ENABLING LIFE

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Many biotechnology products are living organisms that are essentially "made" by a trial and error process of directing evolution in a laboratory. Decades ago, the Supreme Court in Chakrabarty *settled the threshold question of patent eligibility for life forms, stating clearly that living things are patentable. Nevertheless, the fact that nature assists inventors so heavily in the process of inventing a useful new organism raises the question of whether such organisms meet patent law's enablement requirement—that a patent application must teach a person of ordinary skill in the art how to make and use the invention without undue experimentation. This Note argues that the enablement requirement has been overlooked for patents to genetically engineered organisms, and proposes solutions for updating this requirement to properly incentivize the creation of socially beneficial living things, without allowing inventors to bar access to products of nature.*

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INTRODUCTION

More than three years before the Supreme Court first heard arguments on the patentability of genes,[1] notorious gene patentee Craig Venter had already moved on. A "self-proclaimed maverick" scientist,[2] Venter had pioneered human genome sequencing and filed patents on thousands of genes.[3] By 2010, though, his focus had shifted to entire organisms rather than individual genes, and he announced with characteristic grandiosity that he and his colleagues had created a "synthetic" life form.[4] In reality, what they accomplished wasn't as innovative as Venter let on. Techniques to synthesize the genes of a cell had already been developed, as well as a method to empty an existing cell of its genetic content. With these tools at his disposal, the process was as simple as copy-paste. As Venter admitted, "we didn't create life from scratch."[5]

Naturally, Venter and his team filed for a patent.[6] But are they entitled to receive one? The question of whether inventions derived from products of nature can receive patent protection is a highly significant one for biotechnology, a field defined as "[t]he application of science and technology to the utilization and improvement of living organisms for industrial and agricultural production and . . . other biomedical applications."[7] Of course, all inventions derive from nature at some level, whether they are built from metals mined from the earth or from plastic produced from oil. Biotechnology is different, however, precisely because its inventions are not made "from scratch." Cells are not created by people in the same sense that Thomas Edison created his light bulb or the Wright brothers created their airplane. Though a few prominent scientists aspire to change

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[1] *See* Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107 (2013).

[2] Kristen Philipkoski, *Venter's Side of the Genome Story*, WIRED (Feb. 20, 2001), http://archive.wired.com/science/discoveries/news/2001/02/41892.

[3] Leslie Roberts, *Genome Patent Fight Erupts*, 254 SCI. 184, 184–86 (1991); *Human Gene Patents Defended*, BBC NEWS (Oct. 27, 1999, 10:53 AM), http://news.bbc.co.uk/2/hi/science/nature/487773.stm.

[4] John Bingham, *Synthetic Life: Dr Craig Venter Seeking 'Monopoly', Claims Gene Pioneer*, TELEGRAPH (May 25, 2010, 8:49 AM), http://www.telegraph.co.uk/news/science/science-news/7762711/Synthetic-life-Dr-Craig-Venter-seeking-monopoly-claims-gene-pioneer.html. They nicknamed it "Synthia." *Id.*

[5] *Scientist: 'We Didn't Create Life From Scratch*,' CNN REPORTS (May 21, 2010, 4:45 PM), http://www.cnn.com/2010/HEALTH/05/21/venter.qa/.

[6] *See* U.S. Patent Publication No. 2007/0264688 at [0048] (filed Dec. 6, 2006). A representative claim from the patent application reads "37. A synthetic cell comprising: a microorganism of one species from which part or all of the resident genome has been removed; and a synthetic genome which exhibits at least one property that is different from the resident genome." *Id.*

[7] *Biotechnology, n.*, OXFORD ENGLISH DICTIONARY (3d ed. 2010).

this,[8] the current reality is that engineered cells are not built by a rational design-and-construction process.[9] Rather, they are *evolved* through a trial and error process of natural selection in the lab. A scientist induces the DNA of a cell to mutate by a random process,[10] then selects for desirable traits from the resulting cells. One could say that instead of being built bottom-up, cells are engineered top-down. The inventor guides a cell to develop a new and useful function—without having a detailed understanding of the underlying molecular changes needed to get there.

This blurring of the distinction between invention and evolution creates challenges for the patent system. On one end of the spectrum, some products are considered to be entirely the result of evolution, meaning they are unpatentable products of nature.[11] On the other end, inventors who have designed and built inventions using conventional engineering methods can enjoy the protection afforded by a patent system geared toward such methods. In between, products created with techniques that blend notions of evolution and invention frustrate patent law's attempt to establish clear rules for patentability. The verb "evolve" has taken on an active character—as in "to evolve a protein with a desired function"—quite apart from its traditional meaning, which refers to a gradual, passive, natural process of change.[12] So-called directed evolution methods put pressure on the

[8] *See* Narayana Annaluru et al., *Total Synthesis of a Functional Designer Eukaryotic Chromosome*, 344 SCI. 55, 58 (2014) ("Rapid advances in synthetic biology coupled with ever decreasing costs of DNA synthesis suggest that it will soon become feasible to engineer new eukaryotic genomes, including plant and animal genomes, with synthetic chromosomes encoding desired functions and phenotypic properties based on specific design principles.").

[9] *See* Jon Mooallem, *Do-It-Yourself Genetic Engineering*, N.Y. TIMES MAG., Feb. 10, 2010, at 40, 42, http://www.nytimes.com/2010/02/14/magazine/14Biology-t.html (describing synthetic biology as "still in its infancy").

[10] *See* Yen-Hsiang Wang et al., *Synthetic Biology: Advancing the Design of Diverse Genetic Systems*, 4 ANN. REV. CHEMICAL & BIOMOLECULAR ENGINEERING 69, 76 (2013) (reviewing the process of synthetic biology, including focusing on a desired function, generating genetic diversity, and screening for the desired activities). Mutations can be induced, for example, by exposure to a mutagen such as radiation or mutagenic chemicals. *See Mutagen, n.*, OXFORD ENGLISH DICTIONARY (3d ed. 2003) (defining a "mutagen" as "substance or agent that causes genetic mutation").

[11] *See* Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 133 S. Ct. 2107, 2116 (2013) (explaining that products of nature are not created, and "manifestations . . . of nature [are] free to all men and reserved exclusively to none" (alteration in original) (quoting Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980))).

[12] *See* Andrew Pollack, *Selling Evolution in Ways Darwin Never Imagined; If You Can Build a Better Gene, Investors May Come*, N.Y. TIMES, Oct. 28, 2000, http://www.nytimes.com/2000/10/28/business/selling-evolution-ways-darwin-never-imagined-if-you-can-build-better-gene.html?pagewanted=all (drawing a contrast between directed evolution, used in laboratories to produce molecules or metabolic pathways with desired properties, and natural evolution, which occurs over the course of millions of years).

enablement requirement, which states that, in order to receive protection, a patent specification must describe how to make the invention in "full, clear, concise, and exact terms."[13]

The patentability of synthetically evolved organisms is an important issue, given the rapidly growing use of this form of biotechnology. Biofuel companies are hoping to commercialize microorganisms developed to produce sustainable sources of energy.[14] Researchers are trying to evolve a photosynthesis protein that can be used industrially to capture carbon dioxide from the air.[15] To maximize beneficial innovations like these, it will be necessary to resolve the mismatches between evolved inventions and our patent system. On the other hand, policymakers should consider just how much an inventor deserves patent rights to something developed in collaboration with nature.

This Note argues that, by focusing almost entirely on whether living organisms are patent-eligible subject matter, courts and legal scholars have overlooked the problem that patent claims covering living organisms very often do not meet the enablement requirement for patentability. That these patents often fail the enablement requirement is unsurprising in view of the fact that this requirement, as applied to living things, is largely unworkable. Part I introduces the problem by reviewing the current law on patent eligibility, which boils down to the Supreme Court's deceptively simple doctrine that anything man made is patent eligible. In setting forth this rule, the Court hoped to broadly encourage the development of useful, novel, living organisms, but provided little guidance on how to define the line between things made by people and things made by nature. An examination of the two seminal cases delineating this distinction exposes the fundamental fuzziness of the distinction and its dependence on technology's ability to differentiate between things made by human or by nature. Part II extends this discussion to the disclosure requirements for a patent specification, where the common law takes the position that a written document cannot adequately teach how to make a living

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13 35 U.S.C. § 112 (2012).

14 *See, e.g.*, Matthew L. Wald, *Ethanol Plant Is Switching to Butanol*, N.Y. TIMES (Mar. 10, 2011, 12:07 PM), http://green.blogs.nytimes.com/2011/03/10/ethanol-plant-is-switching-to-butanol/ ("Gevo tinkered with the yeast to turn off its ability to make ethanol and increase its production of isobutanol[,] . . . [which] can be turned into a drop-in component of gasoline, diesel or jet fuel.").

15 *See* Gayathri Vaidyanathan, *Injecting Tiny Proteins into the Hunt for 'Clean Coal,'* N.Y. TIMES (Feb. 15, 2010), http://www.nytimes.com/cwire/2010/02/15/15climatewire-injecting-tiny-proteins-into-the-hunt-for-cl-64718.html ("[S]cientists are engineering proteins found in living things to trap carbon dioxide from coal-fired power plants.").

organism.[16] Instead, the patent system currently requires an inventor to make a biological deposit that enables members of the public to bypass the experimental work done by the inventor in creating the patented organism.[17] Unfortunately, this requirement not only enables people to make and use the invention, as the law requires of patents, but also enables competitors to infringe without detection, or to work around the claims with little effort. Part III concludes by proposing solutions, including updating the concept of undue experimentation, employing means-plus-function claiming, and enlarging the research exemption, in order to help separate patentable invention from purely natural—and therefore unpatentable—evolution.

I
SHIFTING CONCEPTS OF NATURAL AND SYNTHETIC

A. Creation of Novel Organisms by Random Mutation and Selection

The process by which scientists create novel organisms is known as genetic engineering. The term "engineering" might be a misleading one—the products of genetic engineering are often not designed and built from basic chemicals, but derived from natural cells and their components.[18] Genetic engineering is a direct descendant of breeding, which takes advantage of the natural selection process by which organisms evolve in the wild.[19] Genes mutate randomly, and beneficial mutations are more likely than detrimental ones to be inherited

[16] *See* David J. Weitz, *The Biological Deposit Requirement: A Means of Assuring Adequate Disclosure*, 8 HIGH TECH. L.J. 275, 279 (1993) ("Biotechnology differs from most fields in that the 'machinery' used, living matter, cannot always be reproduced from a written description, no matter how comprehensive. There are circumstances where 'life simply cannot be reduced to a written recipe.'" (footnote omitted) (quoting Brief *Amicus Curiae* of The American Type Culture Collection in Support of Petitioners at 4, Genetics Inst., Inc. v. Amgen, Inc. at 4, 502 U.S. 856 (1991) (No. 91-13), 1991 WL 11178446 at *4)).

[17] *See* 37 C.F.R. § 1.802 (2015) (requiring the deposit of biological material where "access to such material is necessary for the satisfaction of the statutory requirements for patentability under 35 U.S.C. 112").

[18] *See* Katherine Xue, *Synthetic Biology's New Menagerie*, HARV. MAG., Sept.–Oct. 2014, at 42, 43 ("'Many of the biomolecular components we're not building from scratch,' says James J. Collins, Warren Distinguished Professor at Boston University. . . . 'We're taking native systems and then modifying them.'"); *see also* Joseph N. Michelotti, *Genes as Intellectual Property*, 11 MICH. ST. U. J. MED. & L. 71, 87 ("To date, no person has actually composed an original base pair sequence for even a relatively short segment of DNA with the expectation that it would encode predictable and useful instructions in a living organism.").

[19] *See* ANTHONY J.F. GRIFFITHS ET AL., AN INTRODUCTION TO GENETIC ANALYSIS 486 (7th ed. 2000) ("[O]ne way of breeding a better crop plant is to make a hybrid and then to select the desired recombinants from the progeny generations. That approach makes use of the variation naturally found between available stocks or isolates from nature.").

through generations.[20] This bias forms the basis for the principle that beneficial traits (which result from beneficial mutations) are systematically favored—i.e., naturally selected.[21] Evolution is the long-term result of repeated natural selection. In the wild, survival of the fittest drives evolution.[22] When humans direct breeding, however, they usually select for traits other than pure ability to survive, like increased milk production in cows or rust resistance in wheat.[23]

Modern biotechnology aims to breed cells or molecules with useful functions, analogous to traditional animal and plant breeding.[24] But while it took more than ten thousand years to go from a wolf to a Chihuahua,[25] genetic engineering works much faster. There are two main reasons for this. First, genetic engineering works primarily with single-celled organisms, which can reproduce rapidly, in minutes or hours.[26] Microorganisms are small, allowing an individual researcher to handle millions at a time in screening for desired traits. Second,

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[20] *See* SIDDHARTHA MUKHERJEE, THE GENE: AN INTIMATE HISTORY 37 (2016) ("[A] variant better adapted for an environment is 'naturally selected.' The best adapted—the 'fittest'—survive. . . . These survivors then reproduce to make more of their kind, thereby driving evolutionary change within a species.").

[21] *See id.*

[22] *See id.*

[23] *See* Manuel Porcar, *Beyond Directed Evolution: Darwinian Selection as a Tool for Synthetic Biology*, 4 SYS. & SYNTHETIC BIOLOGY 1, 3 (2010) ("The mechanism behind both natural and artificial selection is the same: the fittest (with respect to the environment in natural selection and with respect to human requirements for artificial selection) survive.").

[24] A note on terminology: "directed evolution" is a term that typically refers to the laboratory selection of molecules with desired characteristics. *See, e.g.*, Pollack, *supra* note 12 (explaining that directed evolution works by mutating genes to produce mutated proteins, where "[t]he genes for the best proteins can be mutated again and again in hopes of evolving an even better protein"). "Synthetic biology" usually refers to the re-wiring of cells—largely via evolutionary methods—to produce useful products. I will use "genetic engineering" as an umbrella term encompassing both processes. *See, e.g.*, W. Wayt Gibbs, *Synthetic Life*, SCI. AM., May 2004, at 75, 76 ("Synthetic biology has already produced microbes with a variety of unnatural talents. Some produce complex chemical ingredients for drugs; others make artificial amino acids, remove heavy metals from wastewater or perform simple binary logic.").

[25] *See* Adam H. Freedman et al., *Genome Sequencing Highlights the Dynamic Early History of Dogs*, 10 PLOS GENETICS 1, 1 (2014) ("We narrow the plausible range for the date of initial dog domestication to an interval spanning 11–16 thousand years ago, predating the rise of agriculture.").

[26] *See* Kevin M. Esvelt & Harris H. Wang, *Genome-Scale Engineering for Systems and Synthetic Biology*, 9:641 MOLECULAR SYS. BIOLOGY 1, 10 (2013) (explaining that microbes are "the organisms of choice for directed evolution studies," on account of their rapid growth and large population sizes); Kenneth Todar, *The Growth of Bacterial Populations*, TODAR'S ONLINE TEXTBOOK OF BACTERIOLOGY tbl.2 (2012), http://textbookofbacteriology.net/growth_3.html (listing bacterial reproduction times).

genetic engineers have various tools at their disposal for increasing the rate of mutation, thereby accelerating natural selection.[27]

Today, the starting point for evolution-based biotechnology is often a naturally occurring cell or macromolecule. After multiple rounds of inducing random mutations (sometimes in combination with targeted gene manipulations), followed by large-scale selection, the process achieves the goal of a cell or macromolecule that performs a useful function.[28] If the evolved product exhibits a function that the starting material lacked, the inventor can demonstrate (for example, with modern sequencing technology) that the invention is something new that does not exist in nature.[29]

B. Presumed Patent-Eligibility of Nonnaturally Occurring Organisms

The quality of being distinct from anything that exists in nature is a basic requirement for patentability. There are four principal statutes that set forth the requirements for patentability of an invention: 35 U.S.C. §§ 101 (patent eligibility),[30] 102 (novelty),[31] 103 (nonobviousness),[32] and 112 (written requirements).[33] Section 101 is often referred to as a threshold requirement,[34] dictating whether the subject matter of an invention can even be considered for patenting. Laws of nature,

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[27] *See Ex parte* Jackson, No. 463-26, 217 U.S.P.Q. (BNA) 804, 806 (B.P.A.I. Nov. 12, 1982) ("It is very well known that spontaneous mutation is a common occurrence in microorganisms and that mutations can be intentionally produced by a variety of known procedures.").

[28] Pollack, *supra* note 12.

[29] *See* Olga Kuchner & Frances H. Arnold, *Directed Evolution of Enzyme Catalysts*, 15 TRENDS BIOTECHNOLOGY 523, 523 (describing directed evolution as an iterative process of mutation and screening).

[30] *See* 35 U.S.C. § 101 (2012) ("Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.").

[31] *See* 35 U.S.C. § 102 (2012) (providing that a person is entitled to a patent unless the claimed invention was previously "patented, described in a printed publication, or in public use, on sale, or otherwise available to the public before the effective filing date of the claimed invention").

[32] *See* 35 U.S.C. § 103 (2012) (providing that a patent may not be obtained "if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention").

[33] *See* 35 U.S.C. § 112 (2012) (requiring that a patent application "contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art . . . to make and use the same").

[34] *See* Bilski v. Kappos, 561 U.S. 593, 602 (2010) ("The § 101 patent-eligibility inquiry is only a threshold test.").

physical phenomena, and abstract ideas are not patent eligible.[35] When faced with the question of determining to what extent an invented organism is an unpatentable work of nature and to what extent it qualifies as patent-eligible subject matter,[36] the Supreme Court issued a sweeping pronouncement: "[A]nything under the sun that is made by man" is patent eligible, including living organisms.[37]

In the case underlying that grandiose rule, microbiologist Ananda Chakrabarty had produced an improved oil-eating bacterium that was useful for cleaning oil spills and did not occur in nature.[38] To do so, he combined four strains known to digest four different ingredients of oil into a new aggregate strain able to "eat oil faster than any one of the four [could] individually."[39] The Court was impressed with the compelling utility of the bacterium,[40] and showed no hesitation in declaring it a patent-eligible "product of human ingenuity."[41] In so doing, the Court came down strongly in support of a policy encouraging the invention of useful, novel, living organisms.

The Court had spoken so strongly that when the Patent Office granted a patent to Harvard on a mouse genetically modified for use in cancer research the decision went unchallenged in the United States.[42] In Europe, the same patent application was opposed by seventeen parties who argued—ultimately unsuccessfully—that patents covering higher life forms should be banned as contrary to public

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[35] *Id.* at 601 ("The Court's precedents provide three specific exceptions to § 101's broad patent-eligibility principles: 'laws of nature, physical phenomena, and abstract ideas.'" (quoting Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980))).

[36] *See, e.g.*, Linda J. Demaine & Aaron Xavier Fellmeth, *Reinventing the Double Helix: A Novel and Nonobvious Reconceptualization of the Biotechnology Patent*, 55 STAN. L. REV. 303, 392–93 (2002) ("Because of limited creative input in the production of DNA molecules, proteins, and other preexisting products that have been altered in some less than fundamental way, biotechnological innovations typically inhabit a twilight zone between patentable inventions and unpatentable discoveries.").

[37] Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980). Exceptions are "laws of nature, physical phenomena, and abstract ideas." *Id.* at 309. Section 101 permits patents to cover "any new and useful process, machine, manufacture, or composition of matter." 35 U.S.C. § 101 (2012). The *Chakrabarty* Court held that engineered cells constitute a "manufacture" or "composition of matter" within the statute. *Chakrabarty*, 447 U.S. at 309.

[38] *Oil-Eating Bug*, TIME, Sept. 22, 1975, at 52.

[39] *Id.*; *see also* U.S. Patent No. 4,259,444, at [57] (filed June 7, 1972) (describing the creation of a strain combining the "camphor, octane, salicylate and naphthalene degradative pathways").

[40] *See Chakrabarty*, 447 U.S. at 310 ("Here . . . the patentee has produced a new bacterium with markedly different characteristics from any found in nature and one having the potential for significant utility.").

[41] *Id.* at 309.

[42] *See* U.S. Patent No. 4,736,866, at [57] (filed June 22, 1984) (referring to "[a] transgenic non-human eukaryotic animal whose germ cells and somatic cells contain an activated oncogene sequence").

morals.[43] A similar argument prevailed in the Canadian Supreme Court, which rejected the mouse claims and held that higher life forms are simply not patentable in Canada.[44]

In the United States, there are currently no legal limits to the patent eligibility of life forms, so long as they are "made by man."[45] This lone constraint is minimal, but important—the prohibition against patenting anything that already exists in nature is a fundamental corollary to patent law's insistence that all inventions be new and not previously "available to the public."[46] Wild organisms, even if newly discovered, are considered nonnovel and ineligible for patent protection.[47] In short, they are the products of evolution, not invention.

C. Technology-Dependent Definitions of "Nonnatural"

The real question, of course, is how to interpret "made by man." Where is the threshold at which human manipulation of a natural composition rises to the level of an invention? A closer look at *Chakrabarty* suggests this line is blurrier than it appears. The Court

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[43] President and Fellows of Harvard Coll. v. British Union for the Abolition of Vivisection, No. T 0315/03-3.3.8, Decision, Technical Board of Appeal of the European Patent Office (July 6, 2004), http://www.epo.org/law-practice/case-law-appeals/pdf/t030315ex1.pdf. After proceedings lasting more than a decade, the Board dismissed the action, acknowledging that though there was unease in Europe about the potential mistreatment of research animals, "there is nothing before the Board to suggest that such unease could be elevated to the status of moral disapproval." *Id.* at 127.

[44] Harvard Coll. v. Canada (Comm'r of Patents), [2002] 4 S.C.R. 45, 46 (Can.).

[45] *Chakrabarty*, 447 U.S. at 309. A test filing by Stuart Newman in 1997 gave rise to a possible exception for human/animal chimeras. *See* U.S. PATENT & TRADEMARK OFFICE, PRESS RELEASE 98-6, FACTS ON PATENTING LIFE FORMS HAVING A RELATIONSHIP TO HUMANS (1998), http://www.uspto.gov/about-us/news-updates/facts-patenting-life-forms-having-relationship-humans ("It is the position of the PTO that inventions directed to human/non-human chimera could, under certain circumstances, not be patentable because, among other things, they would fail to meet the public policy and morality aspects of the utility requirement."). This statement has been untested by courts because the PTO did not allow claims to the chimeras to issue, and the applicants abandoned their efforts in 2005. *See* Seán M. Coughlin, *The Newman Application and the USPTO's Unnecessary Response: Patentability of Humans and Human Embryos*, 5 CHI.-KENT J. INTELL. PROP. 90, 97 n.84 (2006) (noting that a Notice of Abandonment was mailed in the case on March 2, 2005).

[46] *See* 35 U.S.C. § 102 (2012) ("(a) Novelty; Prior Art.—A person shall be entitled to a patent unless—(1) the claimed invention was patented, described in a printed publication, or in public use, on sale, or otherwise available to the public before the effective filing date of the claimed invention"); Gen. Elec. Co. v. De Forest Radio Co., 28 F.2d 641, 643 (3d Cir. 1928) (invalidating patent claims to purified tungsten as mere discovery of something created by nature).

[47] *See* Demaine & Fellmeth, *supra* note 36, at 347 ("[A] plant, animal, or microbe newly found in the wild, or a mineral or chemical newly discovered in the earth, or any part of a plant, animal, microbe, mineral, or chemical is not patentable subject matter . . . ."); Rebecca S. Eisenberg, *Proprietary Rights and the Norms of Science in Biotechnology Research*, 97 YALE L.J. 177, 188 (1987) ("[N]aturally-occurring organisms are not new.").

distinguished the facts of *Chakrabarty* from those of *Funk Bros. Seed Co. v. Kalo Inoculant Co.*,[48] in which it had held that a mixture of naturally occurring bacteria was not patent eligible. The *Chakrabarty* Court found the contrast between the two cases to be quite dramatic, distinguishing *Funk Bros.* on the grounds that Chakrabarty had "produced a new bacterium with markedly different characteristics from any found in nature,"[49] whereas the bacteria in *Funk Bros.* were merely mixed together, such that the individual cells were unaffected.[50]

This *Chakrabarty* Court's view of the two cases both overstates the *Chakrabarty* invention, and understates the product created by Varley Sherman Bond, the patentee in *Funk Bros.* The factual distinction between these two cases is not all that clear. To start, both inventors set out to solve remarkably similar problems. In Chakrabarty's case, different bacterial strains were known to digest different components of oil, and these strains were commonly mixed to treat oil spills. Unfortunately, because the bacteria would compete against one another, scientists observed that "the use of a mixed culture leads to the ultimate survival of but a portion of the initial collection of bacterial strains" leaving "the bulk of the oil . . . free to spread or sink."[51] Bond faced the same problem in the context of treating legume plants. Different bacteria strains were known to work for different types of plants (for example, alfalfa, soy, and peas), but previous attempts to mix the bacteria for general use were frustrated by the fact that "different species of the Rhizobia bacteria produced an inhibitory effect on each other . . . with the result that their efficiency was reduced."[52]

Chakrabarty concluded that the solution was to fuse the different bacterial genes for oil digestion to create an aggregate strain that would not be hampered by competition between strains.[53] Bacterial genetics was still in its infancy at the time, and Chakrabarty was forced to use a laborious trial and error process to produce his strain. He mixed different bacteria together, allowed them to exchange genetic material (as bacteria naturally will), and irradiated them with

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[48] 333 U.S. 127 (1948).

[49] *Chakrabarty*, 447 U.S. at 310.

[50] *See Funk Bros.*, 333 U.S. at 131 ("The combination of species produces no new bacteria, no change in the six species of bacteria, and no enlargement of the range of their utility.").

[51] U.S. Patent No. 4,259,444 col. 5 l. 31 (filed June 7, 1972).

[52] *Funk Bros.*, 333 U.S. at 129–30.

[53] *See* '444 Patent at col. 3 l. 11 ("Having established the existence of (and transmissibility of) plasmid-borne capabilities for specifying separate degradative pathways for salicylate and naphthalene, unique single-cell microbes have been developed containing various stable combinations of [those] plasmids.").

ultraviolet light, a method known to promote gene fusions.[54] Chakrabarty's hope was that genes from different strains that would normally clash with one another could be made compatible by permanently connecting them.[55] He had no way to control when and where fusion occurred, but he could observe it after the fact by looking at which oil components the bacteria could digest. Bond's work predated Chakrabarty's by three decades, and more closely resembled traditional breeding methods. He isolated individual strains in the laboratory and used trial and error to find ones that were compatible with each other, meaning they could promote nitrogen fixation by host plants without mutual inhibition.[56] Bond called these more neighborly bacteria "alpha" strains, and filed for a patent covering mixtures of alpha strains.[57]

Of course, however one measures nonnaturalness, Chakrabarty's aggregate bacterium would almost certainly exhibit more of it than Bond's alpha bacteria. The aggregate strain was the product of irradiation, a deliberate attempt to induce gene fusions, whereas the alpha bacteria were obtained by passive selection without active gene disruption.[58] Nevertheless, it might not make sense to draw the line for patent eligibility between these two bacterial strains. Though Chakrabarty set out to alter bacterial DNA, his process was uncontrolled—the same result could technically be accomplished (albeit much more slowly) without human intervention, by random exposure of bacteria mixtures to ultraviolet rays like those present in sunlight.[59] Chakrabarty himself took a modest view of his achievement, saying, "I simply shuffled genes, changing bacteria that already existed[,] . . .

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[54] *See id.* at col. 13 l. 65 (discussing the use of "UV irradiation or X-ray exposure" to render plasmids compatible).

[55] *See id.* at col. 4, l. 62 (declaring that "the problem of plasmid instability has now been solved by bringing about fusion of the plasmids in the recipient cell").

[56] U.S. Patent No. 2,200,532 p. 5 col. 1 l. 56 (filed Aug. 24, 1938).

[57] Bond designated the selected strains "alpha" to mean "those strains of the species of Rhizobia which are mutually noninhibitive of each other." *Id.* at l. 58.

[58] Filed in 1938, Bond's patent preceded the discovery of the structure of DNA and the subsequent ability to manipulate genes by fifteen years. *See* J.D. Watson & F.H.C. Crick, *Genetical Implications of the Structure of Deoxyribonucleic Acid*, 171 NATURE 964, 965 (1953) (remarking that "no evidence has been presented to show how [DNA] might carry out the essential operation required of a genetic material, that of exact self-duplication" and reporting a proposed structure which "immediately suggests a mechanism for its self-duplication").

[59] *See, e.g.*, Gerd P. Pfeifer et al., *Mutations Induced by Ultraviolet Light*, 571 MUTATION RES. 19, 21 (2005) (explaining "sunlight-induced formation" of a mutagenic DNA lesion prevalent in skin cancer).

like teaching your pet cat a few new tricks."[60] (Still, he did apply for a patent.)

More to the point, there is no way to be certain that Bond's process of selecting and pairing strains in the laboratory did not alter them from their natural state, as is now known to occur.[61] At the very least, Bond cultivated bacterial strains that exhibited enhanced efficiency.[62] These were useful products, and it would be hard to argue that they differ meaningfully in patenting terms from a patented lettuce plant bred for resistance to aphids, for example.[63] Perhaps Bond's achievement was merely the unpatentable isolation of the best of naturally existing strains. Or perhaps the way Bond processed the strains in the laboratory produced something new, improved, and patentable. We will never know for sure, but it seems likely that, had genome sequencing been readily available, Bond would have been able to show he had created something that did not exist in nature.

Recently, in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, a landmark opinion on gene patenting, the Supreme Court revisited the comparison between *Chakrabarty* and *Funk Bros.*[64] The claims at issue covered isolated forms of two naturally occurring genes for which mutations increased the risk of ovarian and breast cancer—and thus the ability to use these genes in diagnostic testing.[65] The Court held isolated genes to be unpatentable by

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[60] Giovanna Breu, *An Illinois Biochemist Wins a Crucial Patent Fight, and a New Era of Life in a Test Tube Begins*, PEOPLE 37 (July 14, 1980), http://www.people.com/people/archive/article/0,,20076962,00.html.

[61] Laboratory yeast strains differ significantly at the genetic level from their undomesticated relatives in the wild. *See, e.g.*, Gianni Liti et al., *Population Genomics of Domestic and Wild Yeasts*, 458 NATURE 337, 340 (2009) (sequencing the genomes of various domestic and wild yeast strains and concluding that there are "extensive differences" among them); James Ronald et al., *Genomewide Evolutionary Rates in Laboratory and Wild Yeast*, 174 GENETICS 541, 542 (2006) (reporting that a laboratory yeast strain "evolved at a slow-to-intermediate rate relative to two natural isolates").

[62] *See* U.S. Patent No. 2,200,532 p. 2 col. 2 l. 51 (filed Aug. 24, 1938) (describing an object of the invention as providing "a mixed culture the component strains of which are selected in such a manner that optimum efficiency results").

[63] *See* 35 U.S.C. § 161 (2012) ("Whoever invents or discovers and asexually reproduces any distinct and new variety of plant, including cultivated sports, mutants, hybrids, and newly found seedlings, . . . may obtain a patent therefor . . . ."); *see also* U.S. Patent No. 5,977,443, at [57] (filed Nov. 12, 1996) (directed to plants genetically engineered for aphid resistance). Because the plant breeder actively cross-pollinates existing strains to generate new ones, he might appear to exert more active control over his organisms than the bacteriologist. Bacteria, however, exchange genetic material in the form of plasmids, when they are mixed together. *See* MUKHERJEE, *supra* note 20 at 213 (relating the story of the realization that bacterial plasmids could be harnessed to duplicate genes of interest, since "[b]acteria, after all, were capable of trading genetic material like gossip"). The analogy between Bond's method and plant breeding holds.

[64] 133 S. Ct. 2107 (2013).

[65] *Id.* at 2110–11.

drawing a direct comparison to the *Funk Bros.* strains and a direct contrast to *Chakrabarty*.[66] Deservedly or not, *Funk Bros.* now stands firmly for the rule that a product of nature is unpatentable when it remains unaltered from its natural state—even though it may be transported to a new context.[67] This is a clearly articulated and useful rule, though the results of its application will shift over time as technology changes our ability to distinguish unnatural from natural at the molecular level. As technological advancements make it increasingly easy to identify something as nonnaturally occurring, the bar for patent eligibility will be lowered.

II
The Challenge of Enabling Claims to Evolved Products

Though the rule that separates *Chakrabarty* and *Funk Bros.* can be clearly stated, if not always clearly implemented, it suggests a problem for the enablement requirement, which requires patents to teach skilled persons to make and use the claimed invention. Biotechnology's increased reliance on evolution-based methods means it places a heavy emphasis on the end product over how to make it—on function over mechanism. The selection process chooses cells and molecules that have useful traits, without concern for molecular underpinnings. Chakrabarty had little knowledge of the underlying structure of his bacterium, so he defined it mainly by its "energy-generating" functions.[68] Bond knew virtually nothing about his bacteria strains at a molecular level, but even if he had been able to identify the mechanism, his interest would still have been in *what* the bacteria could do, not necessarily *how* they did it. Defining an invention by *what* it is often suffices to meet subject-matter requirements, but the enablement requirement provides that an inventor must also disclose *how* to make and use an invention. 35 U.S.C. § 112 sets forth this requirement:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled

[66] *See id.* at 2117 ("[T]he patent holder [in *Funk Bros.*] did not alter the bacteria in any way. His patent claim thus fell squarely within the law of nature exception. So do Myriad's." (citation omitted)).

[67] The PTO guidelines require a "marked difference," defined broadly to include a product of nature "and a solubilizing agent." *Nature-Based Products*, USPTO 3–4, http://www.uspto.gov/patents/law/exam/mdc_examples_nature-based_products.pdf.

[68] U.S. Patent No. 4,259,444 col. 16 l. 23 (filed June 7, 1972).

> in the art to which it pertains, or with which it is most nearly connected, to make and use the same . . . .[69]

The enablement requirement lies at the heart of the patent system's goal to foster innovation by granting rights in exchange for publication of information. In exchange for a patent granting and announcing their temporary right to exclude others from using their invention, inventors must disclose the inner workings of their inventions within the patent application, a public document.[70] The disclosure requirement encapsulates an enablement standard, meaning the patent specification must teach a person having ordinary skill in the art how to make and use the invention without undue experimentation.[71] Publishing the instructions benefits the public with knowledge and allows other inventors to make improvements.

A. Assumptions of Nonenablement for Written Disclosures of Evolved Products

The trouble for biotechnology patent applicants is that methods of making genetically engineered products are inherently experimental.[72] Evolution-based methods utilize random mutation and are therefore unpredictable. Chakrabarty's use of ultraviolet radiation and random gene fusion meant that he himself could never perfectly repeat what he did to create his aggregate strain, much less instruct others how to do so. Once Thomas Edison had identified and published the recipe for a material that would glow brightly and stably when electrified, a skilled engineer could build a light bulb in far less time than the years spent on the initial invention. In contrast, though it might not take the original six years, a skilled bacteriologist or even Chakrabarty himself, using the tools available in 1980, would likely still need to spend years to create a second bacterium with the patented properties.

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69 35 U.S.C. § 112 (2012).

70 This foundational quid pro quo concept is neatly spelled out in the Constitution. U.S. Const. art. I, § 8, cl. 8 (empowering Congress "[t]o promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries").

71 *See* 35 U.S.C. § 112 (2012).

72 *See* Karen Goodyear Krueger, *Building a Better Bacterium: Genetic Engineering and the Patent Law After* Diamond v. Chakrabarty, 81 Colum. L. Rev. 159, 170 (1981) ("[M]any of the processes by which useful microorganisms are isolated or created are not reliably reproducible, which complicates still more the task of description."); *see also* Alison E. Cantor, *Using the Written Description and Enablement Requirements to Limit Biotechnology Patents*, 14 Harv. J.L. & Tech. 267, 278–79 (2000) (making a similar argument for recombinant DNA).

The judicially created litmus test for enablement is undue experimentation.[73] Because a skilled engineer can fill in gaps with common knowledge or routine screening,[74] a patent "need not disclose what is well known in the art."[75] The Federal Circuit has provided a lengthy list of factors to consider when gauging whether experimentation is undue. These include:

> (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.[76]

Because biotechnology is thought to be unpredictable,[77] the quantity of experimentation needed to reproduce the invention will often be found to be too high to deem the disclosure enabling. When following the instructions set forth in a patent amounts to largely duplicating the inventor's efforts in developing the invention—as will often necessarily be the case for evolution-based methods—courts will likely find the instructions nonenabling.[78]

Significantly, the first case to consider the question of whether animals can be patented sidestepped that issue and rejected the patent for failure to adequately claim its improved chicken.[79] Today we would cast this deficiency as a problem of nonenablement: that the teachings provided will too often fail to produce the claimed invention. Specifically, the court complained that the process described for breeding the chicken was subject to the random nature of genetic inheritance, which meant that practicing the claim would only produce

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[73] *See, e.g.*, Minerals Separation, Ltd. v. Hyde, 242 U.S. 261, 270 (1916) (asking whether necessary experimentation is reasonable); United States v. Telectronics, Inc., 857 F.2d 778, 785 (Fed. Cir. 1988) ("The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.").

[74] *See In re* Wands, 858 F.2d 731, 736–37 (Fed. Cir. 1988).

[75] Lindemann Maschinenfabrik GmbH v. Am. Hoist & Derrick Co., 730 F.2d 1452, 1463 (Fed. Cir. 1984).

[76] *Wands*, 858 F.2d at 737.

[77] *See* AbbVie Deutschland GmbH & Co. v. Janssen Biotech, Inc., 759 F.3d 1285, 1301 (Fed. Cir. 2014) (saying biotechnology is "highly unpredictable" because of difficulty in defining a structure-function correlation for the entire genus).

[78] *See* Weitz, *supra* note 16, at 290 (describing an early biotechnology case in which the court struck down as nonenabled a patent claiming a bacterium isolated from a soil sample, stating that it "would be experimentation to employ the same type of routine and known procedures followed in discovering new antibiotics in the first place" (quoting *Ex parte* Kropp, 143 U.S.P.Q. (BNA) 148 (B.P.A.I. Nov. 24, 1959))).

[79] *See In re* Merat, 519 F.2d 1390, 1394 (C.C.P.A. 1975).

the desired chicken between one-third and half of the time.[80] Modern biotechnology methods are also subject to random genetic inheritance but with a much lower success rate than one-third or half the time. Desired cells are selected from many—even thousands[81]—of generations of laboratory-cultivated strains.

Congress recognized the difficulty of enabling a person to create an organism when it enacted the Plant Patent Act of 1930.[82] It chose to handle this problem by simply eliminating the enablement requirement for plant patents.[83] Similarly, courts take the view that when a patent disclosure depends on the use of living materials, organisms, or cultured cells—which biotechnology methods nearly always do—it "may be impossible to enable the public to make the invention (i.e., to obtain these living materials) solely by means of a written disclo-

[80] *See id.* at 1395–96. The court drew Punnett square diagrams to illustrate its analysis. Technically, the claims were rejected for lacking definiteness because they embraced a degree of genetic unpredictability. However, you could equally argue that the patent failed to teach how to breed the improved chicken with certainty. *Id.* at 1395 ("Under the Echelon A definition of 'normal,' only 50% normal chickens are produced by the process; under the Echelon B definition the characteristics of the offspring cannot be predicted.").

[81] *See* Zachary D. Blount et al., *Historical Contingency and the Evolution of a Key Innovation in an Experimental Population of* Escherichia coli, 105 PROC. NAT'L ACAD. SCI. 7899, 7899 (reporting that, though *E. coli* cannot use citrate as a carbon source, a "citrate-using (Cit^+) variant finally evolved in one [laboratory] population by 31,500 generations").

[82] *See* Max Stul Oppenheimer, *The "Reasonable Plant" Test: When Progress Outruns the Constitution*, 9 MINN. J.L. SCI. & TECH. 417, 425 (2008) (describing difficulties with early plant patents under the 1930 Plant Patent Act). In a case that was decided after the Plant Patent Act was enacted, the Patent Office Board of Interference Examiners noted that "[t]he mere filing of an application for a patent for a new variety of plant would not enable anyone to reproduce such a plant." Dunn v. Ragin, 50 U.S.P.Q. (BNA) 472, 474 (B.P.A.I. 1941). The same principle led to the Court of Customs and Patent Appeals' decision (again following enactment of the Plant Patent Act) that a photograph of a rose bush could not defeat a patent on the same rose bush since the photograph could not enable the public to produce the plant. *See In re* LeGrice, 301 F.2d 929, 944 (C.C.P.A. 1962) (noting that "mere description of the plant is not necessarily an 'enabling' disclosure," and that the published photographs were "incapable of placing these roses in the public domain by their descriptions").

[83] *See* John M. Czarnetzky, Note, *Altering Nature's Blueprints for Profit: Patenting Multicellular Animals*, 74 VA. L. REV. 1327, 1359 (1988). The Plant Patent Act stipulates that a plant should be described as fully as reasonably possible. The Plant Variety Protection Act (PVPA), on the other hand, simply requires a deposit of seed in a public repository and disclosure of the plant's breeding history and genealogy. *See* Mark D. Janis & Jay P. Kesan, *U.S. Plant Variety Protection: Sound and Fury . . . ?*, 39 HOUS. L. REV. 727, 747–48 (2002) (discussing impact of PVPA). The PVPA regime includes no adequacy of disclosure requirements comparable to those found in conventional utility patent law's Section 112. Specifically, the PVPA does not require applicants to provide a teaching disclosure of the type that would be required under the enablement standard. Likewise, the PVPA does not extract a disclosure that would satisfy the written description requirement. Despite these lesser requirements, biotechnology inventors greatly prefer utility patents over plant patents because plant patents must be limited to specific genetic profiles, making them relatively easy to work around.

sure."[84] Instead, inventors are required to make a biological deposit that would allow the public to circumvent the screening process. This was the approach taken by Chakrabarty, who deposited his two oil-digesting strains with the U.S. Department of Agriculture.[85] Today, an examiner would likely ask the inventor of a jet-fuel-producing yeast strain to publicly deposit the cell line,[86] in a form capable of self-replication.[87] The inventor of a new anticancer antibody would need to disclose its sequence in a sequence listing, allowing anyone with access to molecular biology tools to synthesize the gene and produce the antibody in cells. Biological deposits and sequence listings are the ultimate dispositive proof of enablement,[88] putting to rest the question of whether the inventor has taught the person of ordinary skill in the art how to make and use the invention by providing the invention itself.

B. Unworkable Existing Routes to Enablement of Evolved Products: Biological Deposits and Sequence Listings

Unfortunately, biological deposits and sequence listings are preferred not only by courts and patent examiners as evidence, but by infringers seeking to free ride on the disclosed invention.[89] Cells and DNA are self-replicating. The biological deposit may work too well as a solution to the enablement problem, such that it becomes self-defeating.[90] As Karen Krueger puts it, "if the inventor is required to provide the public with a working and readily reproducible sample of

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[84] *In re* Wands, 858 F.2d 731, 735 (Fed. Cir. 1988); *see also In re* Argoudelis, 434 F.2d 1390, 1392 (C.C.P.A. 1970) ("[A] unique aspect of using microorganisms as starting materials is that a sufficient description of how to obtain the microorganism from nature cannot be given. Such a description could only detail an experimental screening program similar to the screening programs followed in discovering the microorganism in the first instance.").

[85] *See* U.S. Patent No. 4,259,444 at [57] ("Living cultures of two strains of Pseudomonas (*P. aeruginosa* [NRRL B-5472] and *P. putida* [NRRL B-5473]) have been deposited with the United States Department of Agriculture, Agricultural Research Service, Northern Marketing and Nutrient Research Division, Peoria, Ill.").

[86] *See* Amy Yee, *Airlines Fly the Skies on a Sugar High*, N.Y. TIMES (Oct. 7, 2014), http://www.nytimes.com/2014/10/08/business/energy-environment/airlines-fly-the-skies-on-a-sugar-high.html.

[87] *See* 37 C.F.R. § 1.801 (1999) ("[T]he term biological material shall include material that is capable of self-replication either directly or indirectly.").

[88] *See* 7 U.S.C. § 2422(4) (2012) (requiring application for protection to contain declaration that viable seed samples will be maintained in public depository); *In re* Argoudelis, 434 F.2d at 1393 (finding the deposit satisfies the requirements of Section 112).

[89] *See* Eisenberg, *supra* note 47, at 197 ("By sharing access to unique materials, however, the publishing scientist not only enables other scientists to replicate her claims; she also allows them to compete with her more effectively in making new discoveries.").

[90] *See* Weitz, *supra* note 16, at 297 ("[B]iological deposits have been criticized for increasing the risk of piracy of biotechnology inventions.").

the invention, protection against infringement becomes extremely difficult, if not impossible."[91] Reverse engineering is not even necessary in such cases, because no engineering at all is needed to make and use the invention.

Infringement based on sequence listings and, to a lesser extent, biological deposits[92] could be undetectable, frustrating any efforts to enforce the inventor's patent rights. Though the patent notifies the public of the inventor's right to exclude others from using the invention, the inventor can only act on that right by suing or threatening to sue infringers. The inventor bears the burden of identifying infringers. This is relatively easy to do when a patent has a claim directly covering a commercially valuable product or use of a product. The originator of a blockbuster antibody drug will know that a competitor infringes if the competing product falls within the scope of the claim covering the original product. Infringement of a claimed use of the product is also readily determined when the competitor's product has a label directing use in a manner that would infringe. But infringement of biotechnology patents may be more difficult to detect. If the invention is a cell that provides a cheaper way to make saffron, the public result of infringement might only be that the market is flooded with cheaper saffron, by itself a natural product not protectable by a patent.[93] In that case, an infringer would also likely be able to undercut the inventor's prices, having invested nothing to develop the invention. The Supreme Court has held that using a self-replicated version of an invention is still infringement,[94] but for that decision to have effect, the patentee must still be aware of infringement in the first place.

Another problem is that biotechnology inventions are susceptible to workarounds. As the products of millions of years of natural evolution, biological materials are robust. For the most part, the sequence

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[91] Krueger, *supra* note 72, at 178. The same difficulty applies to plants. *See* Janis & Kesan, *supra* note 83, at 730 ("Plant innovation is borne in seeds, and . . . seeds make hundreds of copies of themselves in the natural growth process. From the standpoint of a producer of innovation, the notion of a self-replicating invention presents as compelling a case for intellectual property intervention as can be imagined.").

[92] The depositor is entitled to notice of furnishing of a sample, as well as the "name and address of the requesting party." 37 C.F.R. § 1.808(b)(2) (1999).

[93] It could be possible to tag the saffron with a molecular signature that could be used to identify improper sources, analogous to a practice in copyright. *See* Andrew Clark, *Copying Maps Costs AA £20m*, THE GUARDIAN (Mar. 6, 2001), https://www.theguardian.com/uk/2001/mar/06/andrewclark ("[A copyright plaintiff's experts] identified unique 'fingerprints' in these publications which proved that the AA was using its maps as a source. These included stylistic features and proportions—such as the width of roads in each drawing.").

[94] *See* Bowman v. Monsanto Co., 133 S. Ct. 1761, 1768–69 (2013).

of a biological macromolecule can be altered quite dramatically without significant consequences for function.[95] If Chakrabarty had claimed his bacteria based on exact gene sequences, it would be a fairly simple task for a competitor to access the deposit and tweak its sequence, thereby producing a noninfringing bacteria that retained the ability to clean oil spills. A would-be infringer could also copy a claimed DNA sequence using synthetic techniques, without accessing the biological deposit, with minor modifications added to escape infringement. In this way, existing approaches to combat the difficulty of expressing biological inventions in words overcompensate and force patent applicants to write unduly narrow claims that are limited to specific sequences or deposited materials.

C. Problems with Broad Biotechnology Claims

To solve the problems posed by sequence listings and biological deposits, it may seem that inventors can simply draft broader claims.[96] After all, Chakrabarty was able to claim any *Pseudomonas* bacterium containing at least two stable energy-generating plasmids (the natural bacteria only stably contained one such plasmid[97]). But because genetic engineers often lack a detailed understanding of their inventions, attempts to draft broad claims may inadvertently exclude that which was made. One can question whether Chakrabarty's claim to a bacterium with "at least two stable energy-generating plasmids"[98] actually covered his invented strain. Chakrabarty did not know which genes were energy generating, though he knew they were carried on exchangeable plasmids.[99] The plasmids tended to be lost during cell division, and Chakrabarty's contribution was to fuse the plasmids so that they would be inherited together through generations of cells.[100]

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[95] *See* Patrick Brian Giles, *How to Claim a Gene: Application of the Patent Disclosure Requirements to Genetic Sequences*, 27 GA. ST. U. L. REV. 695, 696 (2011) ("[I]n some cases, 50% or more of the amino acid positions within the sequence of a protein can be substituted without substantially altering protein function.").

[96] *See* Jennifer L. Davis, Comment, *The Test of Primary Cloning: A New Approach to the Written Description Requirement in Biotechnological Patents*, 20 SANTA CLARA COMPUTER & HIGH TECH. L.J. 469, 485 (2004) ("[B]road claims that describe the DNA by characteristics other than sequence, such as by a structure-function relationship, will prevent patent infringers from avoiding liability by making minor changes to the claimed invention.").

[97] *See* U.S. Patent No. 4,259,444 col. 6 l. 37 (listing four previously known bacterial strains, each of which bears a single degradative pathway contained on a plasmid).

[98] *Id.* at col. 16 l. 24.

[99] *See id.* at col. 5 l. 37 (describing that the invention establishes that degradative pathways "are specified by genes borne by transmissible plasmids").

[100] *See id.* (claiming credit for "the discovery that plasmids can be rendered stable . . . by fusion of the plasmids").

As a result, one could reasonably argue that the bacterium made by Chakrabarty contained multiple energy-generating functions on a *single* plasmid, not the "at least two stable energy-generating plasmids,"[101] described by his own patent claim.

Even when genetic engineers can use modern technology to determine the exact genetic sequence of their inventions—thus avoiding the problem of accidentally failing to claim their invention—they will still struggle to draft valid broad claims to cover them. For one reason, the patent law imposes a written description requirement—separate from enablement—that the patent disclose the invention in terms sufficient to prove that the patentee possessed the claimed invention.[102]

To meet the written description requirement, a genetic engineer who has evolved a useful biological product can narrowly claim the product itself (sometimes called a "picture claim" for its detailed depiction of the product[103]). The claim may be enabled by providing the sequence or making a biological deposit. A product produced by an evolution-based method contains many changes from the natural original that are irrelevant to the desired function, frustrating efforts to extract a thesis for the invention in the form of a broader "genus" claim that will block workarounds. Without knowing which aspects of the sequence are important for the desired function, the inventor will gravitate towards using functional language to describe the invention by what it does rather than what it is.[104] When claims are drafted in functional terms, courts will rightly worry that the patentee is attempting to claim too much, and will tend to reject such claims for failure to meet the written description requirement.[105] To satisfy written description, a genus claim must reference unifying structural features that outline the genus, or the patent must disclose representa-

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101 *Id.* at col. 16 l. 24.

102 *See* Ariad Pharm., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1344 (Fed. Cir. 2010) (holding that Section 112 "contains two separate description requirements": written description and enablement).

103 *See* M. Eagles Tool Warehouse, Inc. v. Fisher Tooling Co., 439 F.3d 1335, 1341–42 (Fed. Cir. 2006) (defining a "picture claim" as one that's narrow and "recites in detail nearly all of the features of the invention").

104 *See* Qin Shi, *Patent System Meets New Sciences: Is the Law Responsive to Changing Technologies and Industries?*, 61 N.Y.U. ANN. SURV. AM. L. 317, 327 (2005) ("[D]escrib[ing] what the invention is . . . may not be possible for certain evolving technologies or new sciences where discoveries are conceived, made, and taught only in terms of 'what it does,' not 'what it is.'").

105 *See* AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc., 759 F.3d 1285, 1301 (Fed. Cir. 2014) ("Functionally defined genus claims can be inherently vulnerable to invalidity challenge for lack of written description support, especially . . . where it is difficult to establish a correlation between structure and function for the whole genus or to predict what would be covered by the functionally claimed genus.").

tive species to fill the scope of the genus.[106] Evolution-based biotechnology is not amenable to structural claiming, and the bar for showing sufficient representative species is high: Courts require that representative species do more than populate a corner of the claimed territory and that the patent does more than "merely drawing a fence around a perceived genus."[107]

As an illustration, suppose that by using directed evolution, a scientist produced a photosynthesis protein capable of removing carbon dioxide from the inside of factory smokestacks. She would sequence the protein and claim its sequence with a species claim, but this claim would not prevent competitors from reading the sequence off the patent, modifying it slightly, and creating a knockoff with minimal effort. To prevent this, she would need a genus claim. Without knowing which structural elements of the protein confer the ability to sequester carbon from industrial waste, she would be unable to write a structural genus claim. Instead, she might try a genus claim encompassing proteins that reduce carbon emissions from smokestacks by a certain percentage (assuming her protein does so). Because a skilled molecular biologist could easily reproduce her protein using the disclosed sequence, the functional claims would likely meet the enablement requirement. But a court would probably find the functional claims lacking in written description.[108] The genus of all proteins that can reduce carbon emissions from smokestacks by a certain percentage is vast. It includes all mutations and combinations of mutations that can be made to the sequence of the invented protein without affecting its function, easily numbering in the many thousands. Not only that, but the claim would cover a completely unrelated type of protein with this ability, including types yet to be discovered.[109]

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[106] *See Ariad*, 598 F.3d at 1350 ("[A] sufficient description of a genus . . . requires the disclosure of either a representative number of species . . . or structural features common to the members of the genus so that one of skill in the art can 'visualize or recognize' the members of the genus.").

[107] *AbbVie*, 759 F.3d at 1300.

[108] *See, e.g.*, *Regents v. Eli Lilly & Co.*, 119 F.3d at 1568 (rejecting functional definitions of a genus because they do not allow persons skilled in the art to "visualize or recognize the identity of the members of the genus").

[109] Patent law permits patents to enable insubstantial variations that were discovered after the patent was filed, known as after-arising equivalents, but this power is limited by the written description requirement. *See* Kevin Emerson Collins, *An Initial Comment on* Ariad*: Written Description and the Baseline of Patent Protection for After-Arising Technology*, 2010 PATENTLY-O PAT. L.J. 60, 62 http://patentlyo.com/media/docs/2010/04/collins.ariad.pdf ("Written description curtails the reach of claims into after-arising technology.").

Currently, the inventor who employs evolution-based processes to develop a biotechnology invention faces a claim dilemma without a workable solution. Structural claims require knowledge that is inherently absent for inventions produced in this way. Species claims are too narrow and easily circumvented. Functional claims are too broad and are vulnerable to attack for lack of written description. Just as it is difficult to distill structural principles that outline a genus claim, it can be very challenging for a biotechnology inventor to delineate valid boundaries for a functional claim. Evolution-based methods are incredibly powerful, but they struggle against a patent system developed for conventional engineering.

III
Striking the Balance Between Too Broad and Too Narrow

In contemplating how best to overcome the poor fit between our patent system and evolution-based biotechnology, we start by considering two opposing views of the inventor's agency. In the first view, the inventor prods cells to mutate faster and selects desirable ones, but natural cellular processes perform essentially all the work of constructing the invention.[110] Under this view, the inventor's patent rights should be limited to a scope commensurate with her role and level of understanding of the invention. This is the view taken by the patent system when it restricts inventors (on the basis of written description) to claiming only the evolved product they made (enabled by sequence disclosure or biological deposit). Patent incentives in this regime are low indeed, as they are prone to severe infringement and workaround hazards. The inventor is left with a dilemma—the patent bargain is unappealing, but biological inventions are difficult to maintain as trade secrets.[111] The lack of good options for protecting the invention in this scenario may result in an undesirable chilling of evolution-based biotechnology research as a whole.

In the other view, the inventor has expended laudable efforts to produce a useful product and deserves the reward of the right to exclude others. In its 2013 decision in *Bowman v. Monsanto*, the

[110] *See* Nathan A. Busch, *Genetically Modified Plants Are Not "Inventions" and Are, Therefore, Not Patentable*, 10 Drake J. Agric. L. 387, 415–19 (2005) (arguing that Monsanto did not invent a genetically engineered plant because it had simply transplanted a gene to a single plant cell, and that nature had done all the work to grow the plant and express the gene).

[111] *See* Eisenberg, *supra* note 47, at 193 ("Microorganism cultures are especially difficult to maintain as trade secrets because they are easily stolen without detection and propagate rapidly.").

Supreme Court took the view that people exercise agency when overseeing the reproduction of living organisms. The Court found that a defendant who planted patented seeds could not escape liability by saying the beans, not he, infringed the patent.[112] But when we give inventors credit for guiding evolution, we risk allowing them to claim their inventions broadly and in functional terms. Such claims have the tendency to close off broad avenues of innovation because they can potentially reach any activity that produces the claimed function.

In a sense, then, the first view requires that claims be overly narrow, shrinking patent incentives almost to zero and chilling investment in research. The second view allows claims to be overly broad, granting the inventors overly large rights in exchange for their disclosures, and stifling follow-on innovation. This Part examines ways to temper each extreme to create a workable solution.

A. Broadening the Reach of the Overly Narrow

Courts can help by updating their concept of undue experimentation. "The fact that experimentation may be complex . . . does not necessarily make it undue, if the art typically engages in such experimentation."[113] Courts are wary of inherently uncertain genetic processes and the potential for the creation of harmful organisms through accident or abuse. These methods are routine in biotechnology because, with enough trials, they are statistically certain. Flipping a coin is random, but if you flip a coin ten or a hundred times, it is effectively guaranteed that you will get heads at least once. The method used by Chakrabarty was useful, not because it fails millions of times, but because it reproducibly gives the desired outcome.

In addition, courts can recognize that improvements in technology may remove the need for working biological deposits. Given that inventors can describe how to make evolved products from the starting point of a natural organism with a guarantee of success—despite inherent uncertainty of the procedure—it should often suffice to refer the public to a source of a suitable starting material. The patent disclosure would then describe how to make and use the invention starting from that point, without those efforts being considered undue experimentation. This procedure might seem too duplicative of the inventor's original efforts, but in reality disclosure of the proper

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[112] *See* Bowman v. Monsanto Co., 133 S. Ct. 1761, 1769 (2013) ("[W]e think that blame-the-bean defense tough to credit. Bowman was not a passive observer of his soybeans' multiplication . . . .").

[113] *See In re* Certain Limited-Charge Cell Culture Microcarriers, Inv. No. 337-TA-129, USITC Pub. No. 1486 (1983) (Final), *aff'd*, *sub nom.* Mass. Inst. of Tech. v. AB Fortia, 774 F.2d 1104 (Fed. Cir. 1985).

conditions for guiding evolution of the desired function is very valuable information that should greatly speed up the manufacturing process. Furthermore, gene-editing technology is sophisticated enough that simply providing the sequence of the evolved product should suffice to either synthesize it from basic chemicals or produce it by genetic manipulation of a natural organism.[114] Biological deposits could even be sealed until expiration of the patent,[115] though this would hinder the ability of experimental researchers to reproduce the work of others.[116]

B. Narrowing the Scope of the Overly Broad

As much as evolved products can be conceptualized and claimed as chemical structures, they also have much in common with software, a field that has been attacked for generating bad patents. Like software, evolved biotechnology products are self-replicating or self-templating.[117] There is little economic value in narrowly patenting code because, like patents on specific gene sequences, such claims could be easily circumvented. Instead, inventors gravitate toward functional claiming, to the dismay of many who find such claims excessively broad and impeding of progress.[118] Broad functional claims have also been implicated in controversy surrounding "patent trolls" (also known as non-practicing entities or patent assertion enti-

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[114] *See* Esvelt & Wang, *supra* note 26, at 3–7 (reviewing various methods for targeted gene modification, and noting the "explosion of modifications achieved" using some of these techniques).

[115] *See* Krueger, *supra* note 72, at 178 ("A better course would be for the PTO to require that the deposit be made on or before the filing date, but that the public be given free access to it under the depository agreement only upon expiration of the patent.").

[116] *See* Eisenberg, *supra* note 47, at 197 ("[F]or research involving the use of unique biological materials, such as bacterial strains and other types of self-replicating cells, publication in writing alone may not be sufficient to satisfy this replicability norm. To replicate the authors' results, subsequent investigators may need access to identical materials."). Such research may fall within the common-law experimental use defense to patent infringement, but this doctrine is narrowly construed to exclude any inquiry with "definite, cognizable, and not insubstantial commercial purposes." Embrex, Inc. v. Serv. Eng'g Corp., 216 F.3d 1343, 1349 (Fed. Cir. 2000) (quoting Roche Prods. v. Bolar Pharm. Co., 733 F.2d 858, 863 (Fed. Cir. 1984)).

[117] *See* Christopher M. Holman, *Copyright for Engineered DNA: An Idea Whose Time Has Come?*, 113 W. VA. L. REV. 699, 715 (2011) ("Another important characteristic shared by software and engineered genetic sequences is that, for both, the cost of development greatly exceeds the cost of duplication owing to the fact that both can serve as the template for their own reproduction.").

[118] *See* Mark A. Lemley, *Software Patents and the Return of Functional Claiming*, 2013 WIS. L. REV. 905, 926–28, 943 (lamenting the proliferation of software claims that claim "not on the basis of the technology the patentee actually developed, but on the basis of the function that technology performs").

ties) that assert patent claims without having played a role in creating the invention.

To address the problem of overly broad functional claims, we can import a suggestion from the software field, where Mark Lemley has advocated a return to the means-plus-function format of claiming.[119] This format allows an inventor to claim means for accomplishing a task and its equivalents. Means-plus-function claims have fallen out of favor over the past fifteen years as a result of courts reading equivalents narrowly, leaving the claims vulnerable to evasion.[120] But means-plus-function claims could be quite well suited to biotechnology by eliminating the problem of trivial workarounds. Inventors would be entitled to the specified means for performing a given function using an evolved product, and its equivalents—in this case, variants of the product with minor sequence differences that do not significantly affect the function.

Concerns about overly broad claims can generally be alleviated by enlarging the research exemption to infringement, as others have suggested.[121] Traditionally, the experimental use defense protected any activity "made or used as an experiment, whether for the gratification of scientific tastes, or for curiosity, or for amusement, [where] the interests of the patentee are not antagonized."[122] But because the interests of the patentee have been circularly defined by the scope of the patent claims,[123] the exemption "has been reduced to a mere *de minimis* exception that bears little relation to the implications of a particular experimental use for follow-on innovation or to effects that a specific use might have on inventor incentives."[124] In its current state, the experimental use exemption fails to protect efforts to develop patentable improvements to inventions.[125] This is at odds with Section 101's patent protection for "any new and useful improve-

119 *Id.* at 943.

120 Lemley, *supra* note 118, at 918 ("[C]ourts in the last fifteen years have not read 'equivalents' broadly . . . [, t]he result [being] that means-plus-function claiming today is viewed as narrow and easy for potential infringers to evade.").

121 *See generally* KATHERINE J. STRANDBURG, THE RESEARCH EXEMPTION TO PATENT INFRINGEMENT: THE DELICATE BALANCE BETWEEN CURRENT AND FUTURE TECHNICAL PROGRESS (2006), http://works.bepress.com/katherine_strandburg/6/.

122 Roche Prods. v. Bolar Pharm. Co., 733 F.2d 858, 862 (Fed. Cir. 1984) (quoting W. ROBINSON, THE LAW OF PATENTS FOR USEFUL INVENTIONS § 898 (1890)).

123 *See* STRANDBURG, *supra* note 121, at 5 ("A patentee's legitimate pecuniary interests are necessarily defined by the legal boundaries of the patentee's rights.").

124 *Id.* at 8.

125 *See* ROBERT PATRICK MERGES & JOHN FITZGERALD DUFFY, PATENT LAW AND POLICY: CASES AND MATERIALS 847 (6th ed. 2013) ("Traditionally, patent law has operated on the assumption that other inventors remain free to seek improvement patents within the claims of an earlier patent.").

ment"[126] of an existing invention, and with the benefit to the public of patent disclosures. A reinvigorated exemption would address this problem—it would "permit the disclosure requirement to achieve its intended result."[127]

Conclusion

Biotechnology has reached new heights in terms of its ability to build upon natural products using processes borrowed from nature. These innovations have the potential to provide great benefits to society, but the patent system struggles to incentivize them within a framework developed for traditional engineering. Though courts have made it clear that inventions derived from wild organisms are patentable, the patent system should adapt to accommodate evolution as a modern mode of invention.

[126] 35 U.S.C. § 101 (2012).

[127] Strandburg, *supra* note 121, at 16.