

SYNTHETIC BIOLOGY: THE BIOECONOMY OF LANDLESSNESS AND HUNGER



For more background see http://www.etcgroup.org/issues/synthetic-biology

Synthetic biology represents a quantum advance on biotechnology, and goes beyond transferring genes between species to constructing entirely new, self-replicating microorganisms that have the potential (partially proven / partially theoretical) to convert any biomass or carbon feedstock into any product that can be produced by fossil carbons – plus many more. In other words, from the perspective of synthetic biology ("synbio"), the resource base for the development of marketable "renewable" materials (that is not from petroleum) is not the world's commercialized 23.8 % of annual terrestrial biomass, but also the other 76.2 % of annual terrestrial biomass that has, thus far, remained outside the market economy.¹

Synthetic biology has already attracted the attention of the United Nations and governments. The technology was on the agenda of the UN Convention on Biological Diversity that met in Hyderabad, India in mid-October 2012, with governments agreeing to continue monitoring the technology and report back to future meetings of the CBD.²

At first blush, a new manufacturing platform built on "re-programming" life forms sounds like the stuff of science fiction and far removed from the realities of agriculture in the global South. However – like previous revolutions in agriculture and manufacturing – the Northern-bred synbio industry is shifting the economic picture for farmers in the South (and at greater speed), driving a new wave of land grabs (for biomass) and competing head to head with the naturally sourced commodities that Southern economies have relied on for decades or even centuries. As well as driving the biomass grab, it is increasing the economic value of natural gas through controversial 'fracking' processes: synthetic microbes are now being re-tooled to use natural gas as their carbon source.3

Synthetic biology by the numbers

In 2012, the synthetic biology industry evolved into a global, well-financed and rapidly expanding sector with products already in the marketplace and many more in the pipeline over the next two to three years.

 Growing Fast: According to BCC Research, global synthetic biology product sales were around \$1,600 million in 2011 and are expected to rise to \$10,800 million by 2016.⁴ A

- recent survey identified almost 3000 active synthetic biology researchers in 40 countries funded by 530 different entities primarily in the USA, Europe, China and Japan.⁵
- **Switching Focus**: Three quarters of the activity has so far been energy and chemical companies (such as BP, Shell, DuPont, Total) developing and marketing artificial microbes that produce next generation biofuels, bioplastics and commodity chemicals. However the industry is now rapidly switching focus to primarily produce materials formerly sourced from natural plant products –such as rubber, food flavours, fragrances and essential oils as well as natural medicinal products. The new waves of investors are the world's largest cosmetics companies, flavours and fragrances brokers, pharmaceutical manufacturers and food ingredient producers (e.g., Novartis, Givaudan, International Flavours & Fragrances Inc., Roquette Frères). A third wave of Synbio partnership is also just beginning that will take advantage of transforming natural gas into high value products. B
- **Big Players**: A 2011 survey by ETC Group and partners found that, overall, the leading global investors and developers of synthetic biology products remain six of the world's ten largest chemical companies, six of the ten largest energy companies, six of the ten largest grain traders and the world's seven largest pharmaceutical companies. Many of these in collaboration with financial players have in turn invested many thousands of millions of dollars of equity in over 100 'pure-play' synthetic biology start-ups.
- Already on Sale: ETC Group has tracked over 20 different products already commercialised or due to be commercialised in 2013. Examples of synthetic biology products already on the market include two maize-based bioplastics sold by DuPont and the Archer Daniels Midland company, biosynthesized 'natural' grapefruit flavour sold by the USA's Allylix Inc, synthetically derived shikimic acid the key ingredient in the drug tamiflu and a cosmetics moisturiser, squalane, as well as cane sugar-based biodiesel sold by Amyris Inc. in Brazil. See Annex for full list.

Enabling the Biomass Grab of the Bioeconomy

It is no coincidence that the synthetic biology industry is surging in the wake of enthusiasm from OECD governments for implementing a new industrial programme dubbed 'the bioeconomy' (or 'bio-based' economy).

The bioeconomy vision involves switching the raw material base of manufacturing away from fossil sources such as oil, coal and gas towards living, theoretically renewable, plant matter such as sugar, woodchips, algae and grasses – collectively known as 'biomass.' Just as sugar-based ethanol has begun to make inroads in fuel production, the hope is to extend the model to other, more efficient fuels and other sectors such as chemicals.

Though the bioeconomy is sold as the way of the future – post-petroleum and "green" – what is often overlooked is that bio-based production requires massive biomass inputs. As we have seen with first generation agrofuels, the quest for biomass inevitably leads to the tropics where 86% of

the planet's biomass grows, and sunlight, water and fertile soil is either abundant or (at least) cheap.¹¹

- The 'next generation' of biofuels is all about synthetic biology. As food prices climb to record levels and 40% of the US corn harvest (15% of the global harvest) continues to be diverted to ethanol,12 OECD countries are renewing efforts to switch biofuel production away from food crops toward so-called 'next generation,' high-performing fuels (made from cellulose, wood chips, algae, seaweed). Both the European Union and US governments have already mandated that next generation fuels be blended into current biofuels and are directing hundreds of millions of dollars of investment to propping up the 'next generation' industry. In all these cases, synthetic biology is considered key. Tellingly, Biofuels Digest's annual lists of the hottest companies in bioenergy and biochemicals are mostly synthetic biology companies or companies that use enzymes and microbes developed through synthetic biology.¹³
- Race for Brazil, Africa and beyond. Although the synthetic biology industry was born in the labs of Europe and North America, tropical biomass is essential to its growth. Brazil is currently the favoured source of biomass to feed synthetic microbes, although synthetic biology companies are also eyeing Africa and beyond. Industry leader Amyris, Inc. (financially supported by Total, Shell, Procter & Gamble and others) is well established in Brazil with two of its own plants, a handful of joint ventures turning sugarcane into a commercial biodiesel, and a cosmetics moisturising product called squalane. Amyris, Inc. CEO John Melo explains his future business plan:

"The vision we have is there is a fantastic opportunity to help some of the African countries to develop new industry by really.. um..er.. exploring some of the agricultural land they have." – John Melo, Amyris Inc. 14

Also building synthetic biology facilities in Brazil are LS9 Inc. (backed by Procter & Gamble), Solazyme (backed by Chevron), Codexis (backed by Shell) and Butamax (backed by BP and DuPont). LS9 (which turns sugar into gasoline using synthetic microbes) is planning to build facilities far larger than any existing biofuel refinery in Brazil and in the medium-term hopes to take the same model elsewhere in the tropics:

"We have plans for multiple sites so total capacity could be 200,000-500,000 tonnes per year in the full-scale phase at around the 2017-2018 time frame. Our first investment will be in sugar-producing regions with secure supplies in Latin America. Once commercialized, it is a natural expansion to invest in other raw material-rich regions in Asia, North America and Europe." – Gary Juncosa, LS9, VP of chemicals¹⁵

• **First up: sugar grabs, cellulose grabs**: The initial feedstock choice of commercial symbio companies has been sugarcane, which is the fastest growing terrestrial source of biomass.

Not only does the cane itself provide an easy-to-ferment substrate for synthetic microbes to feed on, but also the waste bagasse is high in cellulose (a woody sugar). Synthetic biology companies such as Codexis have succeeded in developing enzymes to transform bagasse – increasing the value of sugarcane. ¹⁶ The focus on sugarcane as a biofuel feedstock matches current trends in land grabbing in the tropics as reported by GRAIN and The International Land Coalition (ILC): ILC reports that 78% of recorded land deals are for agricultural production of which three quarters are for biofuels. ¹⁷ GRAIN reports that currently the biggest rise in land grabs is for sugarcane plantations particularly in East Africa (e.g., Mozambique), Latin America and South-East Asia (e.g., Cambodia). ¹⁸ However land grabs for forest cellulose (e.g. eucalyptus) are also on the rise.

Coming soon: desert grabs, coastal grabs: While the primary target of land grabs has so far been prime agricultural and forest land, synthetic biology's ability to convert other biomass sources into products may bring other territories into the global land grab. Biofuels production from algae is now receiving billions of industrial investment, mostly centred on rewiring algae to be more productive, and the aim is to grow algae in large desert ponds potentially encroaching on native and nomadic lands. Algal fuel company Solazyme (whose algae consume sugar) is already building a 300,000 tonne plant in Brazil¹⁹ while Exxon-backed Synthetic Genomics Inc. is building an 81-acre open algae farm on the Mexican/American border. Another synbio start-up, Bio Architecture Lab (BAL), backed by DuPont and Statoil, has developed synthetic organisms to break down farmed seaweed species into cellulosic fuels. BAL is opening a pilot plant in Chile, which harvests seaweed from four ocean farms on the Chilean coast, 20 and reports that they are looking at other Latin American and Asian locations to expand their production. In October 2012, BAL inked a development deal with the China-based Xunshan Group, the largest producer of brown seaweed in the world.²¹ While coastal grabs for seaweed biofuels avoid 'land' conflicts, they potentially open up new conflicts with small-scale fishers and other traditional coastal producers.

Synbio – Synland:

Since the beginning of agriculture – up until the industrial revolution – the route to wealth and power was through the ownership of land. After the industrial revolution – while land continued to be important – the control of the technologies that produced commodities above or below the land became increasingly more important. By the middle of the last century, the "smart money" assumed that peasants – either miners or farmers – should be allowed to work the land while the industries controlled the technologies at enormously less risk.

A few years ago GRAIN produced "land-breaking" research exposing the global pattern of public and private land grabs that posed a profound threat to the wellbeing of marginalized peoples in rural areas. Given climate chaos, the only land we can be sure to have value is land that has water underneath it and – for the moment – reasonable soil quality on top. If the water or the soil quality is in doubt, the land could turn out to be valueless. Furthermore, even if land

and water are available, the disruptive effects of climate change could make profits so unpredictable as to discourage investment. In the long run, then, it seems that the conventional corporate bet that those who control the technologies will control the value of the land prevails. Synthetic biology offers corporate investors an attractive opportunity: to be able to turn any biomass into almost any product. Those who have synbio's artificial microbes can be assured of windfall profits however the climatic winds blow.

To fully understand the dimension of the modern landgrabs, we need to understand, monitor and challenge synthetic biology too.

Beyond land grabs – commodity grabs

The synthetic biology industry's first five years focused on building capacity to transform biomass into commodity fuels and chemicals, already impacting those living on land needed to grow industrial feedstocks. Still, the scale-up needed to meet significant liquid fuel demand has proved difficult: one after another Syn Bio company has found it technically challenging to produce commodity compounds in large enough batches to be economically viable and so have begun to look for high value markets that require smaller production runs to meet demand. The next five years may deliver a deadly double whammy as industry augments biofuels production with an array of valuable niche products currently met by Southern agricultural producers.

'Natural plant products' describes the existing \$6,500 million dollar market22 for compounds harvested from the world's agricultural and forest biodiversity – ranging from bulk commodities such as rubber, silk, and tropical oils to ingredients, flavourings, fragrances and medicinal products, including vanilla, saffron, jasmine, turmeric, liquorice and codeine.

These compounds, known to synthetic biologists as 'secondary metabolites,' are the result of complex biochemical pathways that can now be synthetically 'programmed' to coax synthetic microbes into excreting the natural product of interest. Given that many of these products have a high commercial value and need only be produced in relatively small quantities to match current demand, the synthetic biology industry has seized on these markets as a route to profitability. Synbio companies such as Amyris, Solazyme, Evolva and Allylix are forming joint ventures with cosmetics and ingredient companies and promising to ferment in vats the same compounds currently harvested from tropical fields. In the process, they are dragging down the price and directly competing with small producers. The same companies are also claiming wide-ranging patents on 'metabolic pathways' that cover hundreds of different compounds at a time.²³ Some biosynthesized compounds have already come to market and many others are in the pipeline. Among the near-term targets:

• **Isoprene rubber**: Producing a synbio alternative could affect supply chain for both natural and synthetic rubber. The livelihoods of 20 million smallholder families, mostly in Asia, depend on natural rubber. (The market for Isoprene is \$2 billion per annum).²⁴

- Lauric and Myristic Acid: Derived from coconut and palm kernel oils, they are the staple of the \$3.9 billion oleochemical industry²⁵ and their replacement through synthetic biology could knock economies across Asia, Africa and South America.
- **Artemisinin**: An antimalarial compound currently sourced from Asian and African farmers (~\$90 million market p/a). ²⁶ In April 2013, pharmaceutical giant Sanofi announced it would launch commercial-scale production of a "semi-synthetic" version using synthetic biology.
- **Saffron**: The world's most valuable spice. Iran produces an estimated 90% of the world's saffron, with export markets in over 40 countries (\$660 million market p/a).
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- **Squalene:** a cosmetic moisturiser that used to be made from shark livers and now largely sourced from Mediterranean olives and South American amaranth.
- **Patchouli** –This popular fragrance is largely grown in Southeast Asia. Indonesia, the largest grower cultivates 20,000 ha of patchouli plant producing about 500 tonnes per annum.²⁸
- **Vanillin**: This popular fragrance is largely grown in Southeast Asia. Indonesia, the largest grower, cultivates 20,000 ha of patchouli plant producing about 500 tonnes p/a.²⁹
- **Vetiver oil**: An essential fragrance ingredient used in many cosmetics. In Haiti alone, 60,000 people depend on vetiver production (\$10 million market per annum).³⁰

Endnotes

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²⁷ Edison Investment Research, "Outlook: Evolva," 4 April 2012.

²⁸ FAO factsheet on Patchouli Oil production online at http://www.fao.org/docrep/X5043E/x5043E0i.htm

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Annex – Synthetic biology derived products commercially available or released into the environment 2013

Category	Product	Company	Production Location	Market Status	Additional Info	Sources
Plastic/ textile	Bio-PDO (1-3 propanadeiol) Brand names: Sorona/ Susterra	Du Pont Tate and Lyle	Loudon, Tennessee, USA	Commercial since 2006. Current production 140 million lbs/year.	Synthetic yeast developed by genencor, transforms corn feedstock.	
Plastic/ Textile/ Urethane	Bio-BDO (1,4- butanediol)	BioAmber	Pomacle, France	Commercial since 2012.	BioAmber believes the global addressable market for these products exceeds \$4 billion, principally used to make polyesters, polyurethanes, spandex and biodegradable plastics.	http://www.bio- amber.com/bioamber/en /news/article?id=516
Plastic	PHA (polyhydroxy alkanoates) Brand Names: Mirel, Mvera	Metabolix Inc.	Clinton, Iowa, USA; Leon, Spain	Initial commercial production run with ADM was stopped. Currently selling 5 million pound back-inventory while scaling up new commercial production in Spain for second half of 2013.	Focus on compostable plastic bags, barrier film, protective wrap, agricultural multi film and high strength films.	http://seekingalpha.com/ article/971971- metabolix-s-ceo- discusses-q3-2012- results-earnings-call- transcript?page=2 http://www.plasticsnews. com/article/20120727/N EWS/307279980/metabo lix-finds-new-partner-to- make-biopolymer-mirel
Flavouring/ Flagrance	Bio- Nooktatone	Isobionics (formerly DSM)	Geleen, The Netherlands	Commercial since 2011.		http://www.isobionics.co m/products_nootkatone. htm
Flavouring/ Flagrance	BioValencene	Isobionocs	Geleen, The Netherlands	Commercial since 2011.		http://www.isobionics.co m/press3.htm

Category	Product	Company	Production Location	Market Status	Additional Info	Sources
Flavouring/ Flagrance	Nooktatone (grapefruit flavour)	Allylix	Lexington Kentucky USA; San Diego, California USA	Commercial - Produced in 2000 runs since 2011.	Used as an ingredient in beverages, confections, frozen dairy and baked goods, as well as a fragrance in perfumes and colognes. Also being tested as insect repellent. "It had been selling its biosynthetic terpenes to customers in the flavor and fragrance markets. The company's terpenes are used in products currently found on supermarket shelves."	http://www.cookandsch mid.com/Allylixflavorandf ragranceindustryCarolynF ritzKellyQuigleySanDiego BusinessJournalventure.h tm
Flavouring/ Flagrance	Valencene (orange oil flavour)	Allylix	Lexington Kentucky USA; San Diego, California USA	Commercial - Produced in 2000 runs since 2011.	According to Allylix one commercial fermentation will produce as much valencene as 1.2 million metric tons of oranges.	http://www.slideshare.ne t/cookandschmid/alx- ppt091410bbcems97
Flavouring/ Flagrance	Resveratrol	Evolva (formerly produced by Fluxome)	Copen- hagen, Denmark	Commercial. Self-affirmed as GRAS and European novel foods approved.	Global market \$50.2 million food supplements, chewing gums, beverages and anti-aging moisturizing creams.	http://www.nutraingredie nts.com/Industry/Evolva- pays-550-000-for- Fluxome-resveratrol- business
Flavouring/ Flagrance	Vetivone (vetiver fragrance) Brand name: Epivone (epi- betavetivon)	Allylix	Lexington Kentucky USA; San Diego, California USA	Due to be have been commercialized 3 rd quarter of 2012.	Allylix has obtained Significant intellectual property surrounding Epivone™, including the recent issuance of several patents.	http://www.allylix.com/p ress/allylix- commercialize-novel- specialty-chemical

Category	Product	Company	Production Location	Market Status	Additional Info	Sources
Cosmetics	Squalane Brand name: Neossance	Amyris / Nikko Chemicals Co	Paraiso, Brazil	Commercial since Aug 2011. Nikko sells to Japanese cosmetics market.	Used for face, body and hair care, moisturizing creams, cleansing lotions, sunscreens, lipsticks & lip glosses, makeup primers, foundations, tinted moisturizers, etc.	http://www.businesswire .com/news/home/20110 819005151/en/Amyris- Signs-Multi-Year- Contract-Supply- Renewable-Squalane http://www.centerchem. com/PDFs/NEOSSANCE% 20SQUALANE%20- %20Datasheet%20F%20 0312.pdf
Oils	Algal Dielectric Oil	Solazyme	Peoria, Illinois, USA	Commercial production is expected to exceed 8.5 million gallons starting as early as the second half of 2013.	Full production is sold to Dow Chemical. Dielectric fluids are a \$2 - \$3 billion market – used to insulate electrical transformers.	http://seekingalpha.com/ article/590601-dow- looks-to-corner-the-2- billion-dielectric-fluids- market
Oils	Base Oils (lubricants) Brand name: Novaspec	Novii: Amyris / Cosan Joint venture	Paraiso, Brazil	To begin commercial production 2nd half of 2013.	Engine lubricants.	http://novvi.com.br/ media/imaqes/docs/novvi datasheet 2pg 012612.pdf http://seekingalpha.com/article/1205111-amyrismanagement-discussesq4-2012-resultsearnings-calltranscript?page=5&p=qanda&l=last
Rubber	Liquid farnesene rubber	Amyris and Kuraray		Commercial production and official market launch to begin in second half of 2013 for Kuraray.	For high performance car tyres.	http://seekingalpha.com/ article/1205111-amyris- management-discusses- q4-2012-results- earnings-call- transcript?page=5&p=qa nda&l=last http://www.gupta- verlag.com/general/news /dkt- 2012/11705/Kuraray

Category	Product	Company	Production Location	Market Status	Additional Info	Sources
Fuels	Algal Diesel fuel Brand name: Sola Diesel	Solazyme	Peoria, Illinois, USA	Commercial production at 75,000 liter scale since 2008.	Mostly sold to US Navy for battleships. Now also selling to United Airlines, Volkswagen and to car users through Propel forecourts.	http://seekingalpha.com/ article/1253151- solazyme-s-ceo- presents-at-raymond- james-34th-annual- institutional-investors- conference- transcript?all=true&find= solazyme
Fuels	Isobutanol	Gevo	Luverne, Minnesota, USA	Already commercially produced 150,000 gallons but suspended pending legal and scale-up issues	Selling under contract to Sasol.	http://seekingalpha.com/ article/1249331-gevo-s- ceo-discusses-q4-2012- results-earnings-call- transcript?page=6&p=qa nda&l=last
Fuels	Biodiesel Brand name: "No Compromise"	Amyris	Paraiso, Brazil	Commercial since 2011.	Supplies buses in Sao Paulo, Brazil and other niche fuel markets.	http://www.amyris.com/ News/131/Amyris-to- Supply-S%C3%A3o- Paulo-City-Buses-with- Renewable-Diesel-from- Sugarcane
Pharmaceu tical	Shikimic acid (star anise) used in Oseltamivir (Tamiflu) Anti-viral drug	Roche		Commercial since 2005.	Technology acquired from Draths Corporation. In March 2012 Roche told ETC Group: "For our Tamiflu production we mostly rely on the microbial fermentation process."	http://www.etcgroup.org /sites/www.etcgroup.org/ files/Final_CBD_Star%20 Anise_case_study_TA.pdf
Pharmaceu tical	Sitagliptin- dipeptidyl peptidase-4 inhibitor (Diabetes drug)	Merck/ Codexis		Commercial since 2012 – FDA approved in USA.		http://www.bio.org/articles/current-uses-synthetic-biology?page=show

Category	Product	Company	Production Location	Market Status	Additional Info	Sources
Animal Feed/ Fuel	MGT – Mascoma Grain Technology (grain treated with synthetic enzymes)	Mascoma / Lallemand Ethanol Technology		Commercial since 2012. Approved for animal feed use in the US.	Mascoma reported in 2012 that MGT was used in production of over 20 million gallons of ethanol in commercial trials – expects that it will begin recognizing revenues from its MGT product in the first quarter of 2012.	http://www.mascoma.co m/download/MCM- LETMGT_Update_Press _Release_FINAL.pdf
Chemicals	Succinic Acid /polyester polyols	Myriant	Lake Providence, Louisiana, USA	Due to start commercial production 1st Quarter of 2013.	The plant will produce 30 million pounds of biosuccinic acid annually. This initial capacity is already sold out and plans are in place to expand Myriant's production capacity in 2014 to 170m lb/year Partnering with Piedmont Chemical to produce urethane foams, coatings, adhesives and sealants.	http://www.myriant.com /platform/lake- providence-facility.cfm . http://www.myriant.com /media/press- releases/piedmont- chemical-launches- renewablepolyols- leveraging-renewable- chemicals-from-dupont- and-myriant.cfm
Chemicals	Succinic Acid	Bioamber and Mitsui	Pomacle, France; Sarnia, Ontario, Canada	Commercial since Jan 2010	Currently produces in 350,000 litre fermenter in France. New 17,000 metric tons facility in Ontario to become operational in 2013 in collaboration with Mitsui.	
Crops	Modified corn with built in degrading enzyme. Brand name: Inzyme	Agrivida	Iowa and Indiana, USA	Small open test plots of total less than 100 acres were planted in 2012.		http://www.agrivida.com /news/releases/2012jun5 .html

Category	Product	Company	Production Location	Market Status	Additional Info	Sources
Crops	Modified corn with built in degrading enzyme.	Syngenta/ Verenium	Merill, Iowa, USA	Commercially available. Approved by EPA 2011.	Syngenta is contracting farmers to grow Enogen crop in 2013 for use by ethanol companies – e.g. Plymouth Energy, Siouxland	http://www.syngenta.co m/country/us/en/Enogen /Newsroom/Pages/Plymo uthNewsRelease.aspx
	Brand name: Enogen				Energy, Golden Grain Energy.	