hold will allow [younger, not yet established] researchers to make better use of their data."

Nor does McMahon agree with the idea that structural data are special, "I do not buy the argument that lots of work and resources have gone into deriving the coordinates and therefore they are not equivalent to other scientific data. For example, much work goes into genetic screens in *Drosophila* — a highly competitive field — yet there is a strict policy in that community requiring such reagents be released immediately on publication." Wlodawer cites HIV protease as an example of the spurious nature of the arguments regarding commercial interests. The coordinates for the protease were released immediately on publication, yet "the companies involved in this work have not suffered too badly from their competitors gaining access to the coordinates: the income derived from selling these drugs is already visible on their balance sheets."<sup>2</sup>

If there is to be a change of philosophy regarding the one year hold, how could it best be achieved? Roberts, as the editor of the journal *Nucleic Acids Research*, has had some experience with such matters. "NAR was the first journal to require that authors deposited their sequences and provided an accession number in the paper. We decided unilaterally that it made no sense to publish papers that did not include this information. Admittedly, we were in a strong position to do this; a lot of the sequences (probably as many as 50%) were being published with us at the time. But I think the same is true of *Nature*, *Cell* and *Science*; they publish many of the most interesting structures. If these three journals get together and agree not to publish unless coordinates are made available immediately, all journals would quickly follow suit and the problem would be solved."

"There have been various *ad hoc* efforts to deal with this issue in the past," counters Hendrickson who, in common with many structural biologists, believes that "the way this should be handled is through the IUCr." Roberts is not assuaged: "If you wait for the IUCr to pronounce on the matter it could take five years."

Tom Blundell, at the University of Cambridge, has other concerns about the IUCr approach, "The importance of the IUCr pronouncements are unclear—the rules by which people operate are those which provide gates to their progress. There are three kinds of organizations that influence this: employers, publishers and grant agencies. The greatest pressure comes from the journals; the IUCr can only apply a moral pressure." Huber is a case in point, "I wouldn't care about the IUCr. It is the journals that dictate the rules. That is the only authority I would care about. And I would avoid publishing in those journals that required immediate release."

What of the granting agencies? Jim Cassatt, at the National Institute for General and Medical Sciences (NIGMS): "The National Institutes of Health and the NIGMS presently follow the criteria laid down by the IUCr. Many at the NIGMS are in sympathy with Joel Sussman's editorial. But changing the rules requires a bit more than just being in sympathy, although I am not exactly sure what would be required. We would not unilaterally follow any new criteria laid down by the IUCr, for example."

"The present system catches coordinates at an early stage and gets them into the system. The point at which they are released is almost a second order problem," says Blundell. Although his point is well taken, the one year hold has always been a crutch, which could have only come about because of the very small size of the field, its initially peripheral nature, at least in terms of the general utility of the results (with notable exceptions), and the very small number of structures being determined. Looking to the future, it is clear that withholding coordinates will become an increasingly frustrating impediment to other researchers outside of the immediate structural biology community. If structural biology wants to more quickly integrate itself into the mainstream of biology, structural biologists will have to accept the general scientific principals that researchers in other areas of biology work under.



1. Wlodawer, A. et al. *Science* **279**, 306–307 (1998).  
2. Wlodawer, A. *Nature Struct. Biol.* **4**, 173–174 (1997).