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Synthetic Biology Patent Applications Expected to Present New Challenges

BY VID S. MOHAN-RAM AND J. MARK WAXMAN

Synthetic biology is an emerging but already sensational science that has energized existing technologies in biology, chemistry, and genetics to join forces to create organisms with tailor-made genomes. There is nothing new about manipulating and constructing pieces of DNA that instruct a cell to activate or switch off a particular gene or protein, but the term ''synthetic biology,'' unlike ''genetic engineering,'' aptly captures the design and creation of whole artificial biological systems.

Instead of working within the cellular confines of existing biological tools and networks, synthetic biologists aim to create entirely new structures and new cellular environments designed to perform particular functions and errands. By combining biology, chemistry, and genetics to craft living machines and self-driven molecular tools, scientists can create pre-programmed cellular robots that can be used as biosensors, or self-sufficient factories in which to create new biofuels, drugs, and chemicals.

Synthetic biology is gaining momentum in science and industry as well as with government officials who are becoming more and more willing to lend their ears and coffers to entertain and provide financial aid for fledging ventures. Synthetic biology had lain dormant for some 30 years, but, like most opportunistic organisms, has exploded at just the right time in the scientific community. The PubMed scientific literature database, for example, indicates that while only two articles on synthetic biology were published between 1970 and the end of 1999, nearly 200 articles have appeared since 2000, almost half of which were published in the last 18 months.

Individual journals are seeing the same trend: Since 2002, *Science* published 29 papers and *Nature* 160 papers on synthetic biology. That is striking, especially considering that *Nature* printed only two articles in this field in the preceding 30 years. No doubt, therefore, the term ''synthetic biology'' is becoming the industrial brand-name for these collaborative and integrative technologies.

Since industry and entrepreneurship are intimately tied to patent protection, it is critical for patent practitioners and inventors to understand how the U.S. Patent & Trademark Office (PTO) will react and respond to applications covering synthetic biology inventions. This paper does not aim for an exhaustive assessment of the patent landscape or the scope of protection in this area. Rather, it seeks to summarize the U.S. patent applications that expressly focus on the new and emerging field of synthetic biology, and how the PTO is handling and examining them.

Vid S. Mohan-Ram is a patent agent and member of the Biotechnology and Pharmaceutical Practice at the law firm of Foley & Lardner, Chicago.

J. Mark Waxman is a partner with Foley & Lardner, Boston.

Applications

Despite the increasing prevalence of the term ''synthetic biology'' in the scientific literature, as of April 29 only 11 U.S. patent applications expressly used that phrase. No U.S. patent has yet issued with this phrase in the specification or claims. The 11 published applications claim inventions for creating large DNA molecules, tools for assembling desired genes, and systems for synthesizing genomes. They also cover models and

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computerized simulation methods for evaluating resultant chemical and biological networks, interactions, and cellular dynamics in and between cells made using those genetic tools (*see list following this article for specific application details*).

While the earliest filed application in Class 435 is assigned to the J. Craig Venter Institute (filed on Oct. 12, 2005), it is MathWorks Inc. that, so far, leads the synthetic biology pack with three pending U.S. applications. Mathworks produces software products that computational biologists use ''to analyze and visualize molecular data and to develop accurate diagnostic tools. Researchers perform a variety of biological analysis including biomarker detection, gene expression analysis, sequence analysis, and pathway modeling and analysis.'' In second place is a Canadian governmental agency, the BC Cancer Agency of the Provincial Health Services Authority in British Columbia, which has two U.S. applications. Six remaining applicants, among which are Harvard College and Gene Network Sciences Inc., each have filed one U.S. patent application that somewhere speaks of synthetic biology.

Applicants' Definition of Synthetic Biology

It is interesting to note the context in which each applicant describes synthetic biology. Their ''definitions'' say that synthetic biology:

- ''is an emerging view of cells as assemblages of parts that can be put together to produce an organism with a desired phenotype'';
- ''is an effective means for genome modification'';
- ''[is useful for] making and/or manipulating large polynucleotide constructs'';
- ''optimiz[es] complex biological processes using Darwinian selection [and] combinatorial oligonucleotide synthesis . . . through large stretches . . . of DNA sequence'';
- ''enable[s] parallel multiplex ligation and amplification on surface for making assemblies of nucleic acids of various biological applications and for analysis of biological samples such as DNA, RNA, and proteins'';
- ''uses complex combinations of genetic elements to design circuits with novel properties [that] require the development of new cloning technologies''; and
- ''develop[s] biological nanomachines that might for example be used as programmed drug delivery systems.''

Technological Classifications

The PTO has classified these 11 applications into three examination search ''classes'' based on their respective fields of technology. Seven fall under Class 435 (Chemistry: Molecular Biology & Microbiology), two under Class 702 (Data Processing: Measuring, Calibrating, or Testing), and two under Class 703 (Data Processing: Structural Design, Modeling, Simulation, and Emulation).

The 435 applications describe the genetic tools and engineered enzymes mentioned above for creating large DNA molecules and genomes. The remaining 702/703 applications cover the computerized simulation models and methods for evaluating and predicting newly-designed cellular pathways and networks.

Examining Classifications, Examinations

In terms of manpower, the PTO has divided these applications among five different categories of examiner personnel who reside in different ''Art Units.'' All of the four ''data processing'' (702/703) applications are being examined by Art Unit 1631. The remaining chemistry/molecular biology applications have been routed to Art Units 1637 (three applications), 1636 (two applications), and 1639 and 1652 (one application each).

As of April 29, four applications have undergone substantive examination by PTO. It is interesting to note the examiner's reliance on *In re Nuijten,* 500 F.3d 1346 (2007), in rejecting the claims of Gene Network's application (No. US 2004/0243354) as not being drawn to statutory subject matter.

Petrus Nuijten, the patent applicant, apparently found a way to reduce distortion introduced into digital audio files by embedded electronic watermarks that act as electronic signatures. The watermark signal adds data to the transmission, for example, to indicate source of origin, but it also distorts the original signal. To fix that, Nuijten invented a method for modifying the watermark signal to reconstruct the original sound wave and thereby reduce distortion. The Board of Patent Appeals and Interferences, however, rejected the invention and Nuijten took the case to the Court of Appeals for the Federal Circuit. In the ensuing *Nuijten* case, the court ultimately decided that Nuijten's ''signals'' were transitory and intangible and therefore structurally indefinable. Because of that, the court said the signals could not be patented because they could not be categorized as a process, a machine, a manufacture, or a composition of matter—the four statutory categories under U.S. patent law for determining what can be patented.

Returning to Gene Networks, the applicant there claims a method of inferring cellular networks to identify and model the manner in which cells operate via evaluating computer generated ''biological interaction networks'' that are to some extent based on real biological data. The computer-generated network apparently evolves until the inferences approximate the biology of the target cell. By following that evolution, Gene Networks hopes to create new and more complete models of cellular dynamics.

The PTO examiner asserts, however, that the claimed method in the US 2004/0243354 application covers the step of ''inferring'' cellular networks, which is not something that is ''concrete, tangible, and useful.'' The examiner says that, after *Nuijten*, signals alone are not patentable subject matter, particularly if there is no hardware or ''physical transformation'' of the signal into something that is concrete, tangible, and useful. Patents, therefore, that attempt to cover computer simulations, models, or computer-readable media that estimate or predict the effects of artificially produced cellular pathways and environments will need to address such statutory subject matter concerns. Accordingly, applications that the PTO classifies as Class 703 ''data processing'' technology likely could be more closely scrutinized under the *Nuijten* standard for establishing ''synthetic biology'' subject matter that is eligible for patent protection.

Conclusion

As the term ''synthetic biology'' becomes more and more prevalent in the literature, it is likely to define an industry that is slowly making its presence known in the patent landscape. There are likely to be two arms of synthetic biology: one in which new biological systems

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actually are made in the laboratory using artificially constructed DNA molecules and genomes, and one in which computer software and powerful simulation programs and algorithms are created to evaluate and predict what happens in those new systems and how new cells and organisms operate and interact with one another. These are early days and it will be interesting to follow the effects of U.S. patent law, PTO examination, ethics, and U.S. policy on the evolution of intellectual property protection for synthetic biology.