Synthetic all the way:
Engineering a synthetic yeast genome

Oriol Bárcenas López, Biotechnology B.Sc.
Universitat Autònoma de Barcelona

INTRODUCTION

- Synthetic biology is a rapidly evolving field that aims to design new biological systems (creating a chassis) or improve those already present in nature.
- These advances can provide innovative solutions for the sustainable production of non-native chemicals, as well as improve access to drugs. This would positively impact SDGs.
- The Sc2.0 project aims at generating a completely synthetic *S. cerevisiae* genome, with designer chromosomes and added functionalities. It will become the first synthetic eukaryote, enhancing our knowledge of cellular eukaryotic biology and chromosomal synthesis and organization.

OBJECTIVES

- Present the *Saccharomyces cerevisiae* 2.0 project (Sc2.0), focusing on its modifications and their impact on cellular fitness.
- Study the inducible recombinase system SCRaMbLE and its variants.
- Discuss the biotechnological applications that these technologies may bring: increased biological knowledge of *S. cerevisiae* and easy generation of genetic and phenotypic diversity.

METHODOLOGY

- Evaluate relevant literature regarding synthetic biology.
- Analyze all literature describing the Sc2.0 project, including the basis of the project and checkpoints and breakthroughs in the development.
- Presenting the potential biotechnological applications of the SCRaMbLE technology.

THE Sc2.0 PROJECT

The Sc2.0 Consortium

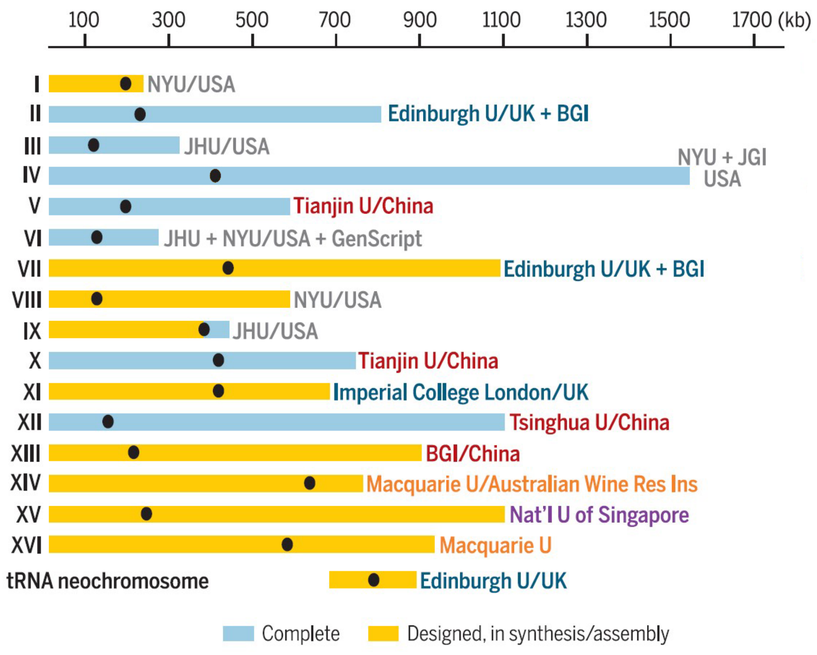


Figure 1. Sc2.0 consortium: international efforts to create synthetic life.

5 different countries are involved (USA, UK, China, Australia, and Singapore). Currently, only 7 of the 17 planned chromosomes have been completely synthesized.

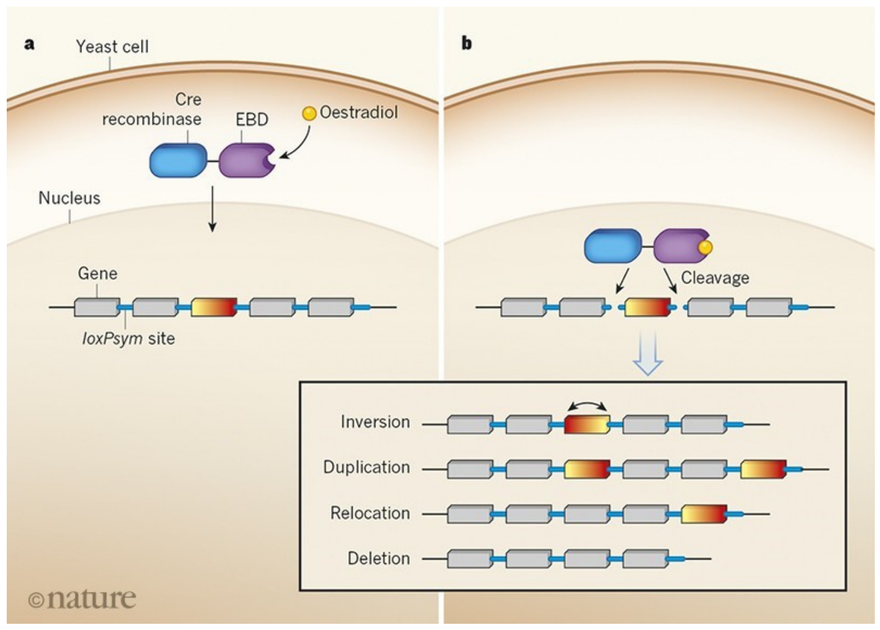
Adapted from ref. 1.

The SCRaMbLE technology

Figure 2. SCRaMbLE: a key tool for genome editing and strain evolution.

The Synthetic Chromosome Rearrangement and Modification by loxP-mediated Evolution enables the rearrangement of non-essential genes to accelerate strain evolution.

Extracted from ref. 3.

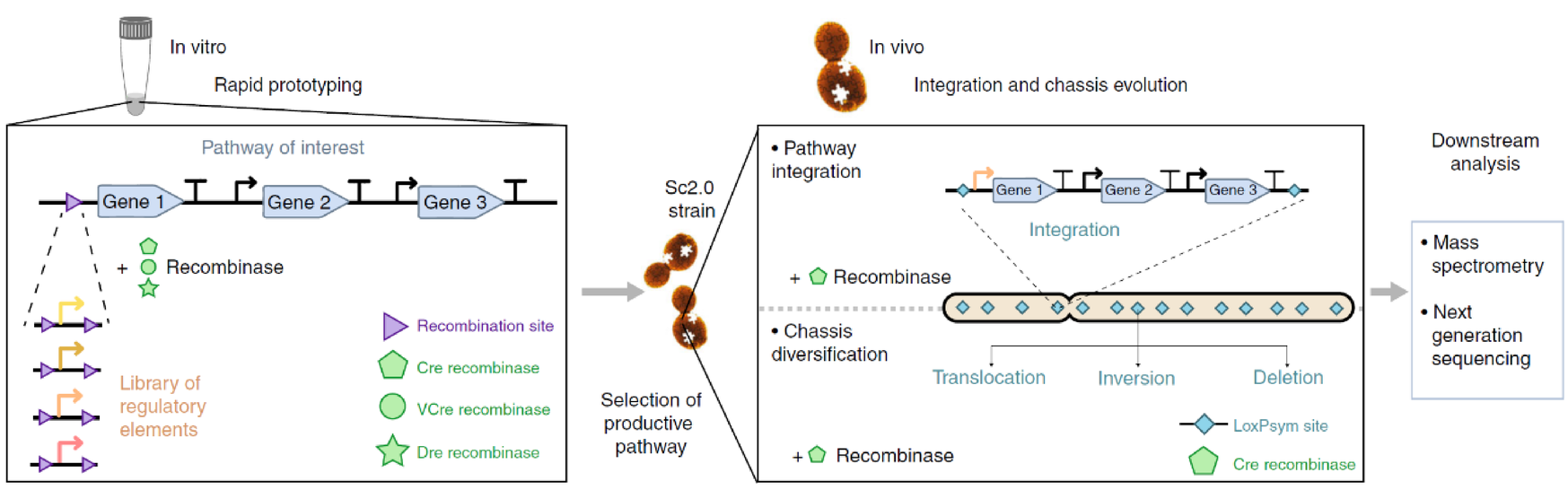


Applications: rapid pathway and strain evolution

Figure 3. SCRaMbLE-in toolkit.

This system enables rapid engineering of productive pathways, followed by their random integration in the genome and the evolution of the productive chassis. The downstream analysis allows for the elucidation of the changes responsible for the observed phenotype. This will deepen our knowledge of environmental stress resistance or the enhanced productivity of a product of interest.

Extracted from ref. 4.



CONCLUSIONS

- The Sc 2.0 project has created a “build-to-understand” organism.
- It enables the identification of previously unknown gene roles, as well as incorporating an easy and reliable inducible recombination technology: SCRaMbLE.
- The recombination system has exhibited low basal activity and can be fine-tuned. No off-site recombinations have been observed, and strains have remained stable for up to 125 mitotic generations (*synIII*).
- However, the system has been yet unproven in large-scale bioreactors: unknown genetic stability and applicability in industrial settings.
- The possibilities offered by this technology are potentially limitless. The induction of SCRaMbLE enables a combinatorial potential never before seen, which will have a deep impact on biotechnology as a whole.

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