Finally, the conclusion that MGED should be rebuilt from scratch seems completely unwarranted. The authors could better have served the community by suggesting a more realistic methodology for improving and cleaning the MGED ontology.

More than anything, the article points to a real need for the community to adopt a set of evaluation arguments to methodologically track consistency, completeness and ontology assessment in the context of known methodologies for evaluating ontologies.

*Mark Miller & Rami Rifaieh*

*San Diego Supercomputer Center, University of California, San Diego, La Jolla, California 92093-0505, USA.*
*e-mail: mmiller@sdsc.edu*

1. Guarino, N. & Welty, C.A. Commun. ACM **45**, 61–65 (2002).

**Larisa Soldatova and Ross King respond:**

We are pleased that our commentary has stimulated debate about the current and future role of ontologies in biology. Our article contained a factual and constructive analysis of the problems in MO. Some of our analysis requires a wider discussion, such as prospective ways of improving and developing ontologies. Other problems could be fixed immediately, such as the names and definitions of classes.

We agree with most of the points made by Musen *et al.* In particular, we agree that "Much of the most influential ontology work in biomedicine has been stimulated by the pressing needs of bench biologists themselves in managing burgeoning quantities of data. As a consequence, many of the ontologies developed thus far are somewhat unprincipled in comparison to what we now know can be achieved." This summarizes our main criticism of MO and other bio-ontologies. We also strongly support the creation by the US National Institutes of Health of the National Center for Biomedical Ontology. Musen *et al.* do, however, misunderstand our proposal for dealing with the problems of ontology use in biology.

Figure 2 in our article clearly shows that our proposal is to create an intermediate ontology of experiments, which will abstract out the key concepts in scientific experiments. This ontology will link down to subject specific experimental ontologies, such as those in the omics, and up to SUMO. Building ontologies as an extension of an upper ontology enhances formalization and axiomatization for logical inference, data mining and knowledge discovery.

We agree less with the points in the letter of Stoeckert *et al.* We are particularly unhappy with the statement: "It is therefore ironic, and of notable concern, that the authors of this commentary have never communicated their analysis, or suggestions for improvements to any of the extended family of MO developers, that includes ontologists in an advisory capacity". We spoke to, and voiced our concern, with several of the authors of the Stoeckert *et al.* letter. We greatly appreciate their and others' work in the bio-ontologies community in organizing biological knowledge. They are undoubtedly pioneers in the application of ontologies to science. We doubly appreciate this because in Aberystwyth, we run the informatics for the UK National Metabolomics Center for Plants and Microbiology, which makes us well aware of the practical difficulties in dealing with modern 'omics' data.

Dealing with the specifics of their letter, we first note that Stoeckert *et al.* do not actually refute any of our original points, and their letter confirms our belief that the designers of MO are hypnotized by the needs of today, rather than planning for the needs of tomorrow. We contend that MO is still relatively small and it is not too late to redesign its structure.

The large amount of support and criticism our commentary has received, both publicly and privately, reflects the growing importance of ontologies in biology, and we would like to thank all our correspondents.

Replying to the letter of Miller & Rifaieh, we are glad that they agree with the majority of the points we made about MO. We agree that the problems we highlighted with MO may not exist in every bio-ontology. However, our commentary aimed to analyze common problems in bio-ontologies, not only those in MO. The most important of these problems is a lack of standards for bio-ontology design. In this regard, we see the value of the OntoClean methodology, but on its own it does not provide the required standards.

Concerning our preference for the use of trees rather than directed acyclic graphs in ontologies (point no. 9), the argument for this is as follows. Consider two classes *A1* with a set of instances *{a1}*, and *A2* with instances *{a2}*, with intrinsic properties *IPA1* and *IPA2*, respectively. And consider the class *B* that is a subclass of both classes *A1* and *A2*. Then, by the definition (see our commentary), the class *B* is populated by instances from both classes *A1* and *A2;* and all instances of B (*{b}*) inherit the properties *IPA1* & *IPA2*. For each individual instance of *B*: or . Therefore either $a1_j$ has *IPA1* & *IPA2* or $a2_k$ has *IPA1* & *IPA2*. This means that either $a1_j$ can be classified as *A2* or $a2_k$ can be classified as *A1*. The result is that an instance, in the same classification system, can be classified into two distinguishable classes, which clearly can cause errors in logical inference.

Finally, given the number of problems in MO (which Miller & Rifaieh accept) we do not consider it to be "completely unwarranted" to call for a complete redesign of MO's structure while preserving its undoubtedly useful parts. All software engineers are aware of occasions when it is necessary to apply lessons learned in an initial version to a clean new design.

It is time for a new generation of bio-ontologies, which should serve not only as controlled terminologies for humans, but also allow computer programs to automate scientific investigations.

# European GMO labeling thresholds impractical and unscientific

**To the editor:**

In the next few months, the European Union (EU) will witness a burst of novel authorizations for genetically modified (GM) plants. In this context, a huge effort is underway in the laboratories of the European Commission (EC), of the Member States, of third countries and of private companies, to elaborate, assess and validate the necessary sampling strategies and molecular analytical procedures required to implement European regulatory requirements[1] for labeling food and feed products containing ingredients from GM organisms (GMOs). It is now three years since the legislation was first introduced, yet enormous technical and scientific challenges remain in reducing regulations to practice.

The EC first introduced labeling thresholds for the accidental unavoidable presence of GM ingredients because of the technical and practical impossibility of ensuring their