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Law and Technology

Unstandard Standardization: The Case of Biology

How applicable are the approaches adopted by information and communication technology standards-setting organizations to biological standards?

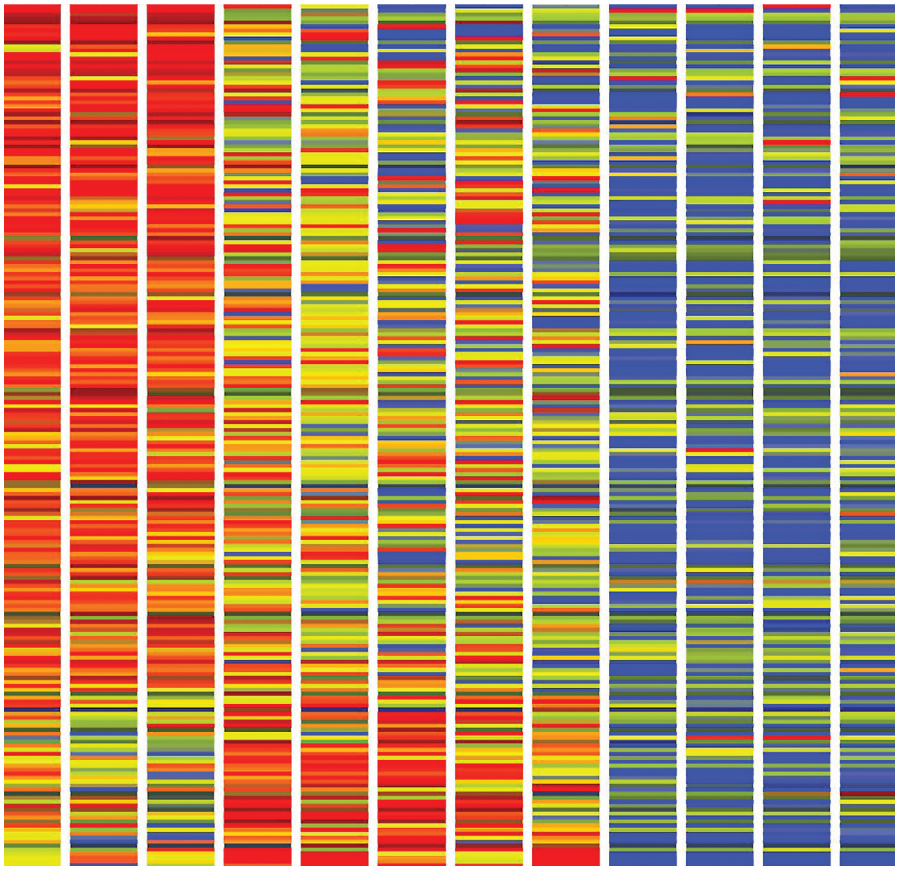
Most engineering-based industries construct products from standard, well-understood components. By contrast, despite the early attachment of the moniker "genetic engineering" to biotechnology, standardization in the biological sciences has been relatively rare. In 2004, MIT computer scientist Tom Knight offered this colorful characterization of the difference between a biologist and an engineer: "A biologist goes into the lab, studies a system, and finds that it is far more complex than anyone suspected. He's delighted; he can spend a lot of time exploring that complexity and writing papers. An engineer goes into the lab and makes the same finding. His response is 'How can I get rid of this?'"[2]

Knight's insightful observation notwithstanding, efforts are currently being made to standardize biology. What lessons (if any) can biology learn from engineering?

Standard-Setting Organizations

The area of engineering where standard setting has been most discussed is information and communication technology (ICT). In the ICT industries, standards often have the potential to read on dozens if not hundreds of patents. Thus standard-setting organizations (SSOs) that make choices among potential standards generally have policies concerning patent disclosure and licensing. The most elaborate policies require disclosure of patents not only by those entities that actually submit technology to the standard but also by other members of the standards organization. As for licensing, patent owners may be required to license royalty-free or, more frequently, on "reasonable and nondiscriminatory terms." At least in theory, such deliberate decision making should lead to the adoption of standards that balance payment of patent licensing royalties with technological superiority.

Through rigorous disclosure and licensing policies, SSOs also hope to avoid future lawsuits in which previously unknown patent owners make assertions of infringement against



A detail of hierarchical clustering and ANOVA of single-cell gene expression data.

IMAGE SOURCE: MARK D. LEVIN . J. CLIN. INVEST. 119:11 DOI:10.1172/JCI39109

product manufacturers that use a widely adopted standard. In such circumstances, the patent holder could arguably extract a royalty in excess of the technical contribution made by the patent.

How applicable are the approaches adopted by SSOs in the ICT industries to biological standards? To a significant extent, the answer depends on the type of standard.

Currently, some of the most advanced standardization efforts involve specifications for the development and presentation of biological data. The Microarray Gene Expression Data Society (MGED) was an early leader in the field. MGED's "Minimum Information About a Microarray Experiment" (MIAME) standard has inspired similar efforts in many other biological fields, including proteomics, metabolomics, and RNA interference.[4] The Minimum Information for Biological and Biomedical Investigations (MIBBI) project takes standardization one step further by attempting to rationalize the varying data standards that have developed in different biological fields. MIBBI's goal is interoperability across data sets from different biological communities.[5]

These data standardization efforts, which emerged from academic institutions, do not appear to have adopted formal policies on patents. But in the case of data standards, the administrative costs associated with establishing an SSO-type apparatus may exceed any challenges that patents pose. At least at this stage, the numbers of patents that could be asserted may not be particularly large.

Biomarker Standards

Another important category of biological standardization efforts involves biomarkers. Biomarkers are biological signs of drug toxicity and efficacy, and the pharmaceutical industry has high hopes that improved biomarkers will yield expedited preclinical drug safety evaluation as well as early indicators of clinical safety and efficacy. With such indicators, firms should be able to reduce the costly drug trial failures that are currently a major contributing factor to diminished biopharmaceutical innovation.

Pharmaceutical companies have formed a number of consortia that pool information and conduct collaborative research to identify consensus biomarker standards. Prominent consortia include the Predictive Safety Testing Consortium (PSTC), which comprises 17 major multinational pharmaceutical firms. The PSTC has already been successful in securing U.S. Food and Drug Administration and European Medicines Evaluation Agency approval for seven new biomarkers that signal kidney injury at the preclinical stage.

The various biomarker standards consortia set up by pharmaceutical firms deal very explicitly with patent rights. To some extent, these consortia adopt policies similar to those of SSOs in the ICT industries. For example, although the PSTC policy does not address the licensing of "background" patents that firms may bring to the collaborative research, it addresses with great care future patents on biomarker standards that may emerge. Specifically, PSTC members assign any future patent rights to a non-profit trusted intermediary, Critical Path. Critical Path, in turn, is obliged to license the rights on "fair, neutral, and commercially reasonable" terms to members of the Consortium as well as third parties. Described another way, in the PSTC, *future* patents are addressed in terms somewhat similar to those used by ICT SSOs for background patents.

The emerging discipline of synthetic biology aims for what is arguably the most comprehensive form of standardization. It hopes to make all of biotechnology a science that relies on standardized, well-characterized DNA "parts." These parts could then be assembled into composite devices and systems with similarly well-defined behavior. When transplanted into suitable model organism "chassis" (which had themselves been standardized), the composite systems could yield outputs ranging from drug therapies to environmentally friendly fuels. Standards would cover not only parts and chassis but, perhaps even more importantly, the interfaces used to assemble parts and the interactions between parts and host cells.

Standardization in Synthetic Biology

The synthetic biology community is still debating precisely how much information about a biological standard is necessary before full standardization can be said to have been achieved.[1] Even so, some progress has been made. The Registry of Standard Biological Parts (http://www.partsregistry.org), an academic effort that receives significant federal funding, now contains about 3,200 parts. Each of these parts adheres to the so-called BioBricks protocol for cloning and physical linking and has specific as-

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sociated inputs and outputs.

The Registry of Standard Biological Parts presents what may be the most interesting, and difficult, challenge for patents on biological standards. As currently constituted, the Registry may well read on a large number of patents. Tens of thousands of U.S. patents have been granted on DNA sequences. Although these patents are not specific to synthetic biology, they could certainly read on various standardized parts. Preliminary patent mapping also reveals a significant number of patents highly relevant to synthetic biology in particular.[3]

Thus far the Registry essentially puts results in the public domain, albeit with a hortatory suggestion that users should contribute back information and data, so as to improve the "community resource." As for background patents that the Registry may infringe, the academic scientists involved appear to be proceeding under the assumption that they will be not be sued because potential plaintiffs will not foresee significant monetary payoffs from such suits. As for potential industry defendants, at this stage it does not appear that Registry parts are being used by industry to make commercially valuable products.

At some point, however, Registry parts may begin to be used by industry. In addition, use of such standardized parts may be difficult to conceal. Thus one apparently common biopharmaceutical industry strategy for avoiding patents on research inputs—secret infringement—may not be possible.[6] Industry users that are contemplating using Registry parts might therefore consider organizing patent mapping efforts to determine whether patents do in fact read on key standards.

The situation the Registry faces arguably bears some similarity to that faced by standards developers for the Web in its early days. For example, in the case of the XML standard for structured data presentation, the critical early work was done by developers from academic and commercial organizations, as well as independent contributors, without any significant thought being given to patents.

As the Web matured, however, the issue of background patents on core technical standards had to be addressed. By 1999, the World Wide Web Consortium had created a patent policy working group. Participants in that group included representatives from the major software, hardware, and telecommunications firms (Apple, AT&T, Hewlett-Packard, IBM, Intel, Motorola, Nokia, Nortel, Sun Microsystems, and Xerox).

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Conclusion

At this stage in the evolution of synthetic biology, it is probably too early to determine whether any of the work done thus far has yielded key standards upon which the community will eventually converge. But as synthetic biologists and other biologists continue work on standardization, they should carefully examine mechanisms (both successful and unsuccessful) for addressing patent issues that have been invoked in the ICT industries. C

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Calendar of Events

January 17–23
POPL '10: The 37th Annual ACM SIGPLAN-SIGACT Symposium on Principles of Programming Lanuguages
Madrid, Spain,
Sponsored: SIGPLAN,
Contact: Manuel V. Hermenegildo,
Phone: 34-91-336-7435,
Email: herme@fi.upm.es

January 18–19
PEPM '10: Partial Evaluation and Program Manipulation (co-located with POPL 2010)
Madrid, Spain,
Sponsored: SIGPLAN,
Contact: John P. Gallagher,
Phone: 45 46742196,
Email: jpg@ruc.dk

January 18–22
The Twelfth Australasian Computing Education Conference
Brisbane, Australia,
Contact: Tony G. Clear,
Phone: 64-9-917-9999,
Email: tony.clear@aut.ac.nz

January 20–23
International Conference on Biomedical Engineering Systems and Technologies
Valencia, Spain,
Contact: Joaquim B. Filipe,
Phone: 351-91-983-3996,
Email: jfilipe@insticc.org

January 22–24
International Conference on Agents and Artificial Intelligence
Valencia, Spain,
Contact: Joaquim B. Filipe,
Phone: 351-91-983-3996,
Email: jfilipe@insticc.org

January 25–27
Fourth International Conference on Tangible, Embedded, and Embodied Interaction
Cambridge, MA,
Sponsored: SIGCHI,
Contact: Jamie Zigelbaum,
Phone: 617-877-4970,
Email: zig@media.mit.edu

January 27–29
Multimedia Systems Conference
Phoenix, AZ,
Sponsored: SIGMM,
Contact: Wu-Chi Feng,
Phone: 503-725-2408,
Email: wuchi@cs.pdx.eduv