

such as sexually transmitted diseases and the need to compete for mates³.

Lacking meiotic recombination, asexual species are often seen as evolutionary dead ends, doomed to extinction owing to genomic decline (an accumulation of detrimental mutations). Yet some asexual species have survived and thrived much longer than expected, puzzling researchers⁴. Ricemeyer and colleagues investigate this phenomenon in the Amazon molly (*Poecilia formosa*). By examining the effects of asexual reproduction on its genome, they provide evidence that the evolutionary potential of an asexual species can be rescued by a mechanism called gene conversion.

The Amazon molly was the first asexual vertebrate known to science⁵. It is a small, all-female fish species that bears live young and inhabits freshwater habitats from north-eastern Mexico to southern Texas. The species is thought to have originated from a single hybridization event between a female Atlantic molly (*Poecilia mexicana*) and a male sailfin molly (*Poecilia latipinna*) near Tampico, Mexico, around 100,000 years ago^{6,7} (Fig. 1). Unlike many asexual vertebrates, the Amazon molly produces clonal eggs by skipping recombination during meiosis, generating eggs that have the same genetic content as all the other cells in its body. The eggs still require contact with sperm to trigger embryo development, so they are pseudo-fertilized by males of co-existing *Poecilia* species, but the sperm's genetic material is typically discarded, resulting in daughters that are genetic clones of their mothers⁸.

The Amazon molly has persisted much longer than indicated by theoretical expectations⁷. How have asexual lineages such as this one managed to survive for so long? The Amazon molly is well placed to address that question, especially given that the sexual parental species, *P. mexicana* and *P. latipinna*, still exist, enabling direct comparison of the evolution of similar genomes in sexual and asexual organisms. Because of their non-recombining nature, asexual genomes are expected to diverge more rapidly (the Meselson effect)⁴, and to accumulate more deleterious mutations (through 'Muller's ratchet')⁹ than are genomes of sexual species. Asexual genomes are also expected to be slower to adapt, given that beneficial alleles cannot be combined as quickly in an asexual individual as they could be in a sexually reproducing species¹⁰.

Ricemeyer *et al.* address those predictions directly through whole-genome sequencing and comparative genomic analyses of the asexual Amazon molly and its sexual parental species. The authors provide evidence of greater mutation accumulation in Amazon molly genomes than in those of their sexual counterparts, supporting predictions of the Meselson effect. However, they found no

evidence for higher accumulation of deleterious mutations in the asexual genomes, in contrast to predictions according to Muller's ratchet. These seemingly contradictory results – faster mutation accumulation but no evidence of deleterious effects – suggest that there must be some molecular mechanism that eliminates deleterious mutations once they emerge.

There are several mechanisms that could reduce the build-up of deleterious mutations, one of them being gene conversion. Unlike meiotic recombination, gene conversion is a 'copy and paste' DNA-repair mechanism that involves copying a segment of DNA from one chromosome to another, typically to repair double-strand breaks¹¹. Experiments have shown that gene conversions eliminate deleterious mutations in the genomes of plant organelles called chloroplasts¹².

Ricemeyer *et al.* demonstrate that gene conversion is a widespread phenomenon in Amazon molly genomes. They show that thousands of pairs of alleles that differ (are heterozygous) in the sexual species are the same (homozygous) in the asexual genomes, indicating that DNA segments have been copied from one chromosome and pasted into the other in the same pair (Fig. 1). Regions of the genome that have undergone gene conversion are commonly found close to regions associated with DNA breaks; they are also more likely to have eliminated, rather than spread, deleterious mutations. Functionally, gene conversions were associated with regions that encode immune proteins, possibly supporting the immune system's ability to fight off pathogens. Gene conversions were also associated with non-coding regulatory regions that might influence the compatibility of the two parental genomes when combined in a

hybrid organism.

Remarkable advances in technologies for genome sequencing are now enabling scientists to investigate some of the most long-standing evolutionary paradoxes. Although it has been proposed that gene conversion prevents genomic decline, the idea has rarely been tested directly at the genomic level. Ricemeyer and colleagues show how gene conversions can interact with natural selection to slow the predicted genomic decay of asexual organisms. In doing so, they have opened up a fresh avenue of research into the dynamic interplay between cellular mechanisms that affect DNA variability, genome evolution and natural selection. Although the role of gene conversion remains to be further explored in other asexual systems, this study represents a landmark in the field and will guide future research on genome evolution and the evolutionary potential of clonal species.

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In retrospect

100 years of synthetic fuels

Ferdi Schüth

The Fischer–Tropsch synthesis shaped history by providing a way of making liquid fuels from coal. It is now causing a stir again as a route to sustainable fuels.

Few industrial chemical processes have a history as winding as that of the Fischer–Tropsch (FT) synthesis, which was reported by Franz Fischer and Hans Tropsch 100 years ago in *Brennstoff-Chemie*. This catalytic process converts syngas – a mixture of carbon monoxide and hydrogen gas – into hydrocarbons. Initially used to synthesize liquid fuels from

coal, it now holds promise as a way to make hydrocarbons, including aviation fuel, from renewable sources of carbon.

At the beginning of the twentieth century, there was much scientific and commercial interest in finding catalytic reactions that converted small molecules into valuable products. For example, the industrial Haber–Bosch

process for synthesizing ammonia (NH_3) from nitrogen and hydrogen was discovered, with the first industrial plant beginning operations in 1913.

The chemistry of syngas was also studied intensively. At that time, syngas was made from coal, but it can, in principle, be prepared from any carbon-containing feedstock. A catalytic synthesis of methane from syngas was reported² in 1902, and a patent³ for a process for making alcohols and hydrocarbons from syngas was published in 1913. In 1922, Fischer and Tropsch discovered⁴ that syngas could be converted into a mixture of oxygen-containing compounds, which contained only trace amounts of hydrocarbons. But their real breakthrough came with the discovery of the process that now bears their names.

Compared with previously published processes involving syngas, the key innovation of the FT synthesis¹ was that it formed higher hydrocarbons – long-chained ones such as those found in liquid fuels and solid waxes – at atmospheric pressure and at relatively low temperatures. The authors reported that iron and cobalt catalysts were more effective at producing higher hydrocarbons than was a previously reported nickel catalyst, which produced mostly methane. The process was found to be rather versatile, tolerating various syngas compositions and forming hydrocarbons with chain lengths that differed depending on the reaction conditions and the exact nature of the catalyst used. The authors also proposed a reaction mechanism involving the formation of carbides (solids in which carbon atoms are located in voids between packed metal atoms).

Given that several patents and publications describing the chemistry of syngas had already been published, it is unsurprising that the patent for the FT process was not immediately granted when it was filed⁵ in 1925. Because of this delay, Fischer was keen to publish a paper to establish that he and Tropsch were the first to discover the process⁶, but without jeopardizing the patent.

The authors therefore tried to deposit a first account of the work in a sealed envelope with the Prussian Academy of Sciences in November 1925. However, such a procedure did not comply with the policy of the academy. That report, together with a second manuscript describing further details of the process, was then filed at the Notgemeinschaft der Deutschen Wissenschaft (the precursor organization of the current German science funding organization, the DFG) in January 1926. Those two accounts were eventually published together with a third instalment as the *Brennstoff-Chemie* paper¹, explaining in the footnote “sehen uns aber jetzt zur Veröffentlichung genötigt” (“we now feel compelled to publish”). The first report was also published separately in a different journal⁷. The patent⁵ was eventually granted in 1929.

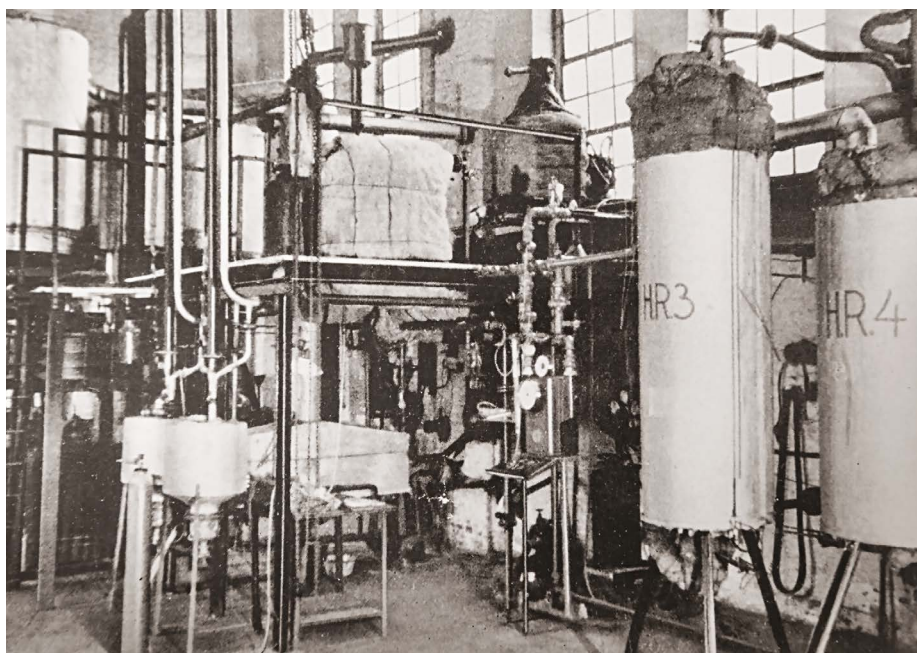


Figure 1 | The early days of the Fischer–Tropsch (FT) process. A FT pilot plant at the Kaiser-Wilhelm-Institute for Coal Research in Mülheim, Germany (now the Max Planck Institute for Coal Research) in the 1930s – the institute at which Franz Fischer and Hans Tropsch discovered the process¹ that is now named after them.

The FT process was quickly adopted for large-scale use (Fig. 1) and was one of the first catalytic processes to be deployed on an industrial scale, mainly to produce liquid hydrocarbons (synthetic petrol) from coal. It met a substantial part of the German demand for fuel during the Second World War, providing the capacity to produce around 740,000 tonnes per year by 1944 (see go.nature.com/4bkz58o). The rest of the demand was met by the Bergius–Pier process – the direct reaction of coal with hydrogen at high pressure – which had a capacity of 4 million tonnes per year⁸.

After the war, with cheap oil becoming increasingly available, the FT process stopped being used industrially in most places, with

“The catalysts identified by Fischer and Tropsch are still relevant in commercial processes today.”

one notable exception: South Africa⁹. The South African Coal, Oil and Gas Corporation (widely known as South African Synthetic Oil limited, or SASOL) took advantage of the country’s abundant coal reserves by using the FT process to make liquid hydrocarbons. For decades, South Africa was subject to international economic sanctions aimed at ending apartheid, culminating with an oil embargo in 1987. During this period, it built up a substantial capacity for petrol production, exceeding 160,000 barrels a day⁹.

The next phase of commercial FT plants saw

a change in feedstock, moving from coal to natural gas. The first such installation outside South Africa was commissioned in Bintulu, Indonesia, in 1993, with several more starting operations in the years thereafter⁹, including the Pearl plant in Ras Laffan, Qatar – now one of the biggest chemical plants in the world. Nevertheless, coal-based plants were still being built, especially in China, to make use of domestic coal.

The iron and cobalt catalysts identified by Fischer and Tropsch are still relevant in commercial processes today, although they have been optimized in many ways over the past 100 years⁹. For example, the size of the catalyst particles has been tuned; additives known as promoters have been added to boost the performance of the catalytically active components; and improvements have been made to the support materials, which provide a structural matrix for the active components and can thereby alter the activity, stability and other properties of the catalytic mixture that affect the outcome of the FT process. Ruthenium was also quickly identified as an excellent catalyst (see ref. 10, for example), but the high cost of this element limits its commercial viability⁹.

The original reactor layout described by Fischer and Tropsch was a type known as a packed-bed reactor, in which the reaction mixture is passed through a stationary bed of catalyst pellets. One of the key challenges for reactor design has been finding ways to dissipate the heat generated by the process. Substantial progress has been achieved in this regard¹¹. This includes the use of multitubular reactors, in which reactants flow through

many catalyst-filled tubes that are connected in parallel and immersed in a coolant-filled container; fluidized bed reactors, in which the reaction gases (the syngas and gaseous products) flow upwards at speeds high enough to suspend the catalyst particles in the reaction mixture; and slurry phase reactors, in which the catalyst is suspended in a liquid through which a gas is bubbled. The type of reactor chosen depends on various factors, including the catalyst used, the temperature and pressure of the process and the composition of the reaction mixture.

The original FT process operated at atmospheric pressure or slightly higher, and at temperatures above 250 °C. Today, two sets of conditions are typically used⁹: low-temperature processes carried out at 180–260 °C yield mainly long hydrocarbon chains; and high-temperature processes at 290–360 °C produce short hydrocarbons. Depending on other parameters of the process, the operating pressures range from slightly above atmospheric pressure up to several tens of atmospheres.

Fischer and Tropsch correctly suggested that their reaction occurs through the polymerization of carbon-containing species at the surface of the catalyst, making it the first example of a surface polymerization reaction to be recognized as such. The process produces a mixture of hydrocarbon molecules with various chain lengths, with the amounts of distinct hydrocarbons governed by the reaction's 'polymerization statistics' – which mathematically describe the probability of a CH₂ group being added to a growing chain versus the probability of a chain desorbing from the catalyst's surface. The resulting statistical distribution of products makes it extremely difficult to tune the FT process to synthesize hydrocarbons with a narrow range of molecular masses, as is generally desirable for applications. The process is therefore often combined with other reactions – such as hydrocracking, which breaks long-chain hydrocarbons into shorter chains – to maximize the yield of products with a desired chain length¹².

Research into FT synthesis continues to be highly active, with the focus now on producing hydrocarbon fuels independently of fossil-fuel resources. For example, FT-derived hydrocarbons have been approved by international bodies for use as commercial aviation fuel, as long as the blend contains at least 50% conventional oil-derived fuel¹³. Making syngas from biomass or municipal solid waste, or from captured carbon dioxide, could substantially reduce the CO₂ footprint of FT-derived fuel. Such efforts also require innovations in industrial processes – for example, companies are already producing sustainable aviation fuel in small, modular FT plants using microchannel reactors (see

go.nature.com/47p8adz). Further substantial developments in this important sustainability technology are surely on the way.

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Precision health

Smart-watch data reveal early insulin resistance

Christopher M. Hartshorn

Patterns in continuous data from wearable devices could reveal early metabolic dysfunction long before routine clinical tests detect it. **See p.451**

Many chronic diseases unfold slowly as continuous biological processes, yet they are typically detected through brief clinical snapshots – at annual visits to a physician or from isolated laboratory tests, for instance. Insulin resistance, a condition in which the body must work harder to regulate blood sugar, can develop for years before it becomes visible in routine diagnostics. On page 451, Metwally *et al.*¹ show that patterns in everyday-life-style data, collected outside the clinic from

of metabolic disease.

Insulin resistance is a compensatory state that precedes overt disease by many years². One reason why insulin resistance is difficult to detect early is that the body compensates for declining metabolic efficiency remarkably well. Blood-sugar levels can remain in the normal range even as the physiological effort required to maintain them steadily increases. Most clinical assessments rely on occasional measurements taken under standardized conditions. This approach is well suited to diagnosing a disease once it has become established, but not to capturing gradual, adaptive change. As a result, early metabolic dysfunction is often invisible until compensatory mechanisms begin to fail, at which point interventions become complex and costly.

Metwally and colleagues address this lack of visibility by focusing on how the body behaves in daily life, rather than on isolated clinical measurements. Continuously collected smart-watch data capture fluctuations in activity, sleep and cardiovascular function over time that, generally, reflect the cumulative demands of metabolic regulation. By integrating these longitudinal signals with demographic characteristics and readily available blood biomarkers, the authors trained a computational model that identifies stable patterns linked to insulin resistance. The

“The authors’ work reflects a broader shift in how health and disease might be understood in the era of continuous data.”

consumer wearable devices, can reveal this hidden phase earlier. Rather than a snapshot, this offers something closer to a ‘movie’ of metabolic health. By drawing on continuous signals from daily life, the authors’ approach highlights physiological strain that is invisible to episodic testing. The work raises the possibility that identifying insulin resistance – a key early feature of type 2 diabetes – earlier could enable simpler interventions and, ultimately, reduce the downstream burden