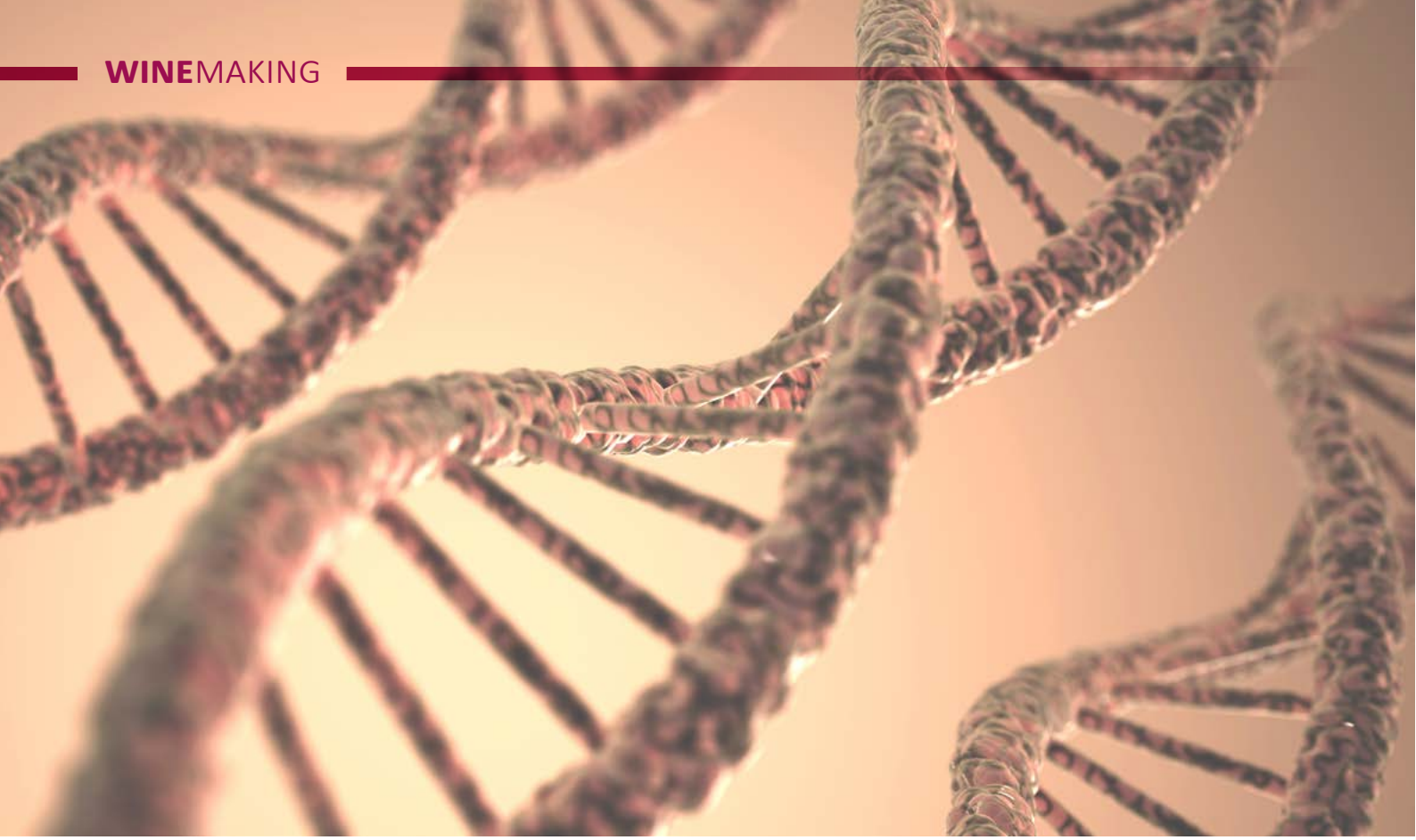

Innovation

Synthetic Biology

What is it and how could it potentially benefit the wine industry?

Writer **Simone Madden-Grey** begins an exploration of so-called Synthetic Biology and its potential application for grape and wine production.

As Australia's relationship with biotechnology evolves, so too has its relationship with the use of Genetically Modified Organisms (GMOs). To date, all mainland states have lifted the moratorium on the use of GMOs moving instead to licencing, and regulating the process through the Office of the Gene Technology Regulator. This means that a number of GMOs are being used to the benefit of the Australian economy and community.

Fundamental to Australia's original nationwide ban on the use of GMOs was the stated goal of allowing sufficient time to pass in which to assess potential risk to human health and welfare. This now being considered passed, the potential benefit biotechnology, including GMOs, could bring to the country is being investigated. The Australian wine industry however maintains its position that no GMOs can be used in the production of wine. Should that position change, the industry's scientific and research communities are ready to assist with the implantation of work they have been undertaking to future-proof the industry.

Wine production faces many challenges, not least of which is climate change and both tradition and technology offer multiple ways in which to respond. Synthetic Biology, which includes GMOs, offers one such technology that may be used in order to strengthen industry response. And if climate change is the measure of how quickly the industry needs to adapt then an increased understanding of Synthetic Biology and how it might benefit the industry without undermining trade relationships, would be timely.

For this to be successful a rational, well-informed, science-based discussion is required in the context of practical application and experience. This will help create a strategy that balances the benefits of this technology with commercial drivers, particularly the response from key export markets.

As the first in a series exploring Synthetic Biology, this article aims to review the

And if climate change is the measure of how quickly the industry needs to adapt then an increased understanding of Synthetic Biology and how it might benefit the industry without undermining trade relationships, would be timely.

definition of Synthetic Biology before considering its regulation, application and perception in the consumer market, with future articles.

What is Synthetic Biology?

The science of Synthetic Biology has continued to evolve in recent years, much like the definition itself. Collaborative and interdisciplinary, Synthetic Biology draws on mathematical and computational, biomolecular, chemical and physical sciences together with information technologies and engineering. It has folded within its definition GMO, Genetic Engineering and Systems Biology to emerge as Engineered Biology in countries such as the USA. Though the scientific community have moved through these definitions as quickly as research has progressed, the wider community has yet to catch up. For the purposes of this article the term Synthetic Biology will be used and assumed to be a synonym of Engineered Biology.

In Australia, the Office of the Gene Technology Regulator defines Synthetic Biology as follows: "A genetically modified organism (GMO) is a plant, animal or other organism that has been modified using gene technology or an organism that has inherited modified traits from a GMO. Gene technology is also known as genetic engineering, biotechnology and genome editing. Synthetic Biology uses gene technology to make synthetic organisms or products. As such, most Synthetic Biology organisms are also GMOs … There is a large amount of overlap between 'gene technology' and the newer term 'Synthetic Biology'."

> Many of the original concerns about GMOs from more than a decade ago are able to be addressed due to the enhanced accuracy of Synthetic Biology techniques.

AWRI Research Manager Dr Anthony Borneman says it can be challenging to define Synthetic Biology because there are multiple definitions used depending on the work at hand. He says the area of Synthetic Biology began when synthetically derived DNA was incorporated into projects, bringing with it an engineering perspective, which until then was a technique that had not been used before. Synthetic Biology is now moving into redesigning synthetic organisms in projects such as the Synthetic Yeast Project 2.0, an international collaboration seeking to synthesize all 16 chromosomes in the yeast strain *Saccharomyces cerevisiae*.

The fundamental role of engineering in Synthetic Biology is highlighted in the paper 'Synthetic genome engineering forging new frontiers for wine yeast', when Isak S. Pretorius writes, "Synthetic Biology combines molecular approaches with engineering principles to 'forward engineer' genetic systems by constructing collections of modular parts to design, build, and fine-tune gene regulatory networks analogous to controllable electrical circuits".

Synthetic Biology process

Synthetic Biology typically consists of four phases. The Design phase draws on research and data input for computational modelling of the experiment. The software also assembles communication protocols with the build instruments. The Build phase involves building the synthetic DNA and automating the development of cells containing the synthetic DNA. The Test or Learn phase tests the new DNA code

While not available for use in Australia, Synthetic Biology-enhanced yeast strains are being used with commercial success in the US.

To successfully navigate this new frontier the industry must proactively address the complexities of integrating these technologies into Australian wine production, whilst protecting existing commercial relationships.

during a full growth cycle. During this phase metabolomics, or a bioinformatic analysis, is used to profile all molecules that have been produced. This ensures no other molecules have been inadvertently created and is done by confirming that the synthetic molecular profile is aligned with the original, non-engineered profile. Iterative Design-Build-Test cycles continue to inform and refine the design until the desired outcome is achieved. The final phase is industrial scaling at low cost.

The Australian scientific community has continued to investigate and publish ground-breaking research in the field of Synthetic Biology and wine, whilst working within the confines of the industry position that prevents the use of GMOs in wine production. Dr Borneman says his work at the AWRI has often used GMO principles for ground truth and proof-of-concept work, in this case with respect to *S. cerevisiae* yeast cells. The example he cites is editing the gene sequence of yeast in the lab to specifically delete a gene and then review the effect on winemaking characteristics. Once this has been proven in the lab, the team can devise strategies to "nudge" biology in order to achieve a natural (non-GMO) mutation in that particular gene. He acknowledges that the non-GMO route can be a time consuming and costly process but the outcome is known and the result not only satisfies the industry's GMO position but ultimately benefits the wine industry.

Many of the original concerns about GMOs from more than a decade ago are able to be addressed due to the enhanced accuracy of Synthetic Biology techniques. Dr Borneman says the convergence of Synthetic Biology with DNA sequencing has facilitated genome sequencing, and the use of techniques such as metabolomics make it possible to track and provide data as to exactly what changes have been made to an edited genome. In other words, Synthetic Biology techniques have allowed scientists to move from sequencing the order of DNA chemical building blocks to sequencing entire sets of genetic instructions within each genome, which includes chromosomes, genes and DNA. Metabolomics testing can provide increased confidence and accuracy in what is being produced by means of a full molecular profile comparison between a GMO yeast and the original non-engineered strain. Using these techniques, for example, the AWRI was the first to successfully design a prototype wine yeast strain (AWRI 1631) that included a synthetic pathway for the production of the potent aroma compound raspberry ketone during fermentation.

Commercial implementation

While not available for use in Australia, Synthetic Biology-enhanced yeast strains are being used with commercial success in the US, where reasonable comparison with a natural organism is the threshold for government approval of GMO implementation.

In the aforementioned paper, Pretorius describes Synthetic Biology as a controversial and disruptive new science, which it undoubtedly is. To successfully navigate this new frontier the industry must proactively address the complexities of integrating these technologies into Australian wine production, whilst protecting existing commercial relationships. Weather events such as bush fires, droughts, floods and so forth together with continued success in export markets will be some of the drivers in this discussion. Should the industry choose a solution not of polarity but of nuanced understanding, it will benefit greatly by investing in understanding this area of science and research.

Simone Madden-Grey is a writer based in Melbourne, Australia writing about the people, places and stories she has discovered on her travels. Her portfolio can be found at happywinewoman.com including articles on climate and sustainability in the wine industry and travel covering the wine, regions and gourmet destinations of Australia and her home country, New Zealand.

Further information

Australian Grape and Wine: www.agw.org.au/policy-and-issues/biosecurity-environment-and-sustainability/genetically-modified-organisms

CSIRO Synthetic Biology Future Science Platform: www.csiro.au/en/research/production/biotechnology/synthetic-biology

Office of the Gene Technology Regulator: www.ogtr.gov.au

Interviews

Borneman, Anthony Dr. Research Manager, AWRI, Adelaide

Pretorius, Isak S. Professor. Deputy Vice-Chancellor, Research, Macquarie University, Sydney

References

Synthetic genome engineering forging new frontiers for wine yeast. Isak S. Pretorius (2017). *Critical Reviews in Biotechnology*, 37:1, 112-136, DOI: 10.1080/07388551.2016.1214945. www.doi.org/10.1080/07388551.2016.1214945

Bioinformational trends in grape and wine biotechnology. Thomas A. Dixon, Department of Modern History, Politics and International Relations, Macquarie University, Sydney, Thomas C. Williams, Department of Molecular Sciences and ARC Centre of Excellence in Synthetic Biology, Centre Headquarters, Macquarie University, Sydney and Isak S. Pretorius, Chancellery, Macquarie University, Sydney. *Trends in Biotechnology*, January 2022, Vol. 40, No. 1. www.doi.org/10.1016/j.tibtech.2021.05.001 GW