Nanobiotechnology Patents

3.172: Patents and Inventions (Fall '05)

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Nanobiotechnology is a result of converging length scales of study in various technological fields. For example, traditional materials engineering focused on the properties of bulk materials, chemistry focused on atomic and molecular level interactions, physics focused on subatomic phenomena, and biology focused on organic molecular and supramolecular interactions. Now, with powerful imaging and computational capabilities, scientists and engineers are finally able to manipulate and create materials and life systems with consideration to nanometer-scale properties.

We are seeing astonishing technological advances at the nanoscale—where basic materials science, chemistry, physics, and biology discoveries result in tremendous progress. For example, materials scientists are mimicking nature's methods for producing highly sophisticated and miniaturized structures [1], employing organisms to clean up contaminated lands [2], and implanting smart materials inside the human body [3].

Current developments are marked by two interesting technological trends: 1) utilizing biological structures and processes to create or interact with non-biological substances, and 2) utilizing synthetic structures and processes to create or interact with biological substances. In this paper, we explore intellectual property implications of this fascinating collision between nanotechnology and biotechnology. The following sections present three linked perspectives on the issue.

I. Patenting biological applications of nanotechnology

Much of today's technical advancements is being made at micron and nanometer length scales. As devices are made smaller with increasing complexity and control, new potential applications and possibilities emerge. One such area includes the interaction of synthetic structures with biological systems. Three patents described below illustrate current trends in patenting artificial biomaterials.

A. Biomaterial

United States Patent 6,666,214
December 23, 2003
Canham; Leigh T

This patent describes a biocompatible form of silicon, constructed by anodizing a porous silicon region onto a silicon wafer. Biocompatibility is indicated by the deposition of apatite onto the porous silicon while in bodily fluids. Previous methods of fabricating silicon chip implants have faced challenges regarding interfacial problems when inserted into the body. This has made it difficult to use electronic chips for long-term applications such as biosensing and drug delivery. This biosilicon material serves as a possible solution to the long-standing goal of electronic biointegration. The primary independent claim of this patent describes:

1. A method of implantation comprising the step of implanting an electronic device within a living human or animal body, wherein the device includes bioactive silicon.

This patent is powerful because the definition of “bioactive silicon” is very broad:

A "biomaterial" is a non-living material used in a medical device which is intended to interact with biological systems. Such materials may be relatively "bioinert", "biocompatible", "bioactive" or "resorbable", depending on their biological response in vivo.

By this definition, anything that is designed to “interact” with biology *in vivo* is considered “bioactive.”

In addition, all modern electronic devices are based on VLSI silicon fabrication methods. As a result, this patent covers virtually any method of implanting an electronic chip into a body. The inventors narrowed the independent claim with the following dependent claim:

6. A method according to claim 1, wherein the bioactive silicon is polycrystalline silicon.

More specifically:

Bulk crystalline silicon can be rendered porous by partial electrochemical dissolution in hydrofluoric acid based solutions, as described in U.S. Pat. No. 5,348,618. This etching process generates a silicon structure that retains the crystallinity and the crystallographic orientation of the original bulk material. The porous silicon thus formed is a form of crystalline silicon.

Consequently, by finding one solution to the silicon-organism interface, this patent can now claim all future discovered methods of inserting silicon devices into the body, whether or not they utilize the same form of porous polycrystalline silicon.

B. DNA-bridged carbon nanotube arrays

United States Patent 6,958,216
October 25, 2005
Kelley, et al.

The ability to detect chemical and biological compounds at very low concentrations is difficult using conventional means. Traditional means often rely on measuring the change in conductivity of a material when the target material absorbs into it. However, these means require high temperature and have many other disadvantages as well. This patent describes a method of detecting chemical or biological agents, in low quantities, using low power. By creating an array of carbon nanotubes with customized binding sites, one can detect the arrival of a specific particle by conduction at the site that binds to it. This is particularly relevant to nucleic acid chains such as DNA. Therefore, this invention is a small and effective method of detecting specific base-pair chains.

This patent claims:

1. An electrically conducting carbon nanotube array comprising:

a) at least one pair of carbon nanotube tubules each having a proximal end and a distal end, said proximal ends attached to a substrate;

b) a metallic material attached to at least a portion of the carbon nanotube tubules including the distal end; and

c) an electrically conductive biological compound attached to the metallic material, and provides electrical connectivity between the pair of nanotube tubules.

Arrays of carbon nanotubes are nothing new, and their high electrical conductivity is well known. One might notice that the entirety of the device itself is this nanotube matrix. It is not possible to patent this device because it is nothing new. Instead, this patent focused on describing the temporary state formed when the detected compound is attached between a pair of nanotubes.

This is one example where existing nanotechnology is adapted to newfound biological applications. In these cases, the invention may be solely in the way an existing device is used. As such, it seems that one method of claiming this new use is to patent the temporary state of interaction at which the device functions.

One enticing application that recently attracted public concern is reflected in the dependent claim:

40. The molecular sensor device of claim 39 wherein the microorganism is Bacillus anthtracis (anthrax).

This claim highlights one potential market that the inventors or assigned entity clearly had in mind.

C. Production of polymer fibres having nanoscale morphologies

United States Patent 6,790,528

September 14, 2004

Wendorff, et al.

This patent describes a porous polymer-based fiber and a method of creating it. These fibers have a wide range of applications, ranging from fabric yarns to insulating materials. Biological applications include scaffolding material in tissue engineering, and for blood vessel and bone implantology. Integration into biological systems often requires highly porous fibers. These are essential for promoting vascularization, and allowing free nutrient and waste fluid flow. This patent claims:

1. Porous fiber comprising a polymeric material, said fiber having a diameter of 20 to 4000 nm and pores in the form of channels extending at least to the core of said fiber and/or through said fiber.

This is simply a description of the physical properties of the polymer fiber. Most of the dependent claims all describe variations in the properties and production of this fiber. This patent is also very broad, as it includes any porous polymer fibers with very small dimensions. The first 11 claims all focus on the fiber, and various methods of fabrication. Later dependent claims mention biological applications of the fiber.

II. Patenting non-biological applications of biotechnology

Many recent technological breakthroughs involve the use of biology to achieve results beyond the capabilities of current synthetic technology. At the nanoscale, the lines separating biological particles/organisms and artificial devices are blurry at best. Consequently, it is becoming commonplace to describe biological components as simply nanoscale devices with specific functionality. This approach has the advantage of keeping the invention as far as possible from controversy involved with patenting biology. It also ensures maximum flexibility for applying the patented technology.

However, as technologies become increasingly biomimetic, care must be taken to ensure that the invention is enforceably "novel" and "non-obvious" despite having natural origins. The following three case studies shed light on patenting strategies used to capture intellectual property space for non-biological applications of biotechnology.

D. Method and apparatus for recovery of metals with hydrocarbon-utilizing bacteria

United States Patent *6,875,356*
April 5, 2005
Perriello

This patent describes the use of microorganisms for "recovering metals from metal-containing support materials such as mineral ores." Specific bacteria and conditions are used to extract certain substances from materials. What is claimed is:

> *1. A method of recovering a metal from a metal-containing support material, the method comprising:*
>
> *contacting the support material with butane to stimulate growth of butane-utilizing bacteria in the support material, wherein the butane is provided as a butane substrate comprising at least about 10 weight percent butane; and*

recovering the metal from the support material.

Such use of microorganisms is known as bioremediation. Techniques like these harness the organisms' unique abilities to process chemicals and materials (e.g., biooxidation). This patent specifically mentions "bacteria"; however, it is possible that another biological or artificial device with similar functionality could be used instead. The "butane-utilizing bacteria" can actually be any active device that can precipitate metal from ore through a number of electrochemical steps under a set of processing conditions. Organisms have long been applied to perform work for humans; for example, cats, the classic "mouse-capturing device", and horses, which are effective "engines fueled by carbohydrates." Despite the advantages of having a more general description, the inventor or author chose to limit the scope of the patent to the use of actual bacteria, possibly to increase the strength and relevance of the claims.

E. Scaffold-organized clusters and electronic made using such clusters

United States Patent *6,872,971*
March 29, 2005
Hutchinson, et al.

This invention "concerns a method for forming organized arrays of metal, alloy, semiconductor and/or magnetic clusters for use in the manufacture of electronic devices." The independent claim is as follows:

1. An electronic device that operates at or about room temperature based on the Coulomb blockade effect, comprising:

a first cluster comprising a metal cluster core having a radius of between about 0.4 nm and about 1.8 nm; and

a second such cluster physically spaced apart from the first metal cluster at a distance of less than about 5 nm, where the physical separation between the first and second clusters is maintained by the clusters being coupled to a biomolecular scaffold.

More specifically, this patent protects a method of using engineered DNA scaffolds to arrange electronic materials. The patent description does not limit the "scaffold" to just DNA, but to "any molecules, including polymers, that can be placed on a substrate in predetermined patterns...and to which clusters can be bonded to provide organized cluster arrays." Here we are treating biological devices as general devices with specific functionality.

Describing DNA as a functional molecule has the advantage of distancing this patent from genetic code patents, even though the specific sequence of the DNA scaffold would affect the structure of the assembled electronic device. It must be noted that this method of assembling devices based on scaffold sequence is alarmingly similar to the natural process of arranging amino acids to form proteins based on RNA sequences. Instead of coding for proteins (nanoscale amino acid "clusters"), the DNA in this invention codes for nanoscale electronic devices consisting of metallic clusters.

F. Biological Control of Nanoparticles

Pub. No.: US 2003/0113714 A1

Pub. Date: Jun. 19, 2003

Belcher et al.

This patent application includes "compositions and methods for selective binding of amino acid oligomers to semiconductor and elemental carbon-containing materials", which includes utilizing genetically engineered viruses to induce the self-assembly of semiconductor materials and nanostructures such as nanowires and quantum dots.

However, to remain as broad as possible, the patent is directed "towards surface recognition of semiconductor materials and elemental carbon-containing materials using organic polymers." Hence, they are describing a virus as simply an "organic polymer"; and the fact that viruses contain genetic information is irrelevant. Interestingly, the primary independent claim is as follows:

> *1. A method for directed semiconductor formation comprising the steps of:*
>
> > *contacting a polymeric organic material that binds a predetermined face specificity semiconductor material with a first ion to create a semiconductor material precursor; and*
> >
> > *adding a second ion to the semiconductor material precursor, wherein the polymeric organic material directs formation of the predetermined face specificity semiconductor material.*

This method is essentially the process of biomineralization—the process reef coral use to grow their rigid skeleton with seawater minerals—but involving semiconductor material precursors instead of naturally-present minerals.

Another independent claim is as follows:

> *52. A biologic scaffold comprising:*

a substrate capable of binding one or more biologic materials;

one or more biologic materials attached to the substrate; and

one or more elemental carbon-containing molecules attached to one or more biologic materials.

The very ambitious claim appears to include most (or all) life forms. Here we observe the puzzling issue of bio-mimetic technology: Albeit innovative and technically groundbreaking, the "invention" simply reproduces or slightly alters natural processes. Consequently, it may be debatable how "novel" and "non-obvious" these aspects really are.

III. Patenting biology

To which extent plants and microorganisms can be patented, is a recurring question. We examine the following three cases in an attempt to observe where the line is drawn.

G. Spider Silk Protein Encoding Nucleic Acids, Polypeptides, Antibodies and Methods of Use?

United States Patent 5,728,810
March 17, 1998
Lewis, et al.

Spider silk exhibits tensile strength comparable to that of high-grade steel while having elastic properties that allow it to be stretched up to 40% of its length without breaking [4]. This patent describes a protein that is responsible for the observed properties of spider silk. The claims refer to specific sequences and combinations of polypeptides that comprise of a specific sequence that makes up the spider protein:

1. A purified recombinant spider silk protein, having a molecular weight of at least 16,000 daltons, comprising a polypeptide selected from the group consisting of:

a polypeptide having the amino acid sequence of SEQ. ID. NO.:2;

a polypeptide comprising tandem repeats of the amino acid sequence of SEQ. ID. NO.:8 linked by a peptide bond to the amino terminus of the amino acid sequence of SEQ. ID. NO.:12 in turn linked by a peptide bond to the amino acid sequence of SEQ. ID. NO.:9;

The nature of the claims indicates that specific genetic sequences and the methods for creating and processing certain sequences are patentable.

H. Mandelvilla plant with double flower

United States Patent 6,300,547
October 9, 2001
Green, et al.

The focus of this patent is the plant, Rita Marie Green. Specific claims are as follows:

1. A plant of a Mandevilla variety "Rita Marie Green" having at least one double flower.

2. The plant of claim 1 wherein said flowers have outer five parted corolla limbs and inner five parted petaloids, said petaloids overlaying the corolla limbs.

3. The plant of claim 1 wherein said flowers have outer five parted corolla limbs and inner five parted petaloids, said petaloids being shorter than the corolla and remaining in a cluster within outer corolla, forming a tight cluster habit of petaloids generally prohibiting a view of the inner throat.

9. A method of producing a double-flowering Mandevilla plant comprising propagating a double-flowering Mandevilla plant of the Rita Marie Green variety to produce a plurality of plants and selecting at least one double-flowering Mandevilla plant from said plurality of plants.

Plants falling under any of the above categories were deemed as Rita Marie Greens. The patent claimed ownership of the Rita Marie Green and implied that all the progeny produced through the Rita Marie Green would also fall under ownership of the patent. It appears that, from this patent, plant reproduction processes and combinations of plan parts are viable patents. A recent decision by the Supreme Court allows utility patents to cover plant technology [5].

I. Transgenic mice depleted in mature T-cells and methods for making transgenic mice

United States Patent 5,175,384
December 29, 1992
Krimpenfort, et al.

Specific claims of this transgenic mouse patent describe:

1. A transgenic mouse having a phenotype characterized by the substantial absence of mature T-cells otherwise naturally occurring in said mouse, said phenotype being conferred by a transgene contained in the somatic and germ cells of said mouse, said transgene comprising the .DELTA.V-TCR.beta. DNA fragment which encodes a T-cell antigen receptor polypeptide variant, and said polypeptide variant being incapable of mediating T-cell maturation in said transgenic mouse.

2. A method for producing a transgenic mouse having a phenotype characterized by the substantial absence of mature T-cells otherwise naturally occurring in said mouse, said method comprising:

(a) introducing a transgene into a zygote of a mouse, said transgene comprising the .DELTA.V-TCR.beta. DNA fragment which encodes a T-cell antigen receptor polypeptide variant, said polypeptide variant being incapable of mediating T-cell maturation in said transgenic mouse,

(b) transplanting said zygote into a pseudopregnant mouse.

(c) allowing said zygote to develop to term, and

(d) identifying at least one transgenic offspring containing said transgene.

This patent indicates that breeding methods and specific genetic sequences of a mouse are patentable. The claims for this patent extend beyond these two areas to cover mouse development and the actual mouse itself.

It appears from these three case studies that, not only are specific sequences patentable, but the method for creating and reproducing entire organisms such as a mouse is patentable as well. The first patent indicates that processes and sequences comprising an organism can be patented. The second patent pushes the line of what aspects of biology are patentable to include components, reproduction processes, and individual parts comprising the organism. The third patent indicates that an entire organism, even one as complex as a mouse, can be patented.

Conclusion

Even though biotechnology patents have already generated much controversy, we expect nanobiotechnology to intensify the debates further. Issues we foresee include:

- **Patents too broad in scope.** Many current nanobiotechnology patents appear focused at first glance because they describe biotechnology applications. However, the patents also encompass future, non-biological applications that are not currently achievable by “those skilled in the art.” These broad patents may become deterrents to innovation.

- **Patentability of biomimetics questionable.** Some of today’s most groundbreaking technologies mimic products and processes of nature. Should man-made products and processes very similar to those of nature be patentable? For example, if scientists create synthetic spider silk, should they be able to patent natural spider silk compositions and properties?

- **Definition of “bio-“ unclear.** At molecular lengthscales, “biological” and “synthetic” products and processes operate on similar (often the exact same) principles. That is, synthetic nanomaterials could be regarded as quasi-biological and vice versa. The legal definition of “bio-“ needs to be carefully defined to outline the subtle yet significant differences (if any) between the biological and the synthetic.

References

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