The Resurgence of Industrial Biotech

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The 20th Century: Early Successes

In 1929, Pfizer began producing citric acid fermentatively using *Aspergillus niger*. Today, citric acid is a commodity chemical produced solely using microbes. An estimated 1.5 million metric tonnes are produced using roughly the same process as developed in 1929, and the chemical sells for less than $0.80/kg. Over the next seventy years, other biologically produced chemicals would follow in the wake of the successful citric acid process. Gluconic acid, itaconic acid, lactic acid, and 1,3-propanediol are all globally traded chemicals produced by microbes. It remains more costly to produce each of these compounds petrochemically than biologically, and these chemicals stand as examples of commercially successful industrial biotech products.

The 2000s: A Race To The Bottom

Despite the success stories of the 20th century, many would say industrial biotech has struggled over the past decade. The science has moved forward, but few companies have been successful in commercializing fermentation-derived small molecules. While failure is not unusual to startups, and an estimated 90% of startups fail, it is difficult for an industry to thrive when technical failure is only realized after constructing a $100M+ production facility.

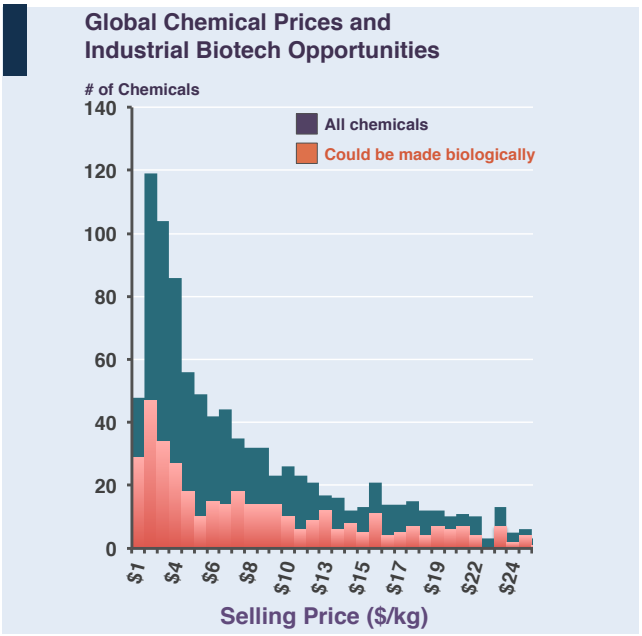
One of the most significant problems in the field is that startups began by chasing after the lowest-value, highest-volume fuels and commodity chemicals. These were pursued, in part, because there was no market risk. If you could make it (cost competitively), it would be bought. Most, however, ran into the problem that all mass is not created equal. Sugar, which remains the feedstock of choice for most fermentation processes, is 53% oxygen and 40% carbon. Nearly all of this oxygen must be stripped from sugar to produce a molecule suitable for use as a fuel. Thus, for biofuels the cost of usable mass is not the cost of sugar (*ca.* $0.30 - 0.35/kg), but something 2- to 5-fold higher. It is already difficult to produce a $1/kg fuel given this feedstock constraint, and there is virtually no room for unexpected process inefficiencies.

The most efficiently produced biofuel today remains ethanol, where a 51% (w/w) yield from sugar is theoretically possible using current strains. The theoretical efficiencies of next-generation biofuel targets, including n-butanol, isobutanol, biodiesel, and farnesane all fall below this standard. It should not be surprising than that when an estimated 10% of U.S. ethanol plants stopped production in 2013 due to high corn costs[1], these less efficient technologies were also struggling to produce fuels commercially.

The 2010s: Rediscovering 20th Century Successes

On a positive note, what the field did take away from the past decade is experience and a recalibration of expectations. There will be industrial biotech successes this decade, and they will likely be had by companies targeting chemicals where biology is inherently advantaged over oil. Like the successes from the 20th century, most of these products will be highly oxidized (*i.e.*, they maintain the oxygen present in sugar) chemicals.

The other piece of the puzzle is identifying chemicals with a bigger potential margin than fuels. At Lygos, we have collected price data on over 1,100 globally traded chemicals (see below) and identified hundred of chemicals that sell for greater than $2/kg. We have mapped out routes to make around 43% of these compounds microbially. While not all make economic sense, many chemicals can be found where the estimated total cost of fermentative production is less than the raw material cost for the incumbent petrochemical process. Moreover, market growth for these products is often held back by their current high cost. These are the products where petroleum cannot compete against industrial biotech and were we believe industrial biotech will thrive.



[1] Eligon J., Wald ML., "Days of promise fade for ethanol." The New York Times (Mar 16, 2013)

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