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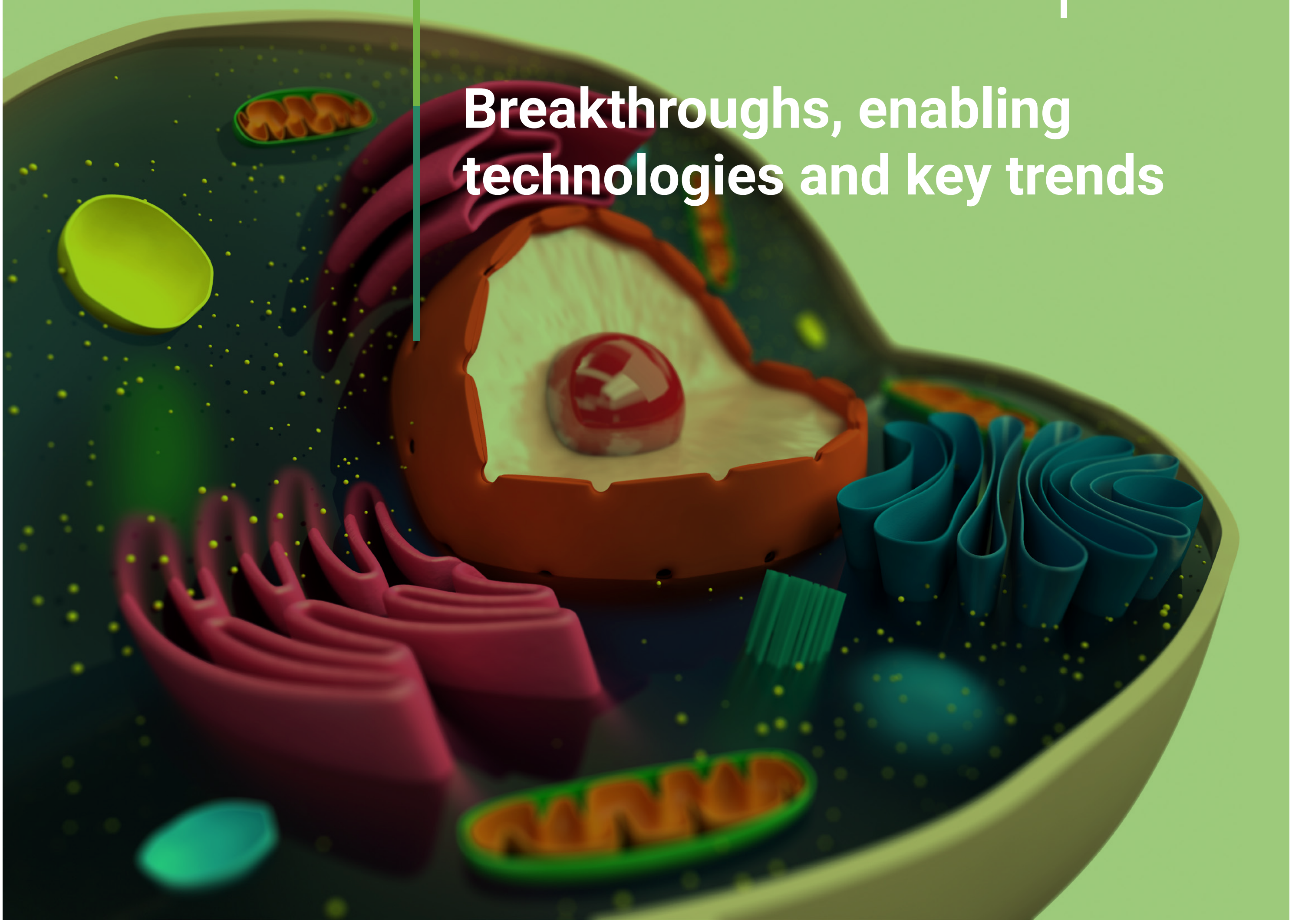
Synthetic biology innovation report

Breakthroughs, enabling technologies and key trends



Content

Overview of major trends

Based on a panoramic exploration of the synthetic biology patent landscape, here are just some of the broad-stroke trends you'll find discussed in this report:

- Many of the institutions leading innovation in this field continue to be academic institutions, with the University of California leading the pack. This has fostered a partnership-friendly vocation—due to the inevitability of technology transfer—where there are many opportunities for joint ventures and licensing deals.
- Microfluidics is a booming area—commercially, and in terms of intellectual property and R&D. This presents opportunities for synthetic biology innovators to commercialise their inventions in adjacent markets, and for innovators in adjacent markets to catalyse progress in synthetic biology with their inventions.
- As synthetic biology grows in significance—commercially and intellectual property-wise—so does the number of patent litigation threats. Aside from well publicised cases, like the CRISPR-Cas9 battle, there are many more legal showdowns taking place below the surface.
- There are several new companies trying to revolutionise healthcare, with technologies on the threshold of reality and fantasy—such as Emulate, which is recreating conditions in the human body on a microscopic scale.
- China's environmental and agricultural challenges have driven the country to become a world leader in synthetic biology—seemingly outmatched only by the United States—and this is reflected in patent trends. This poses threats and opportunities for synthetic biology innovators worldwide.

I hope the analyses here will help you capitalise on all these trends and more.

Introduction

I was recently speaking with Dr Ali Hussein, a biochemistry PhD and PatSnap product director, when he described synthetic biology using a manufacturing-based extended metaphor, which I found quite apt.

There's the physical space or factory in which processes occur (the cell); there's the production line which processes the materials introduced to the factory (cell signalling and pathways); there are the materials of input to the production line (feedstock and energy source) and the materials of output by it (pathway products); and there's the machinery used to engineer this series of activities (enabling tech, e.g. microfluidics and bioreactors).

While I'm aware the definition of *"synthetic biology"* is in flux—spanning everything from genetic engineering to synthetic chemistry—I think this conceit encapsulates meaningfully the fundamentals of the field. Crucially, it provides a good conceptual framework for analysis of trends in patents relating to synthetic biology.

This metaphor tells us synthetic biology involves:

1. Biological objects
2. Cellular infrastructure guiding the behaviours of these biological objects
3. Stimulation of these biological objects
4. Responses by these biological objects
5. Instruments for the manipulation of these biological objects and their environments (internal and external)

This analysis of patent data relating to synthetic biology will give an overview of innovation trends in the field as a whole, but also within components outlined above.

If you're new to the world of patent data, you might wonder why we'd even go digging in patents to better understand and develop the field of synbio. I'll respond by telling you the story of Chris and Chris.

Christopher L. Benson and Christopher L. Magee were scientists at the Massachusetts Institute of Technology's (MIT's) department of engineering, and they often dealt with patent data. Around 2014, they decided to analyse the accuracy of patent data as a signal for technological progress. In short, is patent data any good at telling us whether a technology area is maturating—and which of its components are driving this maturation? Using the cold, unforgiving yardstick of statistics, they concluded in a *peer-reviewed paper*:

> *"The results in this paper establish that information contained in patents in a technological domain is strongly correlated with the rate of technological progress in that domain. The importance of patents in a domain, the recency of patents in a domain and the immediacy of patents in a domain are all strongly correlated with increases in the rate of performance improvement in the domain of interest."*

The correlation coefficient for this analysis was 0.76 and the predictive power remains good for more than 10 years into the future. The authors also explain the attractiveness of patent data as a tool for analysing technology trends:

> *Patents are an attractive choice for analysing technological change because they are: generalizable, objective, quantitative and qualitative. Patents include many technical fields over a long period of time, and thus allow for easier generalization of the research.*

I made a similar case for patent data in this *article about improving the stage gate process*. While the analyses here are not identical to those within the cited paper, that study is still relevant as an exemplification of the ability of patent data—when it is wielded skilfully—to forecast and demystify R&D trends.

So, let's dive into how I discovered that if you're innovating in synthetic biology, you don't want to piss off Whirlpool Corporation, you do want to befriend Agilent Technologies and you should keep an eye on *microfluidics—the macro trend to watch (with the market expected to reach a value of $13.9bn by 2025)*. Could there even be hope for the much-maligned proprietors of Theranos lurking in these pages?

The synthetic biology patent landscape reveals the prominence microfluidics-focussed innovation

Report methodology

All data presented were accurate as of 26 April 2018 but new patents are filed every day.

I analysed synthetic biology-related patent data using the PatSnap IP intelligence platform and a set of modified search queries taken from a 2013 research paper, *"The development of synthetic biology: a patent analysis"*.

Although this paper is old and contains limited analyses (due to the limitations of IP intelligence tools back in 2013), its authors—Doren, Koenigstein and Reiss—did an excellent job of breaking synbio into its constituents, and building a tailored search query for each. They separated (conceptually) the field into 3 main parts:

1. **Knowledge generation and engineering**—*"terms for the objects of biotechnology were combined with terms that indicate the realization of the guiding principles relevant in the synthetic biology research area"*
2. **Enabling technologies of synthetic biology**—terms for *"enabling technologies, that are believed to be crucial for the maturing of synthetic biology or for the realisation of the guiding principles"*
3. **Applications of synthetic biology**—terms *"that indicate potential applications of synthetic biology"*

This allowed me to run analyses on each facet of synthetic biology defined above, and on all 3 combined—meaning this is a 4-part report:

1. Synthetic biology overview
2. Knowledge generation in synthetic biology
3. Enabling technologies in synthetic biology
4. Applications of synthetic biology

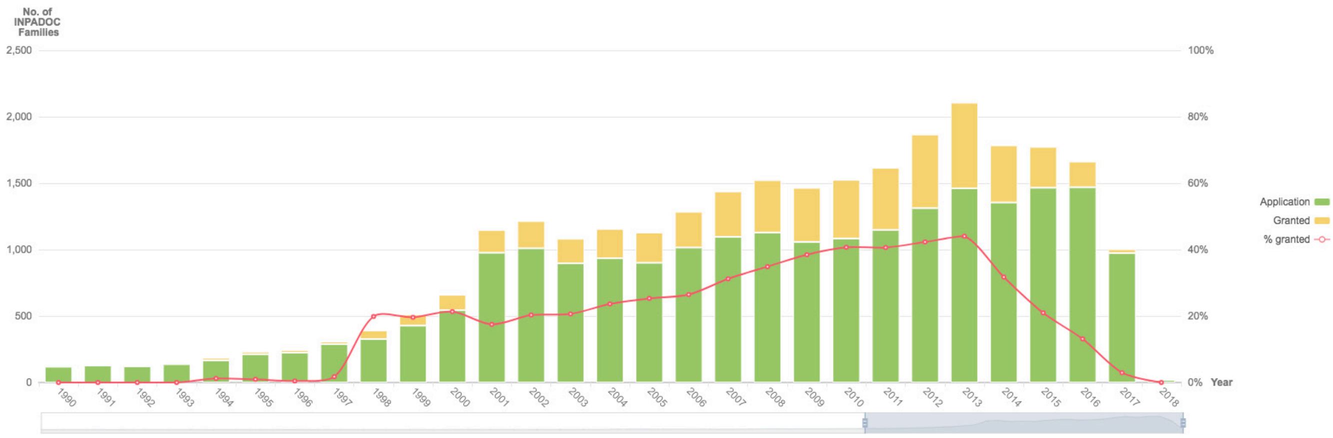
They only change I made to the original query was to search for the specified keywords only in the *title, abstracts and claims (TAC)* of patent documents—where possible—not the entirety of the documents. This is because the occurrence of a keyword in the TAC of a patent suggests it's more integral to the invention being declared (as these are the parts of a patent document where inventive elements are identified). This approach increases the relevance but reduces the volume of patent documents retrieved for analysis.

You can view, reuse and modify the Boolean search queries used here in the last section of this report.

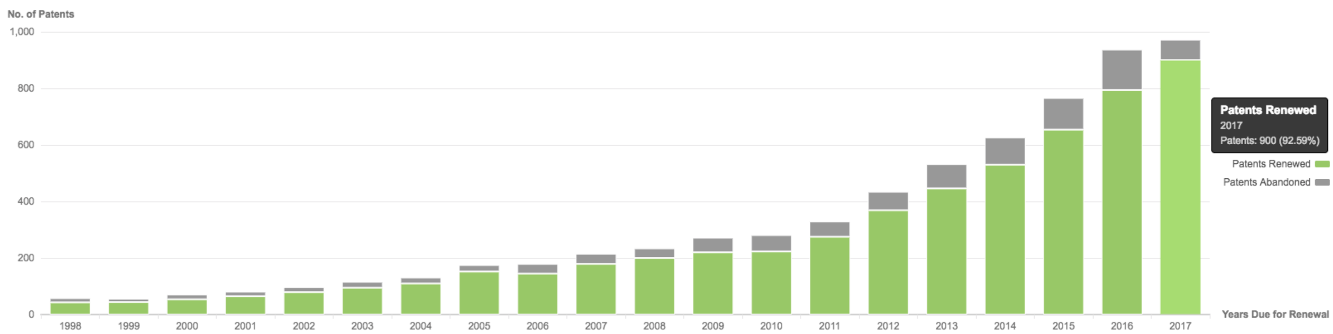
Part I: Synthetic biology overview

My combined search on the entire synbio landscape yielded 24,070 total INPADOC patent family representatives (72,999 total patent docs). Of these, 6226 belong to an academy, 13,648 belong to a company, 5309 belong to a person and 548 belong to a government.

The rate of innovation (as signalled by patent filings) appears to be growing, but not at the blistering pace we might observe in other fields, such as blockchain or drones. It does take up to 18 months before patent filings are publicly disclosed, so the data we're looking at is complete only up till 2016. We may yet see the 2016 and 2017 filing numbers grow.

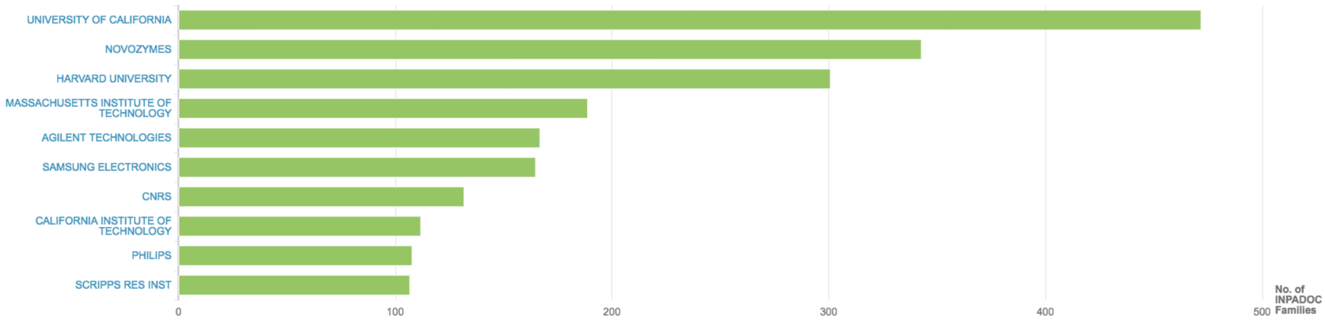


Patent renewal rates are high and rising though, peaking at 93% in 2017. This suggests those who own patents are increasingly optimistic about the technological and commercial value protected by them.



Of these patent owners, the top companies—based on size of patent portfolio—are:

1. University of California (472 patents)
2. Novozymes (343 patents)
3. Harvard University (301 patents)
4. Massachusetts Institute of Technology (189 patents)
5. Agilent Technologies (167 patents)
6. Samsung Electronics (165 patents)
7. Centre National de la Recherche Scientifique aka The French National Centre for Scientific Research (132 patents)
8. California Institute of Technology (112 patents)
9. Philips (108 patents)
10. Scripps Research Institute (107 patents)



There must be something in the water in California… and it probably got in there thanks to a microfluidic device. If we zoom into the synbio patents owned by the University of California, we see they mostly fall under the following International Patent Classifications (IPCs):

- **C12Q1/68**. Involving nucleic acids (99 patents)
- **B01L3/00** Containers or dishes for laboratory use (74 patents)
- **C12N5/10**. Cells modified by introduction of foreign genetic material, e.g. virus-transformed cells (42 patents)

IPCs are a good proxy for understanding the technological areas into which patented inventions fall.

The most dominant terms within the University of California's patents are *"nucleic acid"*, *"microfluidic device"*, *"plant"*, *"synthetic"*, *"DNA"*. And some of the most recurring phrases are *"microorganism engineered to produce"*, *"potential for controlled microfluidic pumping"* and *"squamous cell carcinoma"*.

Some of the patents relating to *"microorganism engineered to produce"* include:

- ***US9540652 Metabolic engineering of the shikimate pathway*** **(valued at $120,000)**
- ***CA2702361A1 Microorganism engineered to produce Isopropanol***
- ***WO2011011568A3 Methods and Compositions for the Production of Fatty Acids in Photosynthetic Prokaryotic Microorganisms***

These trends suggest that rather than adopting a narrow focus, the University of California has broad interests in synthetic biology—from the discovery of new knowledge to the invention of enabling devices. This is not surprising, considering this institution gave us *"synthetic biology's greatest success story so far..."*—to borrow the words of Cosmos Magazine. This is in reference to the discovery of a way to synthesise artemisinin—an anti-malarial lactone—from yeast cells, by turning up the controls on the yeast genes that make FPP (a precursor molecule) and turning down the genes that convert FPP into ergosterol. Jay Keasling, who is also named as an inventor in the patent *"Metabolic Engineering Of The Shikimate Pathway"* (linked above), was a key figure in the synthesis of artemisinin.

Of course, the University of California also gave us some of the inventors of CRISPR—leaving aside the *legal battles with MIT and the Broad Institute of Harvard*. These UC inventors have (incidentally) just been *granted another patent for CRISPR-Cas9 applications*—a patent which has been described as having *"very broad claims"*.

Trends in the University of California's patent portfolio are somewhat reflective of those in the entire industry. The top IPCs at that level are:

- **C12N15** Mutation or genetic engineering; DNA or RNA concerning genetic engineering, vectors; Use of hosts therefor (mutants or genetically engineered micro-organisms); use of medicinal preparations containing genetic material which is inserted into cells of the living body to treat genetic diseases, gene therapy
- **C12Q1** Measuring or testing processes involving enzymes or micro-organisms
- **B01L3** Containers or dishes for laboratory use; apparatus for enzymology or microbiology C12M 1/00); Droppers (receptacles for volumetric purposes G01F)
- **C12N5** Undifferentiated human, animal or plant cells; Culture media therefor

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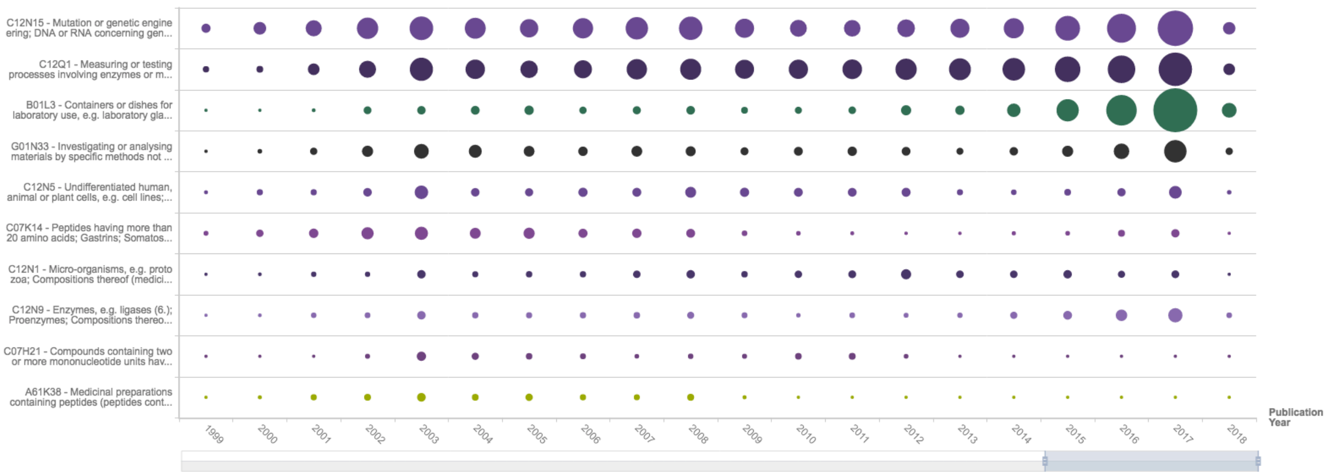
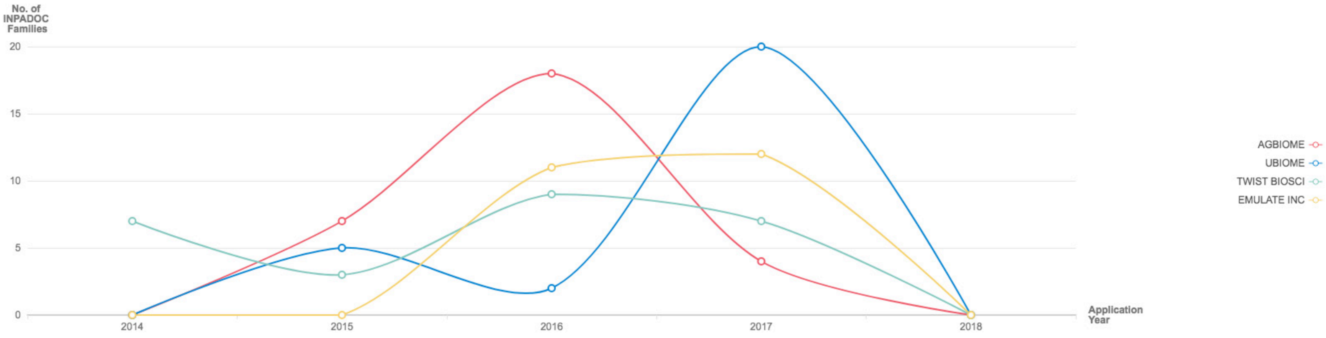


Both IPCs C12Q1 and C12N5 remain in the top 4 list, even when all companies are analysed. And, along with B01L3, these 2 are currently experiencing the greatest acceleration in patent filings. Although outside the remit of this report, it would be worth analysing trends in only the patent filings falling into these IPCs. This can help you discover the areas of science where these booms of innovation are taking place.

What about the companies still at such an embryonic stage, few have noticed the formation of their primitive streaks? The list of companies who've only recently started filing patents relating to synthetic biology includes:

1. *AgBiome* (founded 2012)
2. *uBiome* (founded 2012)
3. *Twist Bioscience* (founded 2013)
4. *Emulate, Inc.* (founded 2014)



AgBiome seems to be focussed on using new knowledge of the plant-associated microbiome, to create novel pest control products.

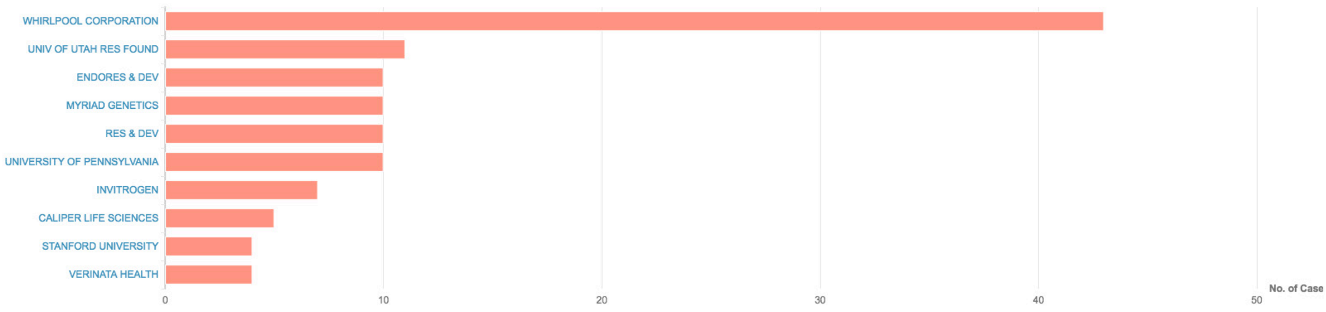
uBiome is using AI to analyse a person's microbiome, so they can better understand and improve specific aspects of their wellbeing (such as gut or vaginal health).

Twist BioScience says it "makes high-quality gene synthesis, oligo pools, exome, NGS target enrichment, variant libraries and other synthetic DNA tools" for genome editing, drug discovery, DNA data storage and more.

Emulate recreates for cells artificial environments akin to those in which they would exist within the body. This helps researchers more accurately predict how a human may respond to diseases, medicines, chemicals and foods—sans actual human testing. This promises to revolutionise bioscience beyond current limitations of cell culture and animal-based testing.

As these new explorers innovate across the synthetic biology landscape, they would be wise to avoid litigation threats—of which there are already many. A list of the most litigious companies in this space includes:

1. Whirlpool Corporation
2. University of Utah
3. Myriad Genetics
4. University of Pennsylvania
5. Invitrogen



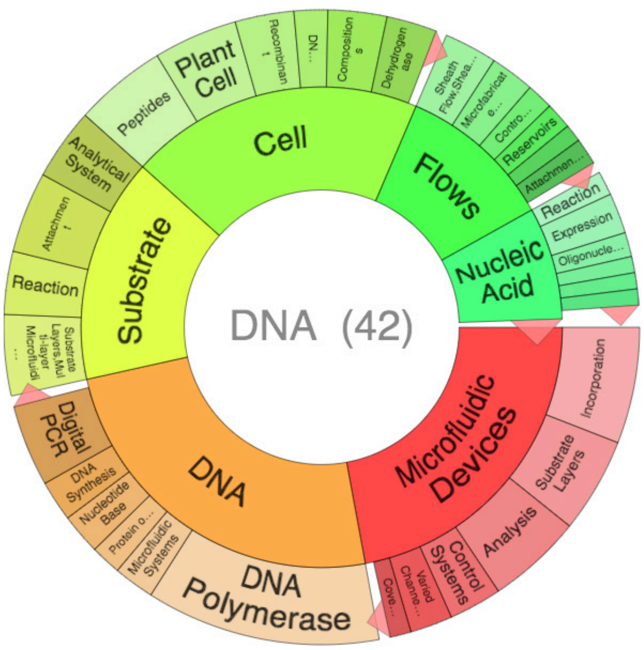
One glance at the litigious companies chart reveals Whirlpool, with 44 court cases, is by far the most active company on the list. All the cases seem to involve one patent (which actually originated from PUR Water Purification Products), *"US7000894 Fluidic cartridges and end pieces thereof"* (valued at $2,380,000).

Whirlpool's focus is currently on filters within appliances, but its patent appears to have some overlap with the field of microfluidics. Due to the relative broadness in applications of microfluidics, it's worth looking at the entirety of litigation threats in that field—not just the areas where it overlaps with synthetic biology.

When I limit my analysis to active patents, the list of most litigious companies includes Perkin Elmer, Caliper Life Sciences, 10X Genomics and Verinata Health.

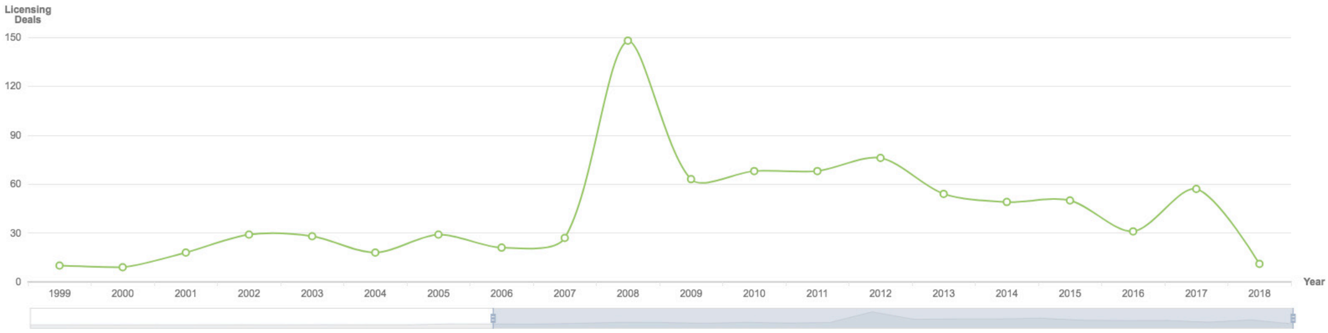
The most litigated concepts—i.e. the concepts most commonly discussed in patents involved in court cases—include:

- DNA (digital PCR, DNA synthesis, nucleotide base and protein or polypeptide)
- Microfluidic devices (incorporation, substrate layers, analysis, control systems, varied channel depths, cover layer and body structure)
- Cell (peptides, plant cells, recombinant cells, DNA sequencing, dehydrogenase)



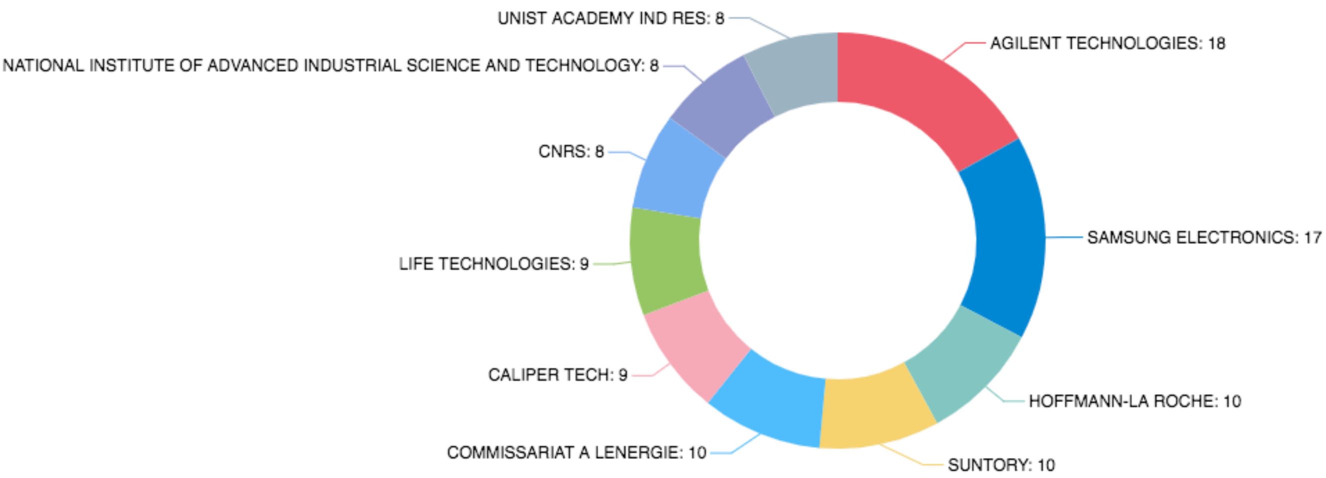
If we zoom into cases focussed on DNA, we see Invitrogen's footprint of 9 litigation occurrences—including against Harvard University, General Electric and Clonetech Laboratories.

Less cynical readers might be more interested in potential partners than looming litigants. Licensing and transfer trends show there's a healthy pattern of collaboration in synthetic biology.



The most active collaborators (in terms of sharing or selling patents) are:

1. Agilent Technologies (focussed on microfluidics)
2. Samsung (focussed on microfluidics)
3. Hoffman-La Roche (focussed on recombinant DNA and genetic engineering)
4. Suntory
5. Commissariat A Lenergie
6. Caliper Tech
7. Life Technologies
8. Centre National de la Recherche Scientifique aka The French National Centre for Scientific Research
9. National Institute of Advanced Industrial Science and Technology
10. Ulsan Institute of Science and Technology (울산과학기술원산학협력단)

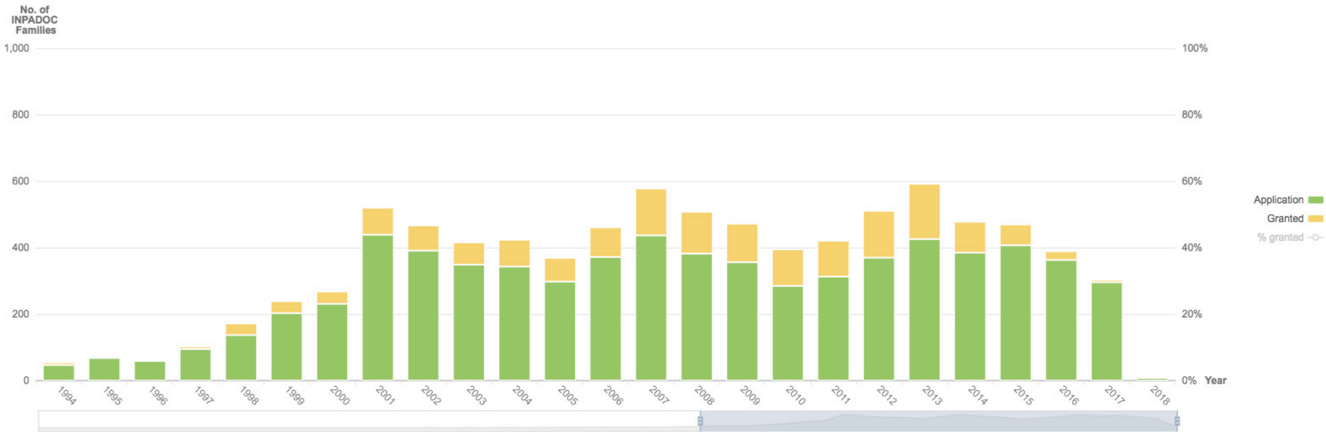


With a general idea of the patent data trends in synthetic biology established, we can delve into specifics.

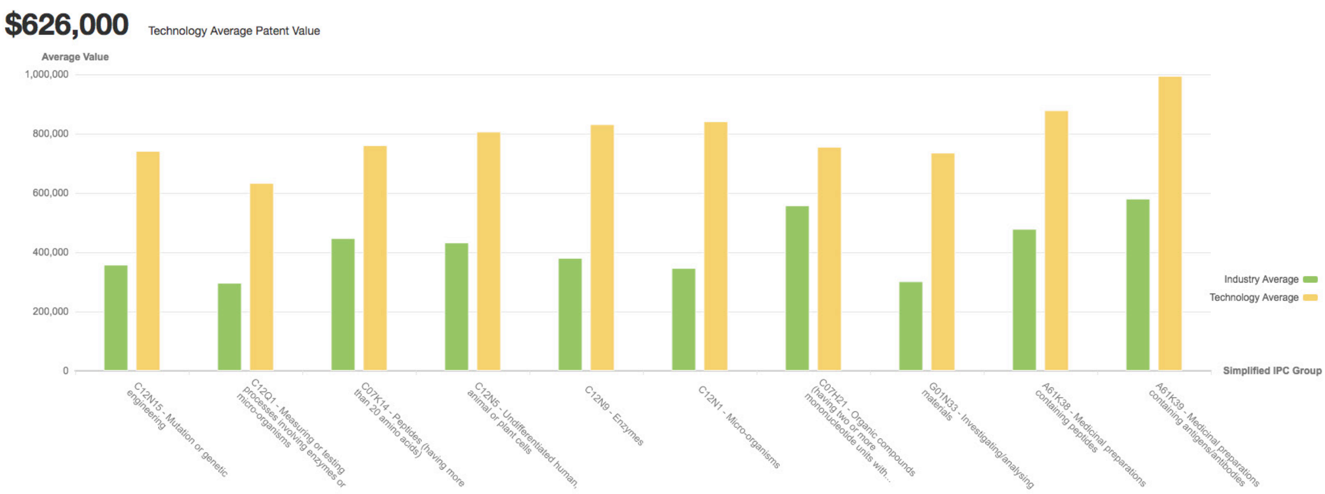
Part II: Knowledge generation in synthetic biology

My search on knowledge generation in synthetic biology yielded 7,234 total INPADOC patent family representatives. Of these, 2051 belong to an academy, 4256 belong to a company, 1536 belong to a person and 196 belong to a government.

The rate of patent filings in this area has remained relatively flat, since an unsustained inflection point around the year 2000.

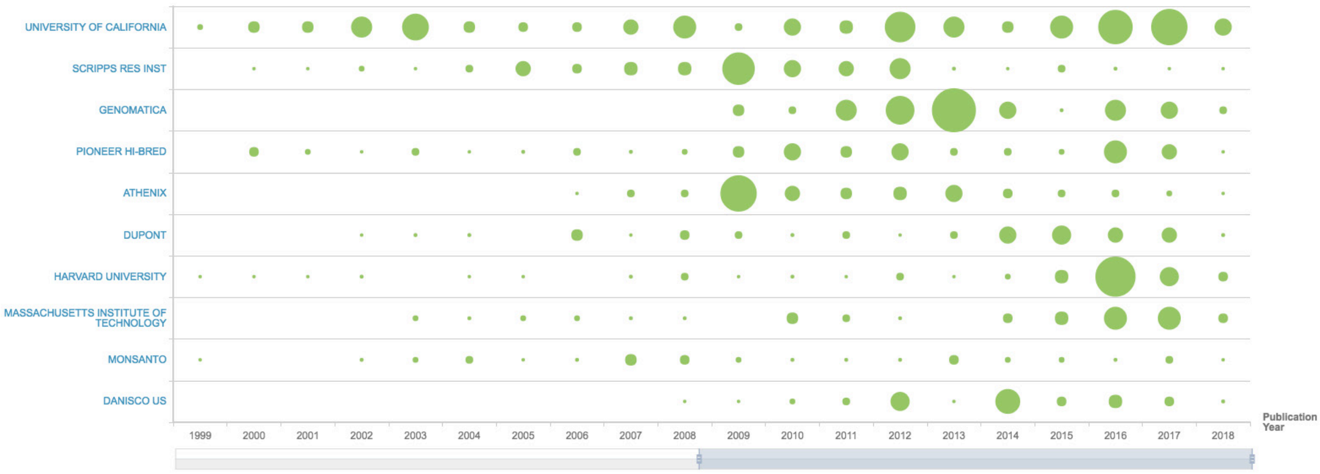


This may be because, as illustrated by the CRISPR legal tug of war, patenting the discovery of new knowledge is tricky. However, patents focussed on knowledge generation in synthetic biology have higher valuations—on average—than patents within the same IPCs which focus on other technologies. This suggests patent protection of new knowledge is—on average—a rewarding strategy.



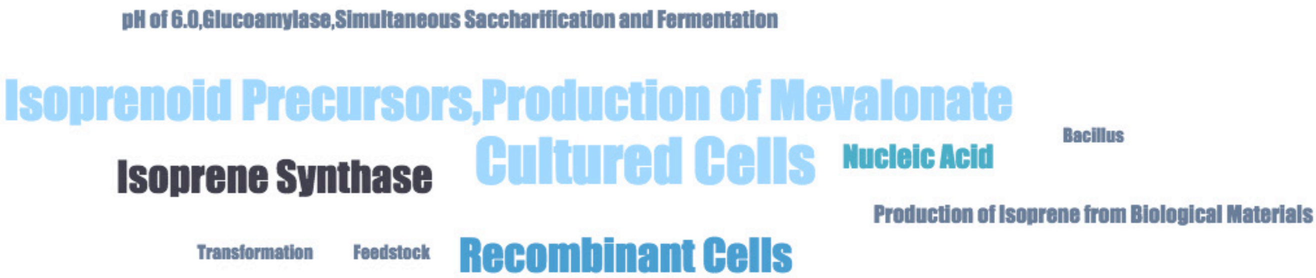
The most patent-intensive organisations in this sub-category are:

1. University of California
2. Scripps Research Institute
3. Genomatica
4. Pioneer Hi-Bred (now DuPont Pioneer)
5. Athenix
6. DuPont
7. Harvard University
8. Massachusetts Institute of Technology
9. Monsanto
10. Danisco US



Danisco, which apparently only began patenting in this area in 2008, has (on the whole) been accelerating its innovation rate. Other companies ramping up patent filings in this area include Harvard, MIT and DuPont. Much of Danisco's innovation appears to be concentrated in the following areas:

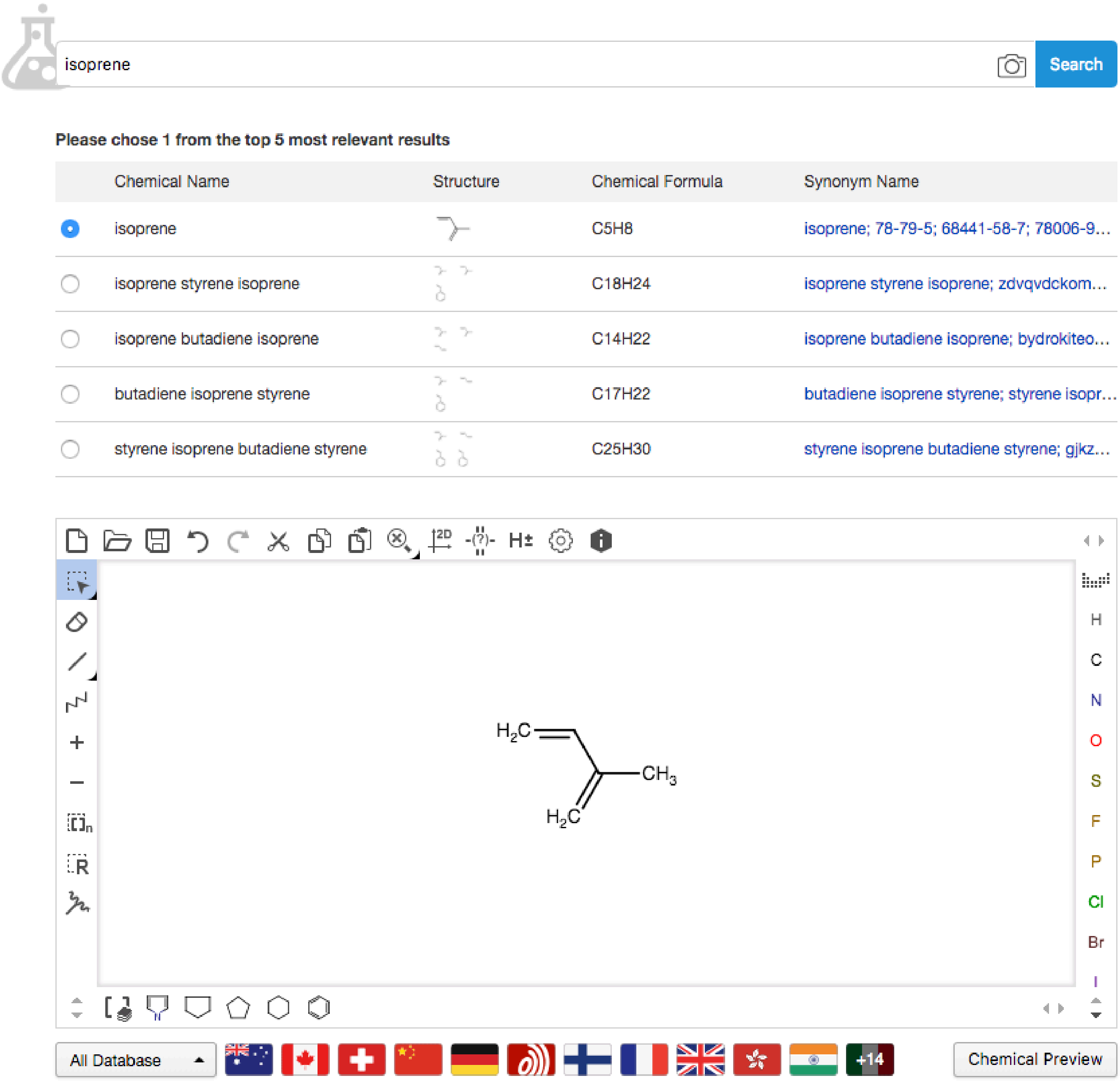
- *"Isoprenoid precursors, production of mevalonate"*
- *"Isoprene synthase"*
- *"Cultured cells"*
- *"Recombinant cells"*
- *"Production of isoprene from biological materials"*



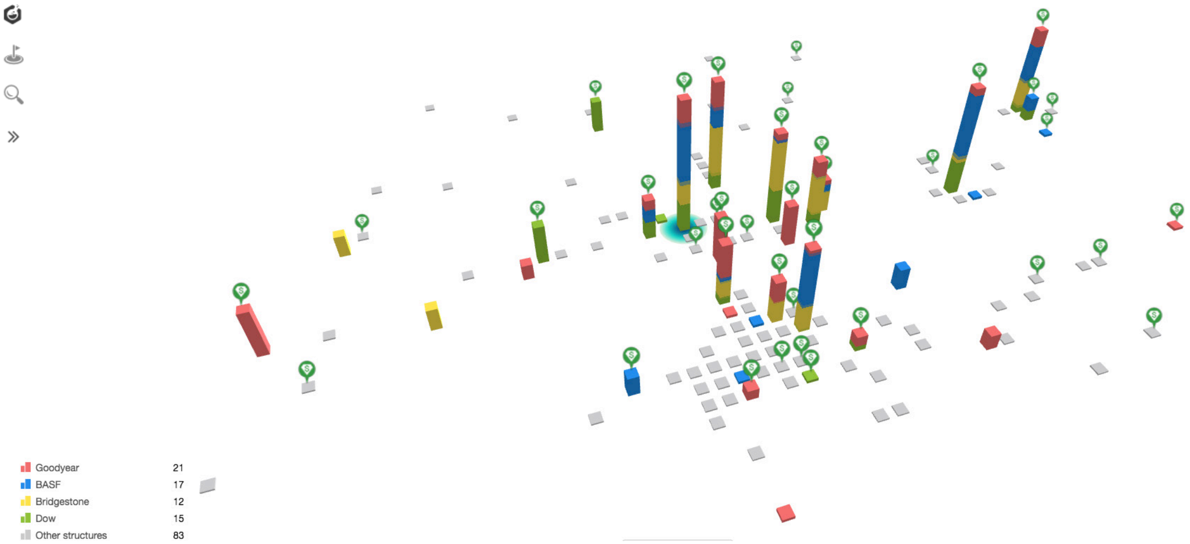
The recurrence of isoprene suggests Danisco, a food company, has some interest in rubber. In fact, its second most highly valued patent in the area of synthetic biology is *"US20160281113A1 Compositions and Methods for Producing Isoprene"* (valued at $2,550,000)—the rubber tire company, Goodyear, is a co-assignee.

All this adds up since *Danisco announced in late 2008 that it would be collaborating with Goodyear* to develop a bio-based alternative ("*bioisoprene*") for the typically Earth-unfriendly compound, isoprene. The recency of the 2016 patent linked above suggests some organisations with a similar innovation focus to Danisco's, could find adjacent market opportunities by looking into trends within the Danish company's overall portfolio. *Companies like Michelin (focussed on bio-butadiene), Pirelli (focussed on Guayule) and Cooper Tire (focussed on guayule-based biopolymers)* are already blazing trails down the same bio-based route taken by Goodyear.

In fact, when I ran a *"similar structures"* search on isoprene, I discovered this is a compound around which there's much innovation—with a dramatically accelerating rate of patent filings and 396 associated chemicals.



A Chemscape (chemical patent landscape) analysis of my isoprene search also reveals there are many areas of highly valued inventive activity. I've identified on the Chemscape some of the main players in this area—Goodyear (red), BASF (blue), Bridgestone (yellow) and Dow (green). The greenish-blue halo at the bottom of the pillar in the centre of the Chemscape, represents our target chemical (isoprene). High-valuation areas are marked with dollar signs.



The list of organisations newly entering this area of innovation includes:

1. Agbiome (covered in Part I)
2. DNA Script (founded 2014)
3. MeiraGTx (founded 2015)

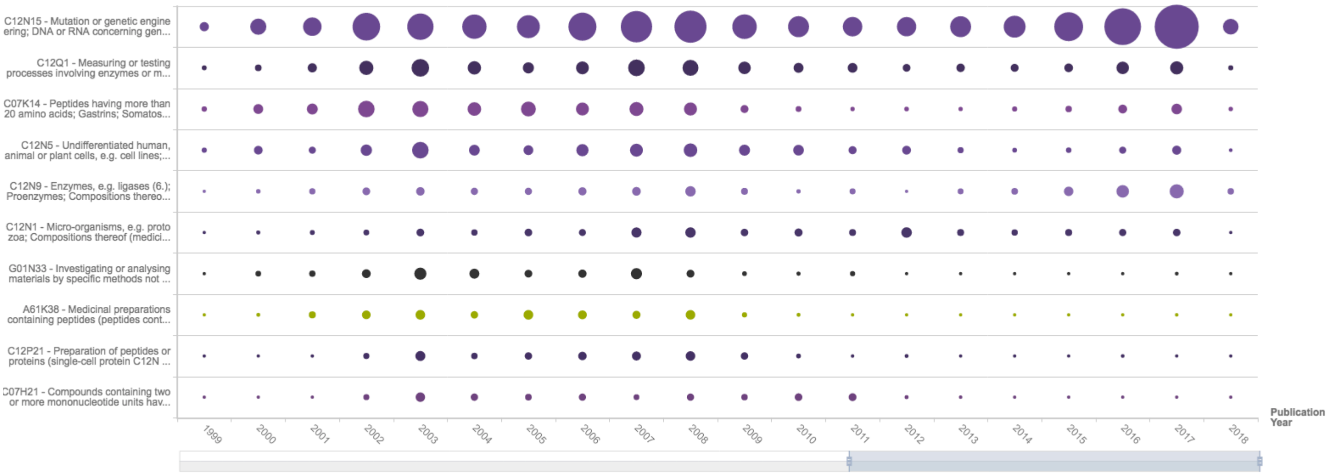
DNA Script says its *"technology overcomes the current inefficiencies of synthetic DNA production, and enable[s] affordable, rapid, high-quality and high throughput production of synthetic biology tools, such as oligonucleotides, genes, pathways and genomes."* The company recently *raised €11m in a Series A funding round* led by Illumina Ventures and Merck Ventures.

MeiraGTx says it's *"developing novel gene therapies for acquired and inherited disorders." The company recently announced a "gene therapy manufacturing collaboration with Oxford Genetics."*

Considering the patent portfolios of these companies are closely tied to their core products and services, it's surprising that they're also somewhat reflective of the macro trends.

Of the top IPCs into which patents in this sub-category fall, these are the fastest growing:

- **C12N15** Mutation or genetic engineering
- **C12N9** Enzymes
- **C07K14** Peptides (having more than 20 amino acids)
- **C12Q1** Measuring or testing processes involving enzymes or micro-organisms

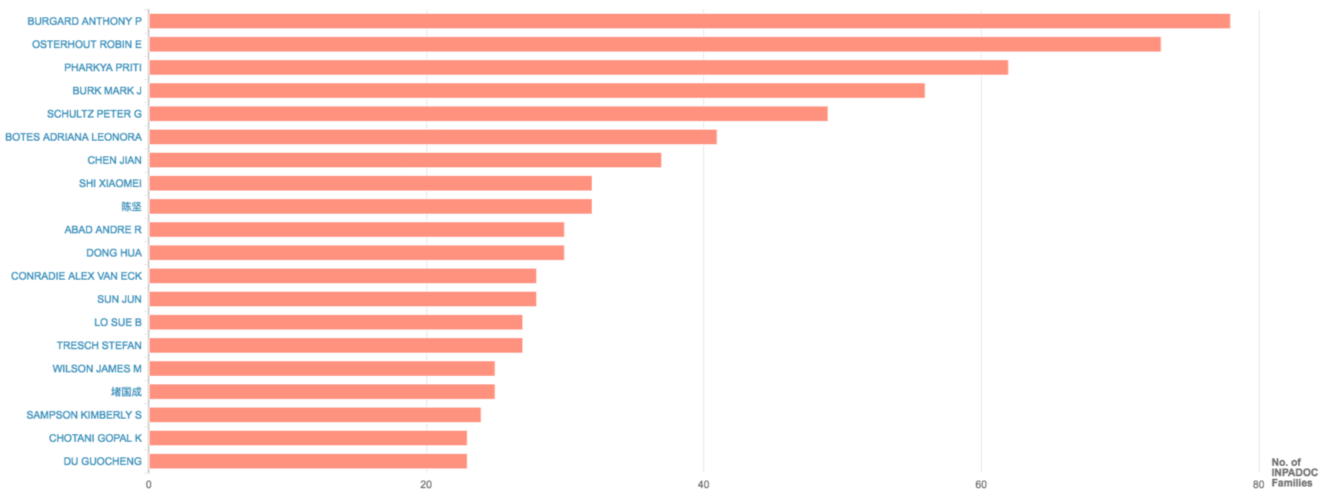


A list of the most cited patents shows some of the landmark inventions driving innovation in these areas:

- ***US5359046 Chimeric Chains for Receptor-Associated Signal Transduction Pathways*** **(C07K14/435)**
- ***WO1995015388A1 Recombinant Binding Proteins and Peptides*** **(C12N15/12)**
- ***US5608144 Plant Group 2 Promoters and Uses Thereof*** **(C12N9/42)**

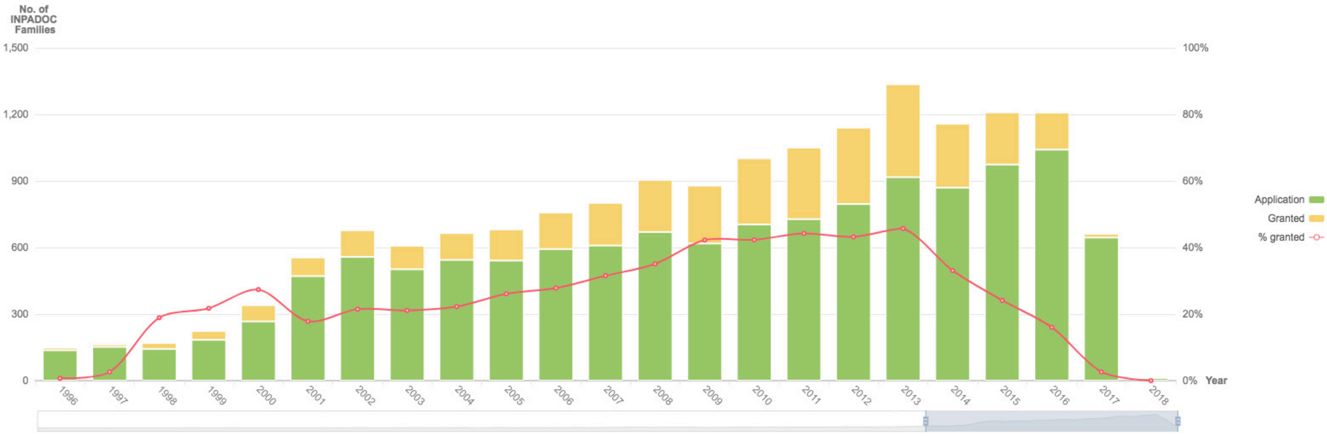
It would feel wrong to conclude this section without a mention of the intrepid inventors synthesising the known with the unknown, to shape our future. The chart for top inventors reveals the following names—and Genomatica as the pack leader:

- Anthony Burgard (Genomatica)
- Robin Osterhout (Genomatica)
- Mark Burk (Genomatica)
- Peter Schultz (Scripps Research Institute)
- Adriana Leonora Botes (Invista North America)



Part III: Enabling technologies

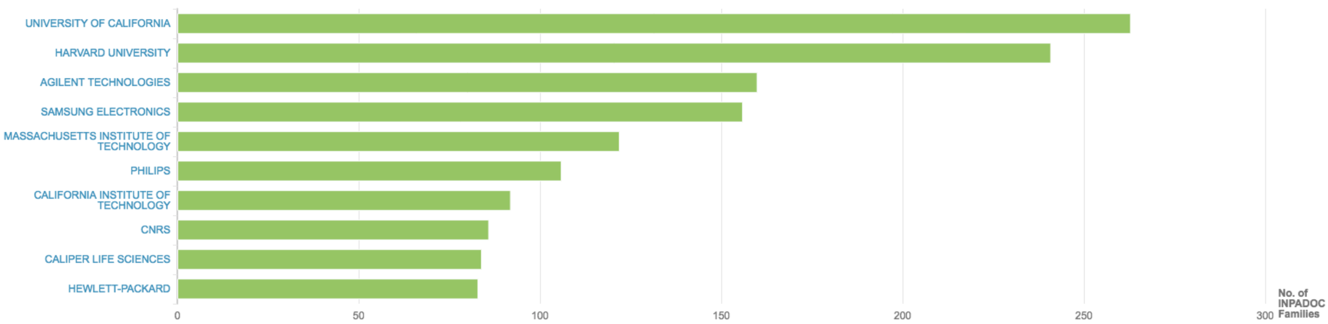
My search on enabling technologies in synthetic biology yielded 15,031 total INPADOC patent family representatives—by far the highest of any of the three facets of synthetic biology analysed here. Of these, 3690 belong to an academy, 8335 belong to a company, 3405 belong to a person and 307 belong to a government.



The rate of innovation in this area is, unsurprisingly, growing—with an all-time high of 1041 patents published in 2016. We expect the numbers for 2016 and 2017 to rise even more.

The most patent-intensive organisations in this area are:

1. University of California
2. Harvard University
3. Agilent Technologies
4. Samsung
5. MIT
6. Philips
7. California Institute of Technology
8. Centre National de la Recherche Scientifique *aka* The French National Centre for Scientific Research
9. Caliper Life Sciences
10. Hewlett Packard



Hewlett Packard (HP) just about makes the top 10 list but it only recently began accelerating filings in this area. In fact, filings in 2018 so far have already exceeded filings in any other year. HP is an established innovator in printer technology (one of the popular application areas for microfluidics), so its appearance on this list isn't necessarily surprising. However, my patent search query is limited to synthetic biology, so the trends we're seeing don't only reflect HP's familiarity with printers—they also reflect its exploration of life sciences.

The company is seeking to apply its microfluidics technologies in adjacent life sciences markets. HP Labs researcher, Anita Rogacs, explains:

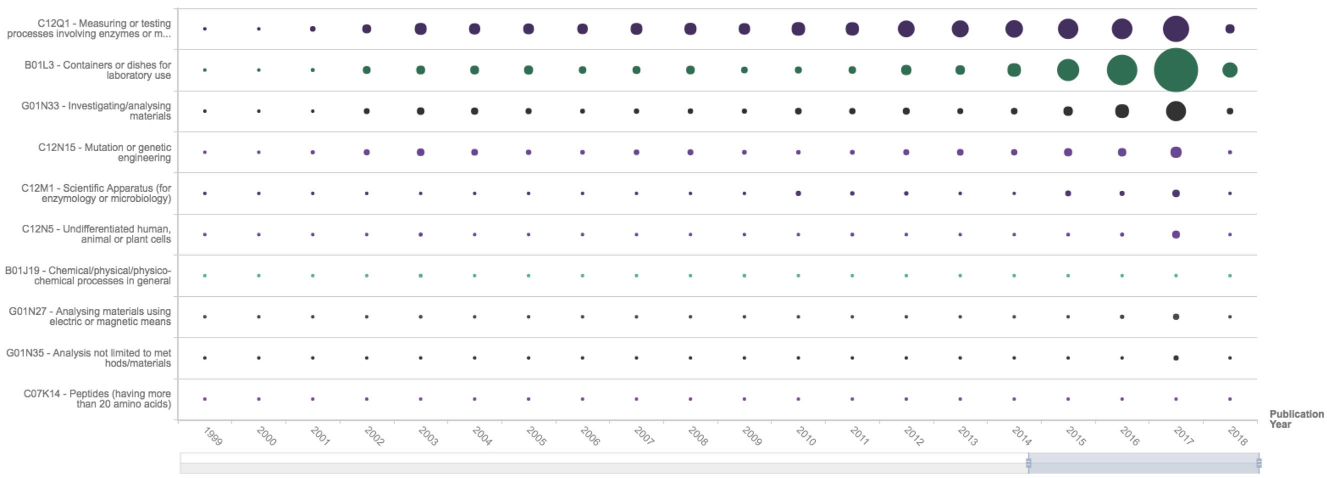
> *…at the heart of every HP printer is a very sophisticated microfluidic chip able to manipulate fluids with a performance unparalleled to almost any other industrial solution today… And microfluidics is one of the most exciting areas in the life sciences at present because it affords an opportunity for decentralization and automation of the biochemical and analytical processes associated with diagnostics, testing, and screening.*

HP even published in the summer 2016 issue of its innovation journal, a paper titled, *"The convergence of microfluidics, commercial mobility & computer technologies for new applications in healthcare"*. As is the case with Danisco's interest in isoprene, HP's interest in life sciences warrants deeper exploration by competitors whose existing R&D activities could have similarly adjacent applications.

Other companies ramping up activity in this area include MIT and Harvard—perhaps in an attempt to re-establish themselves as the leading research institutions in synthetic biology.

Of the top IPCs in which patents are being filed, these are the technology areas seeing the fastest rates of acceleration:

- **C12Q1** Measuring or testing processes involving enzymes or micro-organisms
- **B01L3** Containers or dishes for laboratory use
- **G01N33** Investigating or analysing materials



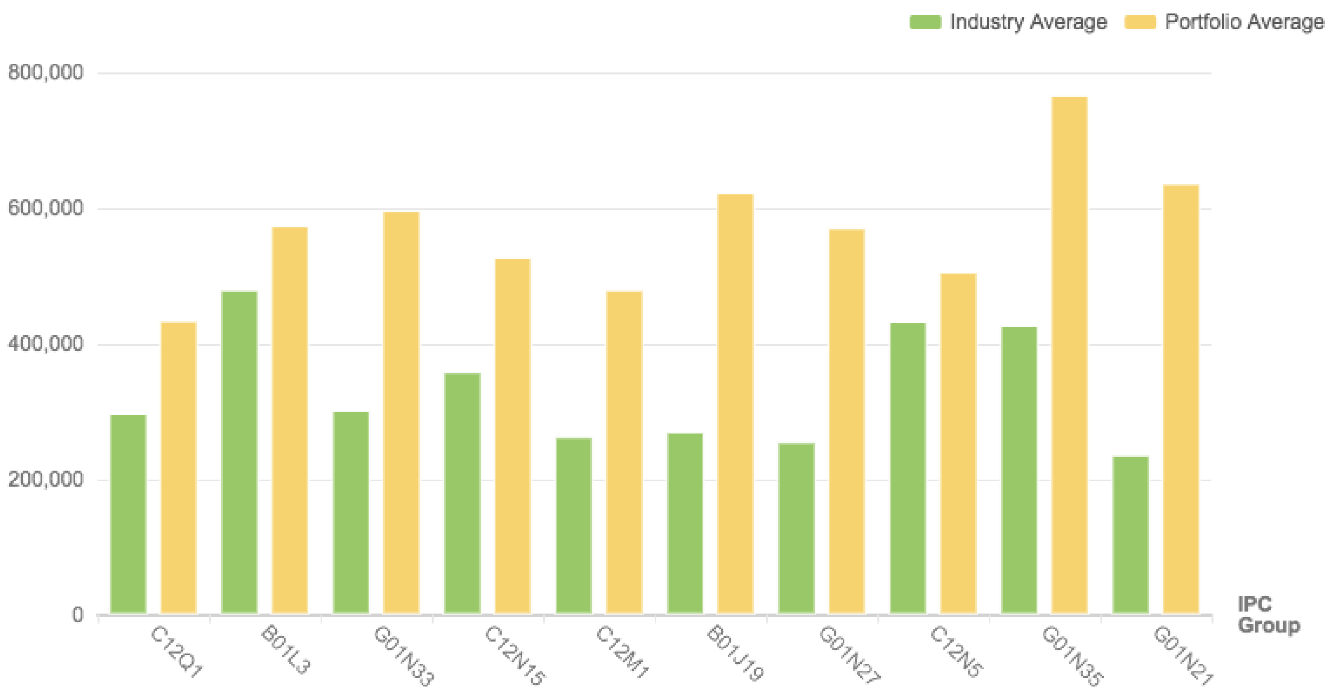
No real surprises here—of all the facets of synthetic biology analysed, enabling tech seems to be the one with the clearest commercial direction. This is reflected not only by the clear dominance of 3 IPCs over all the others—it's also reflected in the relative willingness of organisations to sue each other. Instances of litigation are not only high, they're rising. Lawsuits are very expensive, so they're pursued only as a means of protecting commercial interests so great that legal fees pale in comparison.

In this sub-category, there have been 119 patent lawsuits documented in the PatSnap platform. The most aggressive litigators are:

1. Whirlpool Corporation
2. University of Utah Reservation Foundation
3. Myriad Genetics

The list of most litigious companies here is essentially identical to the list we saw in the synthetic biology overview—which was seemingly skewed by the volume of patents in enabling tech.

Rather than rehash old analyses, I'm going to explore an area that should be of interest to the more commercially driven world of microfluidics—highly valued patents. Enabling technology-focussed patents in synthetic biology have—on average—higher valuations than patents within the same IPCs which focus on other technologies.



Below is a list of the top 3 most highly valued patents:

1. ***US8306757 Methods and Apparatus For Measuring Analytes Using Large Scale FET Arrays*** **(Life Technologies)**
2. **EP1859330B1 Apparatuses and Methods For Manipulating Droplets on a Printed Circuit Board (Duke University)**
3. ***CA2538038C Medical Device for Analyte Monitoring and Drug Delivery*** **(Theranos)**

Patent/Title	Current Owner	Family	IPC Scope	Value (USD)	Estimation Lifespan
US8306757 Methods and apparatus for measuring analytes using large scale FET arrays	LIFE TECHNOLOGIES	47	2	$23,030,000	8 yrs Application Expiry
EP1859330B1 APPARATUSES AND METHODS FOR MANIPULATING DROPLETS ON A PRINTED CIRCUIT BOARD	DUKE UNIVERSITY	15	3	$19,870,000	12 yrs Application Expiry
CA2538038C MEDICAL DEVICE FOR ANALYTE MONITORING AND DRUG DELIVERY	THERANOS	25	6	$17,330,000	14 yrs Application Expiry
IN706MUM2007A CIRCULAR SHACKLE PADLOCK	GODREJ & BOYCE MFG	53	12	$15,500,000	Expiry data unavailable
US20160114320A1 Droplet Manipulation Device	DUKE UNIVERSITY	16	8	$15,280,000	Expiry data unavailable
CN100583434C Optical lens system and method for microfluidic devices	先锋生物科技	20	10	$13,770,000	13 yrs Application Expiry
CA2645225A1 ALDOLASES, NUCLEIC ACIDS ENCODING THEM AND METHODS FOR MAKING AND USING THEM	BASF ENZYMES	18	1	$13,450,000	Expiry data unavailable
MX2010003037A MICROFLUIDIC DEVICE AND METHOD FOR FLUID CLOTTING TIME DETERMINATION.	ILINE MICROSYST	21	2	$13,090,000	10 yrs Application Expiry
US7361313 Methods for uniform metal impregnation into a nanoporous material	INTEL	10	5	$12,610,000	15 yrs Application Expiry
CA2701069C APPARATUS AND METHOD FOR DETECTION OF AN ANALYTE IN A SAMPLE	IBM	8	2	$12,060,000	10 yrs Application Expiry

The name that jumps out here is Theranos. The diagnostics company was once on fire but has evaporated into hot air, with interest in its technologies cooling after its owners were found to have lied about their capabilities. *The latest punishment for Elizabeth Holmes (founder) and her partners is a charge of "massive fraud"*. But Theranos has 6 patents in the area of synthetic biology—one of them highly valued:

- ***KR1020150038155A Methods for Detecting and Measuring Aggregation*** **(valued at $1,240,000)**
- ***HK1156823A Analyte Monitoring and Drug Delivery***
- ***EP1662987A2 Medical Device for Analyte Monitoring and Drug Delivery***
- ***WO2013043203A2 Systems and Methods for Multi-Purpose Analysis***
- ***AU2013201509A1 Point-Of-Care Fluidic Systems and Uses Thereof***
- ***IN9438DELNP2015A Nucleic Acid Amplification***

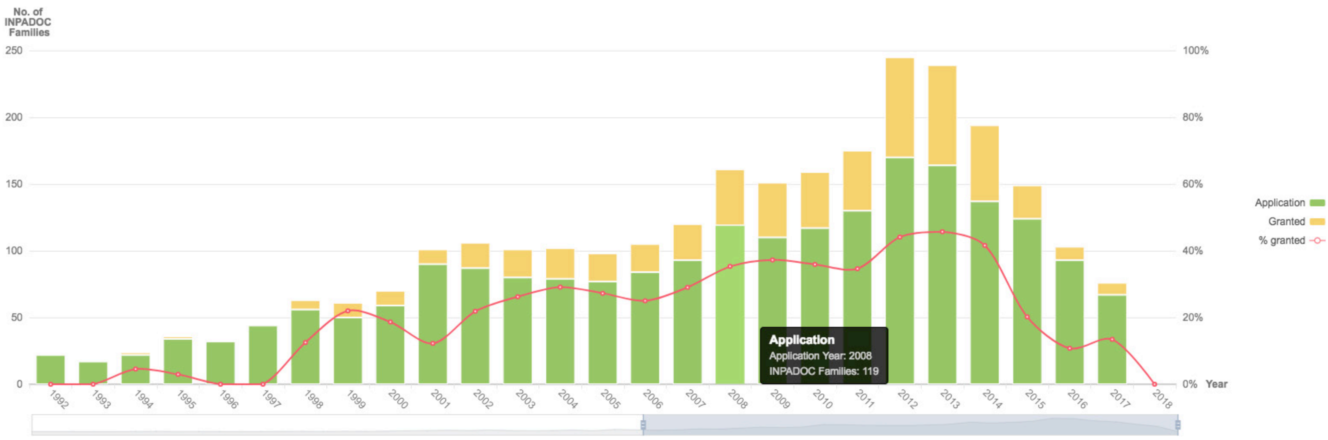
Overall (including patents unrelated to synthetic biology), the company's portfolio comprises 1357 patents (205 INPADOC families), of which 507 are granted and active. The most highly valued patent of these carries a $17,150,00 valuation. A savvy organisation could separate the wheat from the chaff in Theranos' portfolio and acquire some IP bargains in the process. This would also be good for Holmes and co, who will need all the money they can get to pay off a mountain of fines and damages. An interested party could also wait to see if these patents are abandoned, freeing up Theranos' IP for exploitation by all. But if—for whatever reason (e.g. ownership transfer)—this doesn't happen, they might get pipped to the post by a bargain hunter.

Considering the *volume of patent applications was one of the deceptions used by Holmes to dazzle investors*, there's likely lots of crap in Theranos' portfolio… but is it all crap?

Part IV: Applications

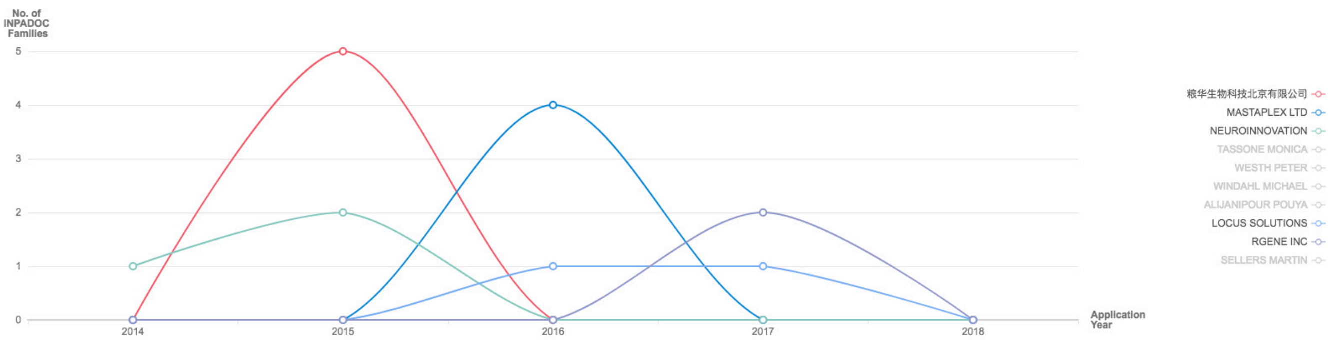
My search on applications of synthetic biology yielded 2363 total INPADOC patent family representatives—making this the area with the least patenting activity. Of these, 614 belong to an academy, 1428 belong to a company, 463 belong to a person and 51 belong to a government.

The innovation rate here isn't exactly bursting to life—patent applications actually began declining in 2012.



However, this sub-category also has the most entries on its list of new companies:

1. Lianghua Biotechnology Beijing (粮华生物科技北京有限公司)
2. Mastaplex Limited
3. Neuroinnovation
4. Locus Solutions
5. Rgene Inc



Even though new companies keep trying their hands at this, we're seeing a decline in the overall number of patent applications. In a way, this makes sense for a developing technology area—many organisations are drawn to it, but none have cracked the most lucrative applications. Hence, we don't see the kinds of trends—such as a sustained increase in patenting activity—present in more mature fields.

Also, unlike in earlier sections, it was hard to find information about two of the new organisations here. Rgene is so nascent that *its website* is a Wordpress template with placeholder text still in it—although it does contain the phrase *"innovative ligases"*. This tallies with the content in the only patent filed by the company so far, *"WO2017139260A1 Multiple Ligase Compositions, Systems, and Methods"*.

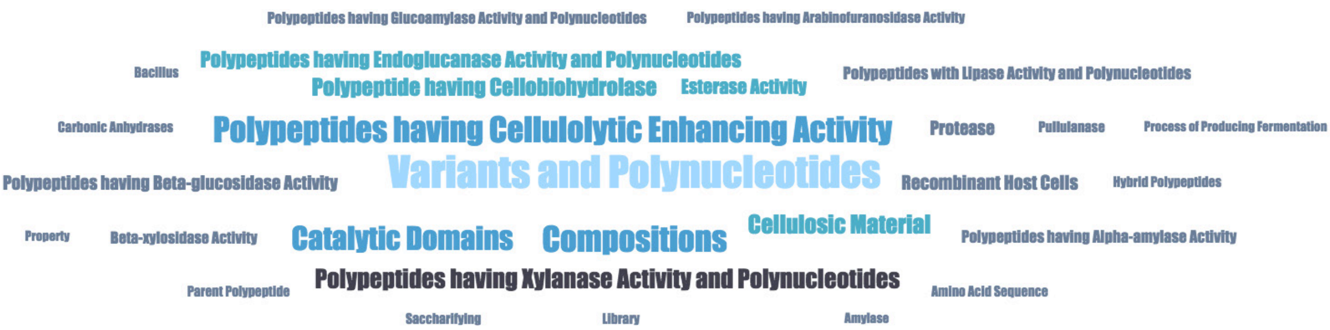
Mastaplex is focussed on *"precise mastitis diagnosis on farm"* and Locus is focussed on *"microbial technology that is 100% environmentally friendly"*. Neuroinnovation appears to be a Spanish company focussed on "scientific research, development and innovation for solutions to cognitive disorders". I could find no conclusive information about *"Lianghua Biotechnology Beijing"*.

The list showing the most patent-intensive organisations contains more recognisable names:

1. Novozymes
2. Genentech
3. University of California
4. DuPont
5. Danisco
6. BASF
7. MIT
8. LS9 (sold to Renewable Energy Group)
9. Qteros
10. REG Life Sciencies

Novozymes, the Danish biotech giant, absolutely dominates this realm. It has filed 29x the number of patents (1413) as the second most patent-intensive company—Genentech has filed 48.

Placing Novozymes' innovation activities under the microscope reveals a focus on *"polypeptides"* and *"polynucleotides"*, with some mention of *"recombinant host cells"*.

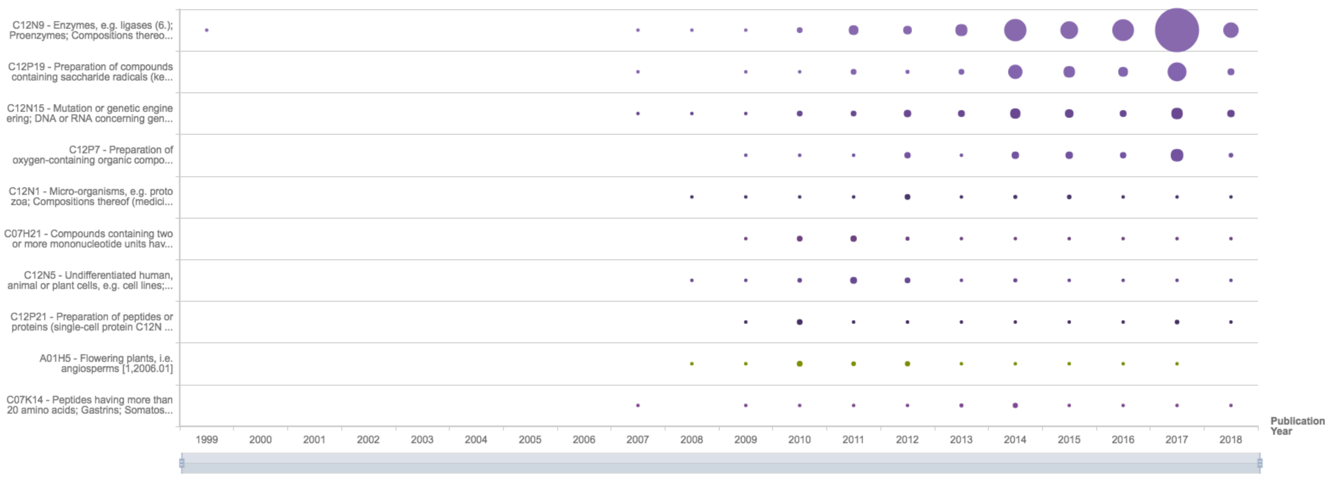


Although outside the scope of this report, zooming into the nature of the inventions in this area would be worthwhile. I can, however, reveal the top IPCs in which Novozymes is filing—particularly IPCs where its innovation rate is accelerating:

C12N9 Enzymes, e.g. ligases (6.); Proenzymes; Compositions thereof (preparations containing enzymes for cleaning teeth A61K 8/66, A61Q 11/00; medicinal preparations containing enzymes or proenzymes A61K 38/43; enzyme containing detergent compositions C11D); Processes for preparing, activating, inhibiting, separating, or purifying enzymes [2006.01]

C12P19 Preparation of compounds containing saccharide radicals (ketoaldonic acids C12P 7/58) [2006.01]

C12N15 Mutation or genetic engineering; DNA or RNA concerning genetic engineering, vectors, e.g. plasmids, or their isolation, preparation or purification; Use of hosts therefor (mutants or genetically engineered micro-organisms C12N 1/00, C12N 5/00, C12N 7/00; new plants A01H; plant reproduction by tissue culture techniques A01H 4/00; new animals A01K 67/00; use of medicinal preparations containing genetic material which is inserted into cells of the living body to treat genetic diseases, gene therapy A61K 48/00; peptides in general C07K) [2006.01]



IPC C12N9 has clearly enjoyed the fastest acceleration in filings—when I ran an analysis on Novozymes' patents covering synthetic biology applications and falling into IPC C12N9, I found this list of high-valuation patents:

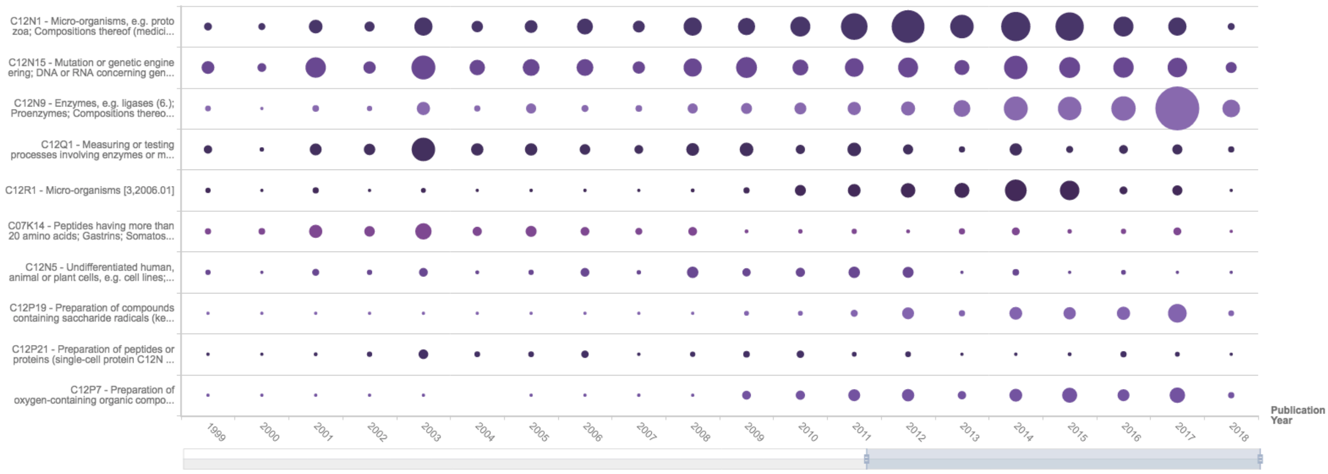
- ***CA2625933C Polypeptides Having Beta-Glucosidase Activity and Polynucleotides Encoding Same*** **(valued at $3,650,000)**
- ***US9506049 Polypeptides Having Cellulolytic Enhancing Activity and Polynucleotides Encoding Same*** **(valued at $3,250,000)**
- ***US9428742 Polypeptides Having Endoglucanase Activity and Polynucleotides Encoding Same*** **(valued at $2,830,000)**

Patent/Title	Current Owner	Simple Family	IPC Scope	Value (USD)	Estimation Lifespan
CA2625933C POLYPEPTIDES HAVING BETA-GLUCOSIDASE ACTIVITY AND POLYNUCLEOTIDES ENCODING SAME	NOVOZYMES	4	6	$3,650,000	12 yrs Application Expiry
US9506049 Polypeptides having cellulolytic enhancing activity and polynucleotides encoding same	NOVOZYMES	5	5	$3,250,000	4 yrs Application Expiry
US9428742 Polypeptides having endoglucanase activity and polynucleotides encoding same	NOVOZYMES	4	2	$2,830,000	5 yrs Application Expiry
CA2682451C FUNGAL PEROXYGENASES AND METHODS OF APPLICATION	NOVOZYMES	6	2	$2,830,000	10 yrs Application Expiry
US20160369253A1 Methods of increasing the cellulolytic enhancing activity of a polypeptide	NOVOZYMES	13	3	$2,790,000	2 yrs Application Expiry
EP2446029B1 HEAT-STABLE CARBONIC ANHYDRASES AND THEIR USE	NOVOZYMES NORTH AMERICA	1	4	$2,760,000	8 yrs Application Expiry
US20170037388A1 ALPHA-AMYLASES	NOVOZYMES	20	4	$2,610,000	2 yrs Application Expiry
US9404091 Dehydrogenase variants and polynucleotides encoding same	NOVOZYMES	9	2	$2,540,000	3 yrs Application Expiry
US20170145457A1 Compositions for saccharification of cellulosic material	NOVOZYMES	10	3	$2,330,000	1 yrs Application Expiry
BRPI0820615A2 POLYPEPTIDES HAVING ACETYLXYLAN ESTERASE ACTIVITY AND POLYNUCLEOTIDES ENCODING SAME	NOVOZYMES	1	2	$2,290,000	9 yrs Application Expiry

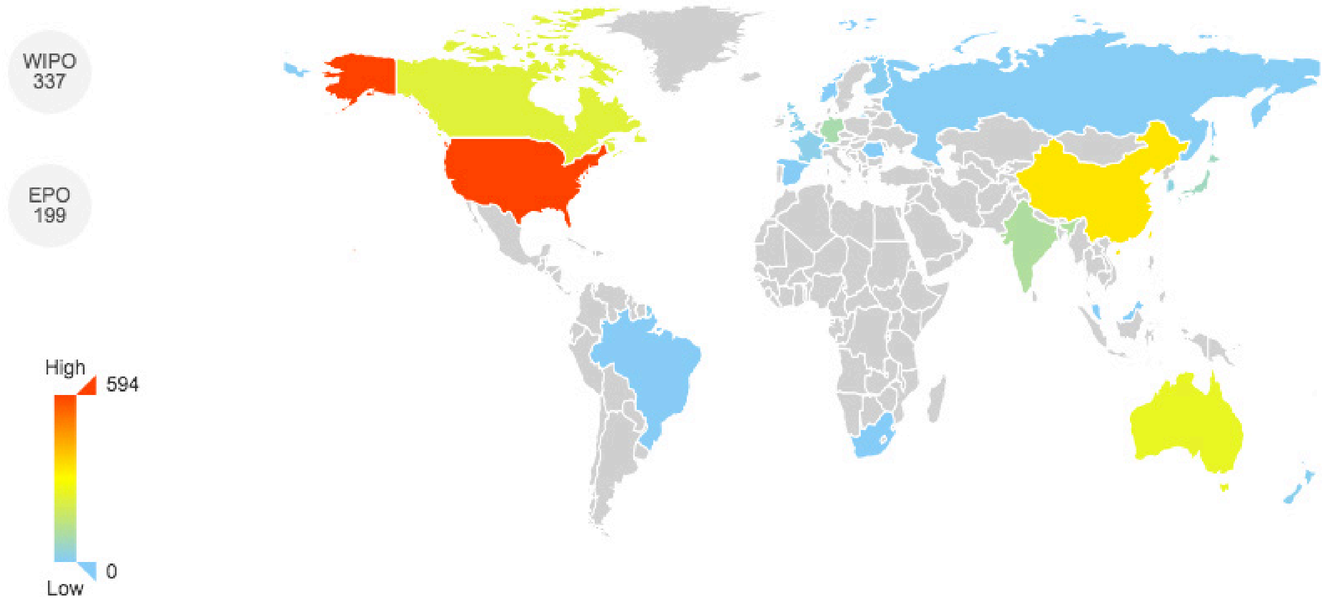
It's a bit like Inception—an analysis, within an analysis, within an analysis. But this kind of digging can be invaluable for understanding a competitor's (or industry's) direction of innovation. You find the areas of accelerating activity, pinpoint the subjects of innovation within those areas, then zoom into individual patents comprising those subjects. To be honest, this took me 5 mins and about 10 clicks—so, with the right tool, the process isn't particularly laborious.

If we zoom back out to the overall landscape, these are the top IPCs with the fastest rates of acceleration:

- **C12N9** Enzymes
- **C12P7** Production of oxygen-containing organic compounds
- **C12P19** Production of organic compounds (having saccharide radicals)



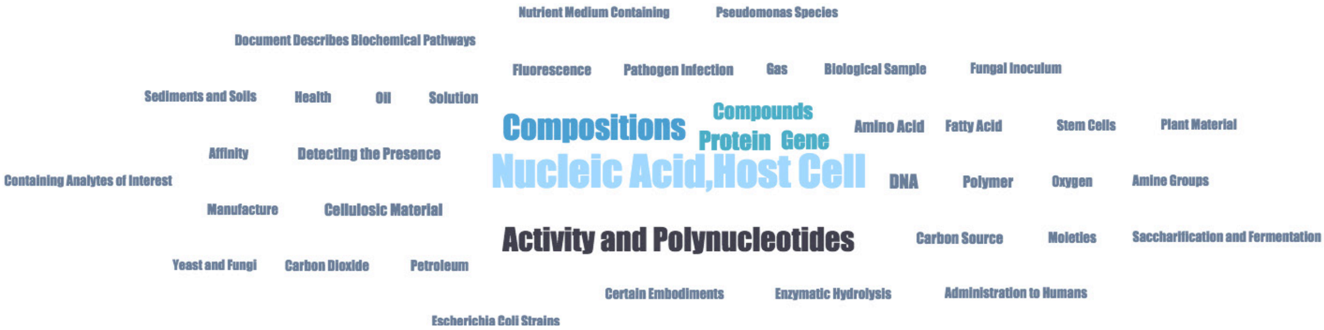
And in which parts of the world is all this innovation taking place? Mainly the US, which has 594 INPADOC families (25% of all filings). Next is China, with 335 INPADOC families (14% of all filings). Completing the top three is Australia, with 246 INPADOC families (10% of all patent filings).



The divergence in focus between patents filed in China and America is interesting.

China's patents seem to revolve around environmental and agricultural applications of synthetic biology—with terms like *"waste water"*, *"soil remediation"* and *"degrading bacteria"* frequently occurring.

American patent filings seem to have a more opaque commercial or practical focus.

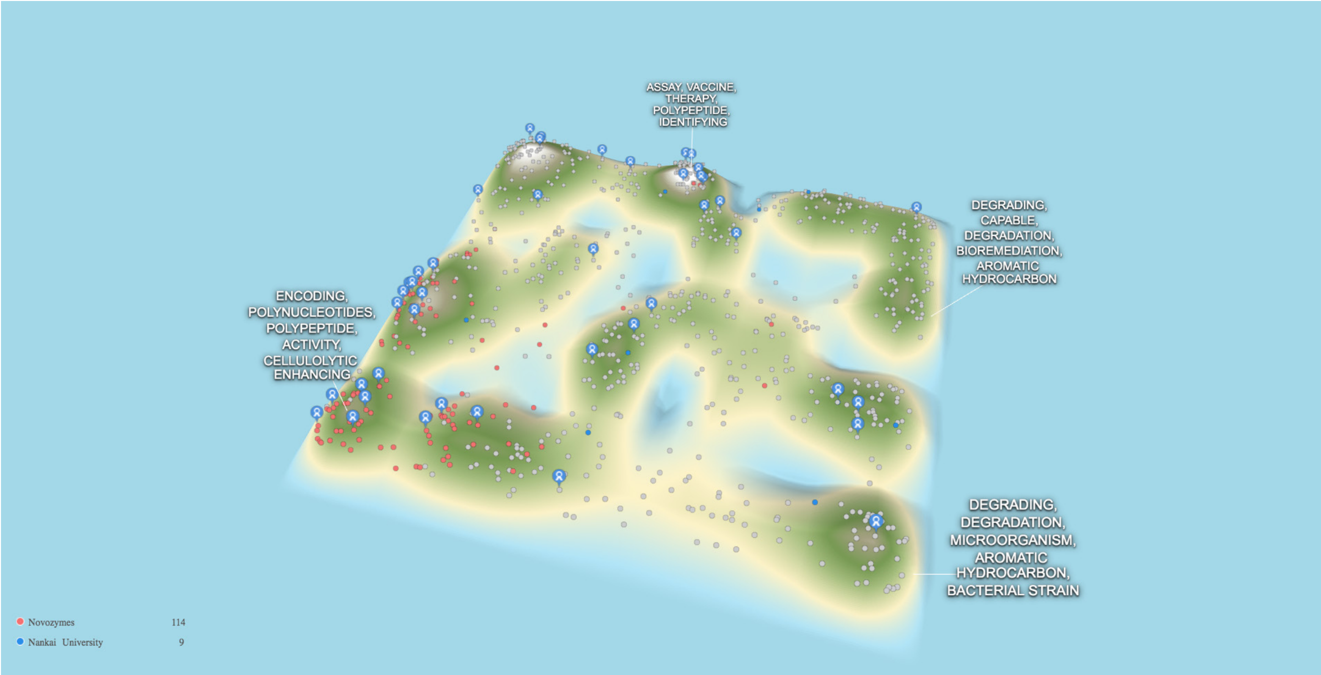


This tallies with *industry analysis of the biotech battle between the US and China*. In a particularly prescient passage, the linked report expounds:

> *With the rise of an environmental movement in China over the past several years, as well as a very public issue with contaminated rice, the development of a cadmium-resistant strain of rice would be popular and necessary. Even with industry consolidation and stricter central government control, reversing the effects of decades of pollution will be slow.*

The main challenges for the United States are the protection of its biotech IP from theft by Chinese agents and (funnily enough) less restricted access to the blossoming Chinese market. But maybe the key lies in partnerships—as seen with Google and Tencent, in the US-China AI battle—rather than confrontations.

Below is the US-China patent landscape (each dot is a patent), with the top 2 companies highlighted—Novozymes (red) and Nankai University (blue). I've also highlighted licensing deals (blue ribbons).



For those exploring the building blocks of life, perhaps the key to finding that decisive technological breakthrough and mass commercial adoption lies in joint exploration.

Boolean search queries

Synthetic biology overview

A merger of all the search queries below.

Knowledge in synthetic biology

TAC:(*"riboswitch*"* OR (*"synthetic biology"* OR *"synthetic amino acid"* OR *"synthetic base pair"* OR *"synthetic genome"* OR *"synthetic genet*"* OR *"synthetic nucleic acids"* OR *"synthetic *nucleotide"* OR *"synthetic sequence"* OR *"artificial amino acid"* OR *"artificial base pair"* OR *"artificial genome"* OR *"artificial genet*"* OR *"artificial nucleic acids"* OR *"artificial *nucleotide"* OR *"artificial sequence"* OR *"genetic circuit"* OR *"signalling pathway"* OR *"systems biology"* OR *"metabolic engineering"* OR *"synthetic protocell"* OR "synthetic cell" OR *"artificial cell"* OR *"minimal cell"* OR *"cell chassis"* OR *"vesicul* bioreactor"* OR *"vesicle bioreactor"* OR *"minimal genome"* OR *"synthetic gene cluster"* OR *"synthetic regulatory network"* OR *"gene circuit design"* OR *"biological parts"* OR *"dna assembly"* OR *"rational protein design"* OR *"computational protein design"* OR *"de novo enzyme design"* OR *"noncanonical amino acid"* OR *"unnatural amino acid"* OR *"rna design"* OR *"rational design"* OR *"dna origami"* OR *"rna nanostructure*"* OR *"dna nanostructure*"* OR *"gene* switch"* OR *"synthetic gene network"* OR *"artificial gene network"* OR *"genome engineering"* OR *"gene oscillator"* OR *"synthetic shRNA"* OR *"artificial shRNA"* OR *"heterologous nucleic acid"* OR *"biological circuit"*) OR (*"molecular machine"* AND *"protein"*) OR (*"molecular machine AND bio"*) OR (*"rna"* AND *"computational design"*) OR (*"rna"* AND *"rational design"*)) AND IPC:(B01 OR C12N OR C12P OR C12Q OR C12S OR C40B)

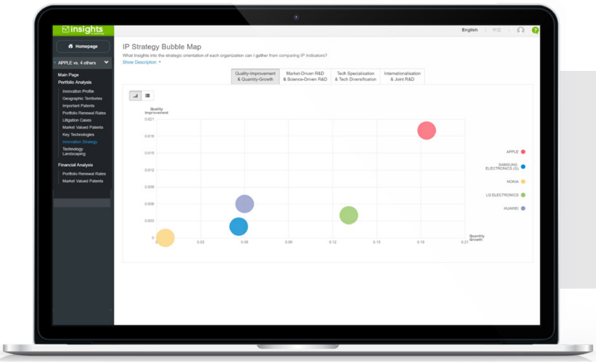
Enabling technologies of synthetic biology

TAC:((*"cad"* OR *"cam"* OR *"microfluidics"*) OR (*"design platform"* OR *"computer aided design"* OR *"systems biology model*"* OR *"metabolomic* model*"* OR *"transcriptomic* model*"* OR *"protein folding model*"* OR *"protein folding prediction"* OR *"rna folding model*"* OR *"rna folding prediction"* OR *"multiplex ligation"* OR *"multiple amplification"* OR *"dna synthesis"* OR *"gene synthesis"*) OR (*"multiplex"* AND *"genome"*) OR (*"multiplex"* AND *"gene"*)) AND IPC:(B01 OR C12N OR C12P OR C12Q OR C12S OR C40B)

Applications of synthetic biology

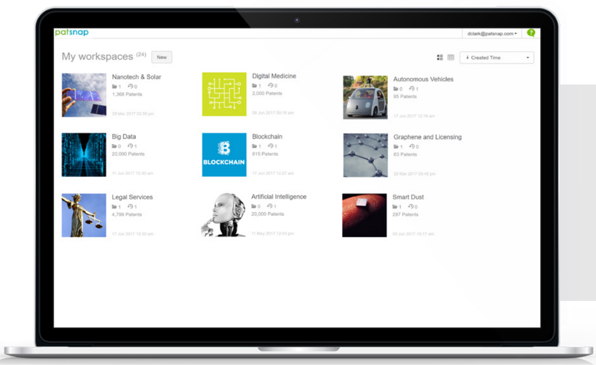
(TAC:(*"environment"* AND *"degradation"*) AND IPC:(C12N OR C12P OR C12Q OR C12S)) OR (((*"medicine"* AND *"bacter*"*) OR (*"photosynth*"* AND *"bacter*"*) OR (*"nano*"* AND *"bacter*"*) OR *("nano" AND "bacter*") OR ("industr*" AND "bacter*") OR ("remediation" AND "bacter*") OR* ("*smart material*" AND "*microbio**") OR ("*fuel*" AND "*microbio**") OR ("*energy*" AND "*microbio**") OR ("*medicine*" AND "*microbio**") OR ("*photosynth**" AND "*microbio**") OR ("*nano**" AND "*microbio**") OR ("*nano*" AND "*microbio**") OR ("*industr**" AND "*microbio**") OR ("*remediation*" AND "*microbio**") OR ("*smart material*" AND "*microbia**") OR ("*fuel*" AND "*microbia**") OR ("*energy*" AND "*microbia**") OR ("*medicine*" AND "*microbia**") OR ("*photosynth**" AND "*microbia**") OR ("*nano**" AND "*microbia**") OR ("*nano*" AND "*microbia**") OR ("*industr**" AND "*microbia**") OR ("*remediation*" AND "*microbia**")) AND IPC:("*C12N*" OR "*C12P*" OR "*C12Q*" OR "*C12S*" OR "*C40B*"))

The PatSnap platform gives your team the data it needs to make better innovation decisions.



R&D is a race against time (and your competitors)

Where is your next million dollar idea?



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