

VersaTile Platform

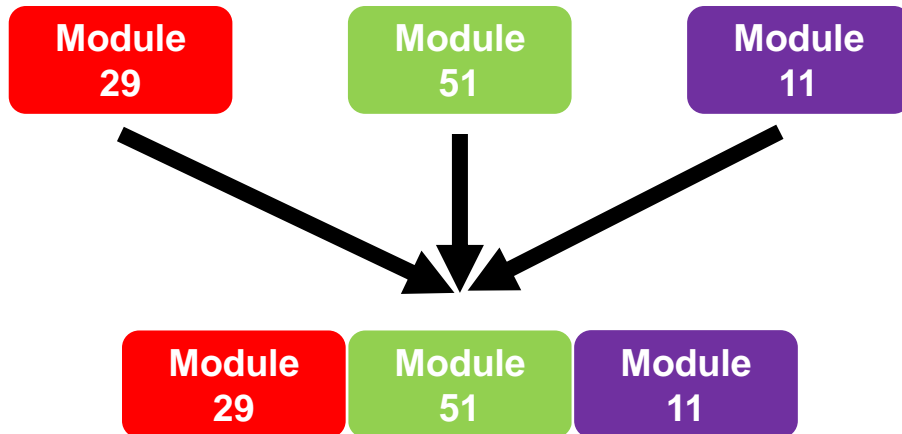
SYNTHETIC BIOLOGY OF MODULAR PROTEINS WITH APPLICATIONS IN INDUSTRIAL AND MEDICAL BIOTECHNOLOGY

Dr. Koen Tyberghein – business developer

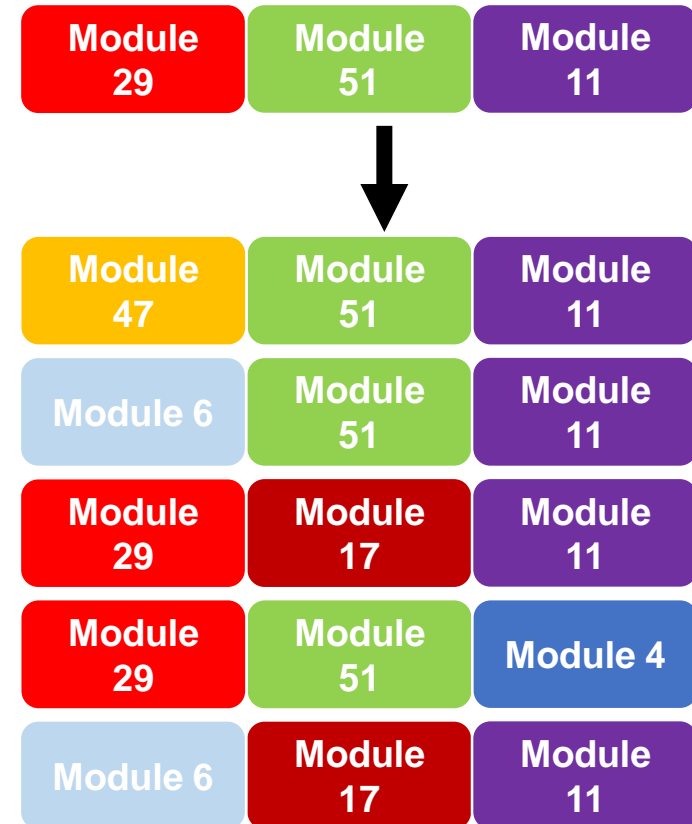
Prof. Yves Briers

SYNTHETIC BIOLOGY OF MODULAR PROTEINS

Neofunctionalization
“New to nature”



Improving properties

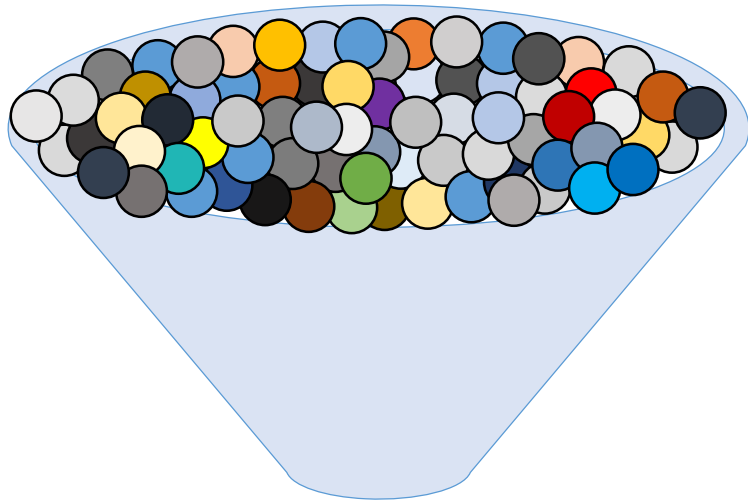


VERSATILE TECHNOLOGY

Step 1:

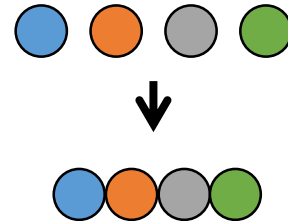
Make your TILE repository

Tile = vector containing module-specific DNA (variants)

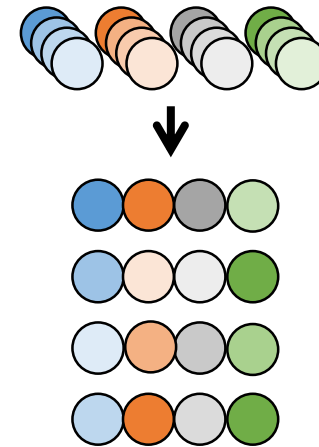


Step 2: Shuffle TILES in a versatile way

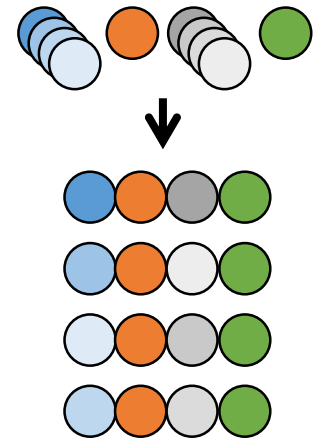
RATIONAL
ASSEMBLY



COMBINATORIAL
ASSEMBLY

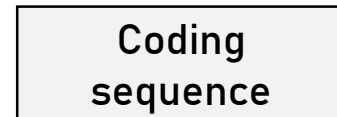


SEMI-RANDOM
ASSEMBLY



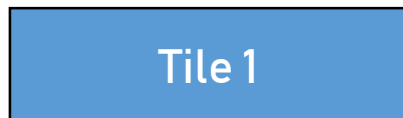
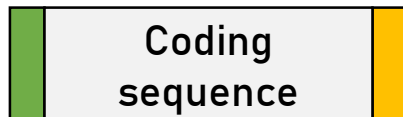
VERSATILE CLONING: TILE CONSTRUCTION

Position tags

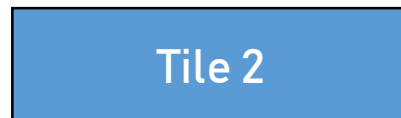
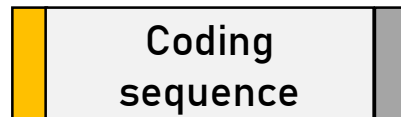


- Position 1  
- Position 2  
- Position 3  
- Position 4  

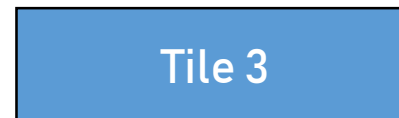
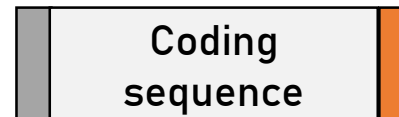
Position 1



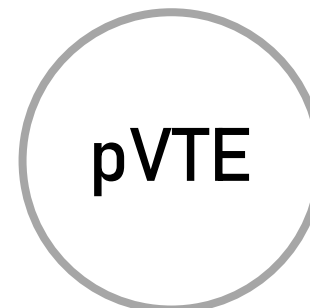
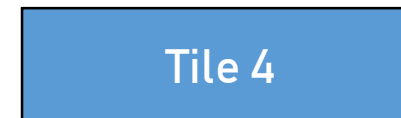
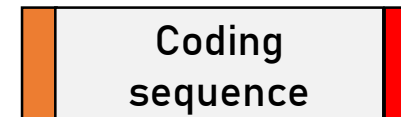
Position 2



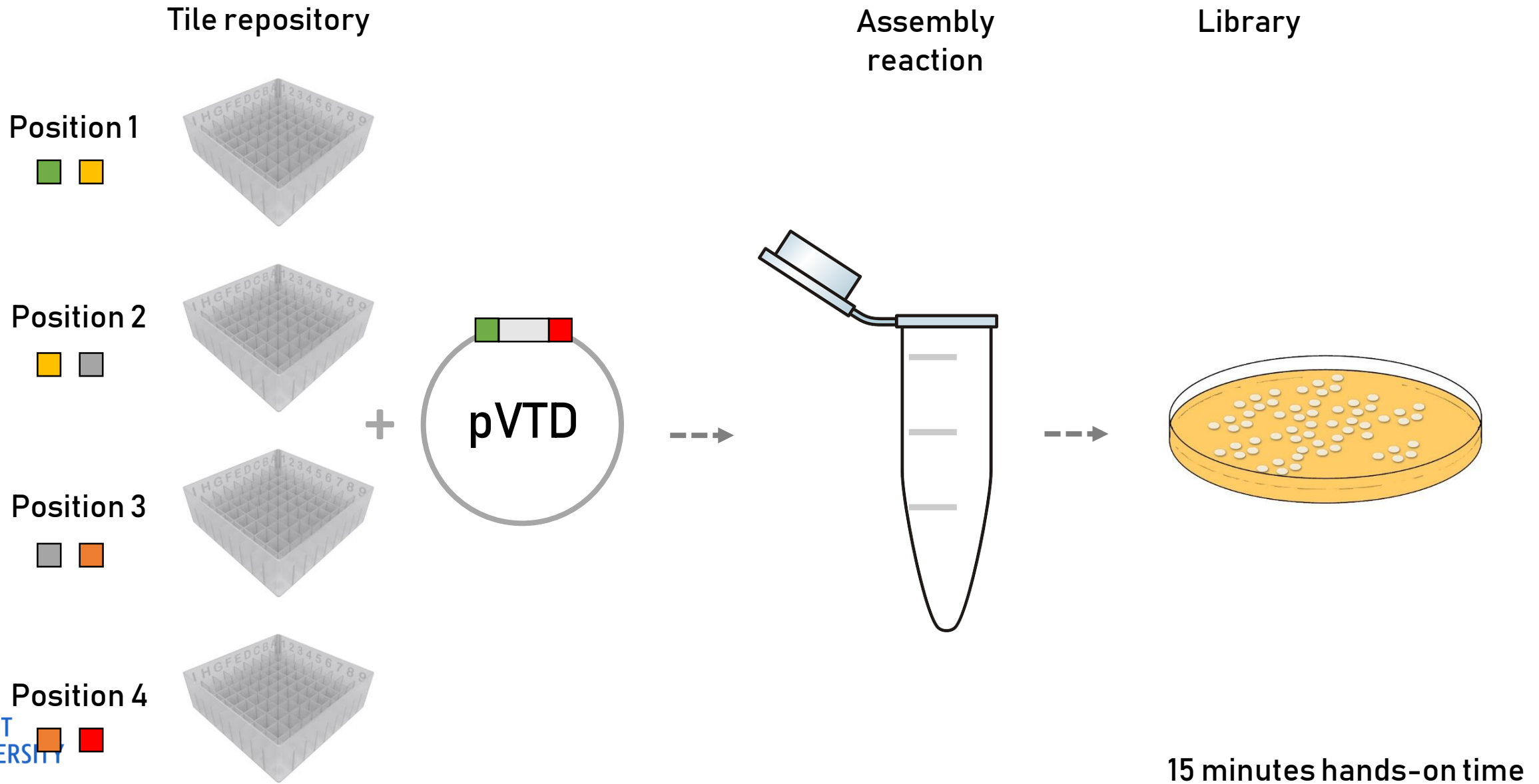
Position 3



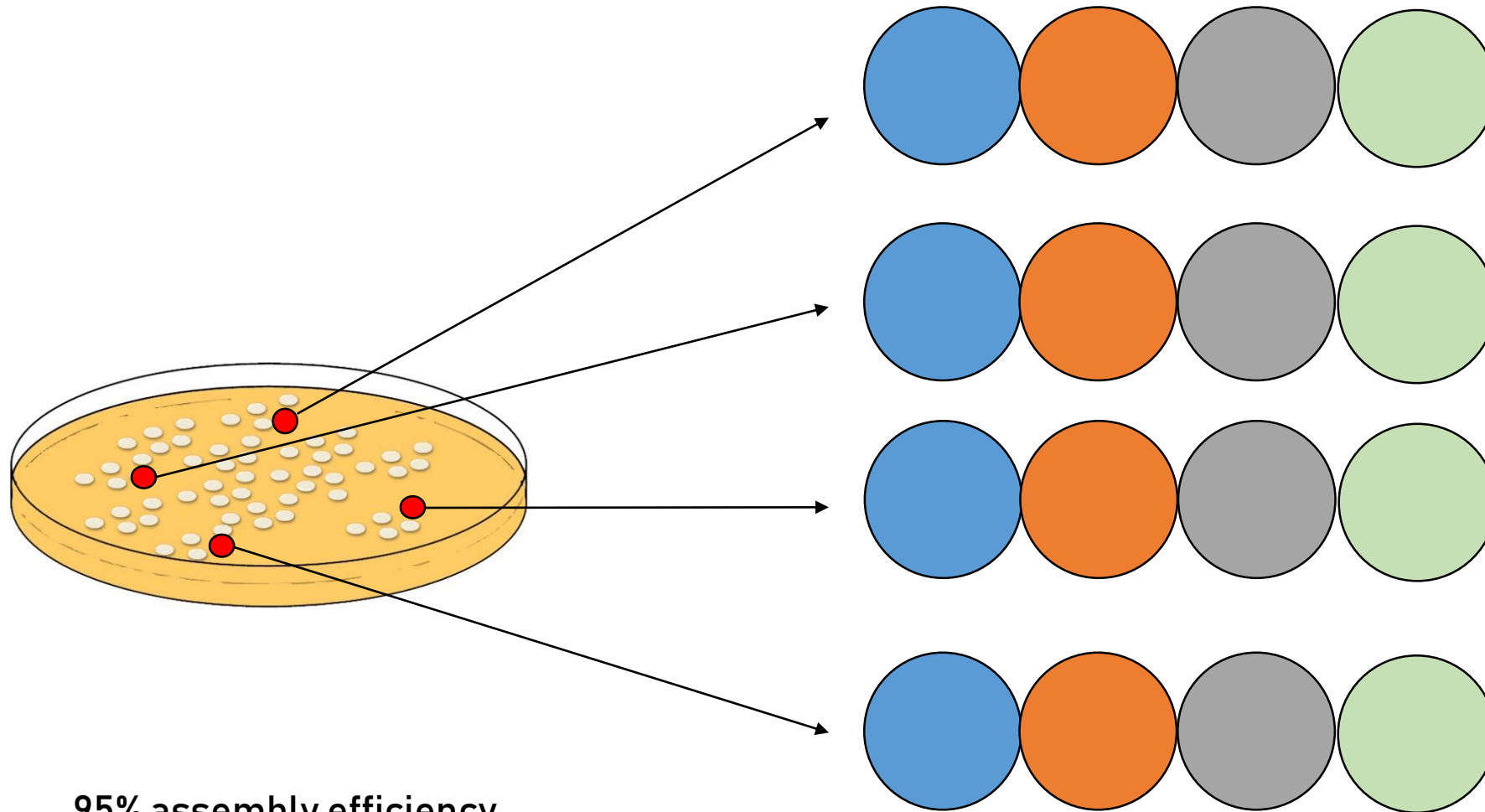
Position 4



VERSATILE SHUFFLING: RATIONAL ASSEMBLY



VERSATILE SHUFFLING: RATIONAL ASSEMBLY



VERSATILE SHUFFLING: COMBINATORIAL ASSEMBLY

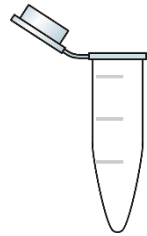
Tile repository

Tile mixture

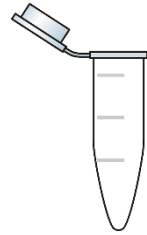
Assembly
reaction

Library

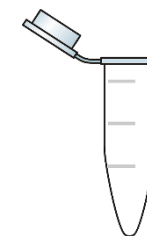
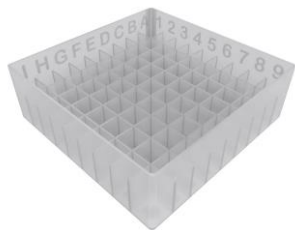
Position 1



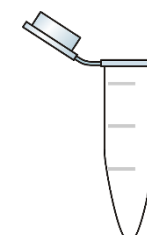
Position 2



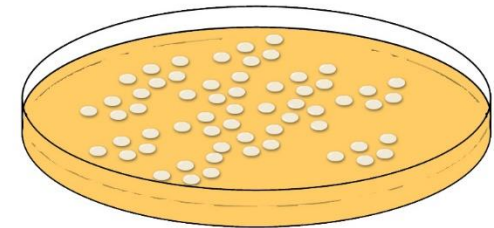
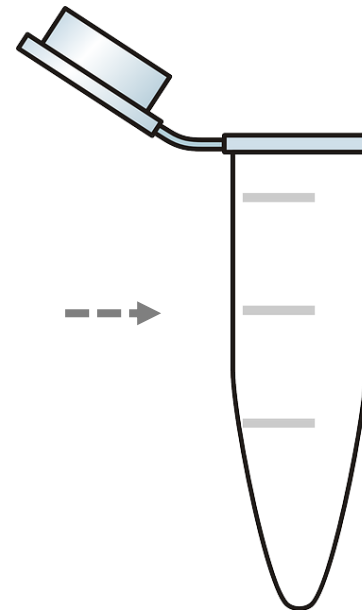
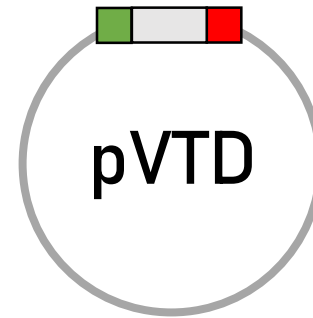
Position 3



Position 4

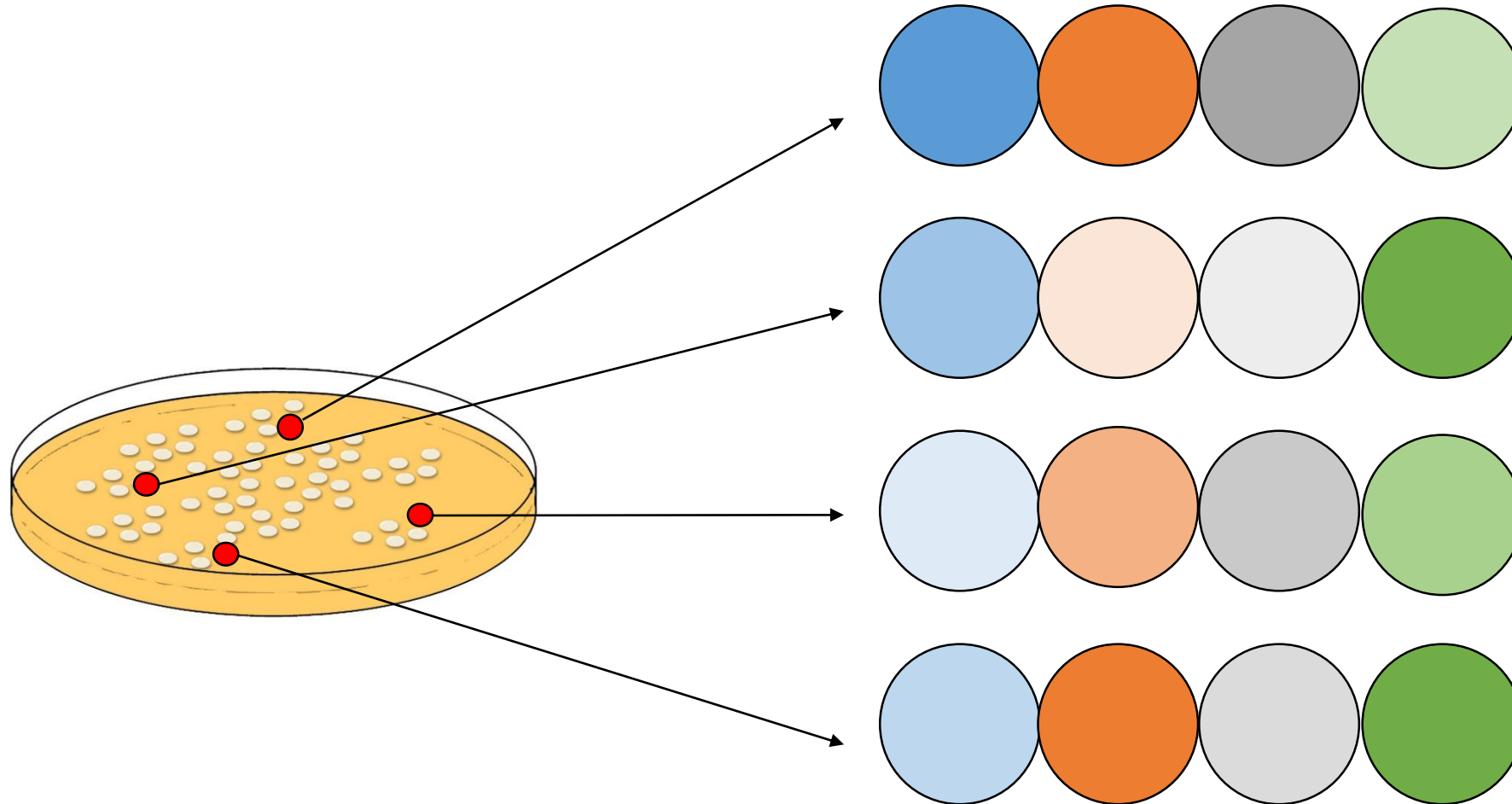


+



30 min to 2 hours hands-on time

VERSATILE SHUFFLING: COMBINATORIAL ASSEMBLY



95% assembly efficiency
Complexity = $a * b * c * d$

VERSATILE TECHNOLOGY APPLICATIONS

VersaTile Technology works for any DNA-encoded biomolecule with modular build-up & across all application areas

- Enzymes
- Antibodies
 - Full length
 - Single domain (VHH)
 - bi- or multi-valent (antibody) constructs
 - ...
- Biopolymers
- ...

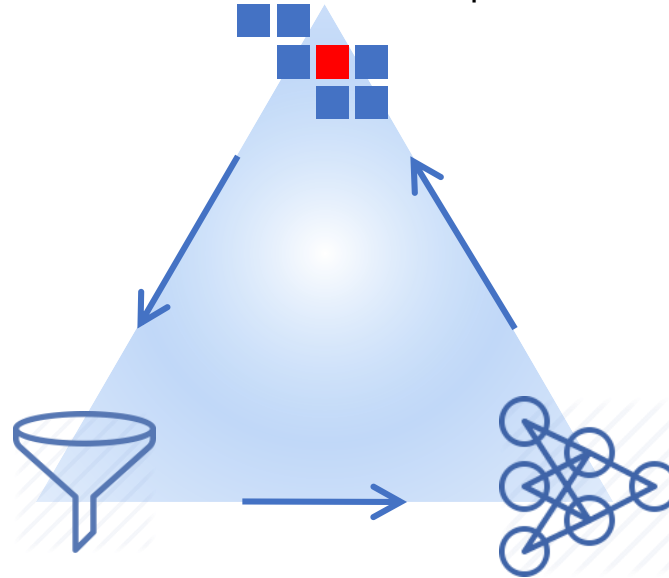
LEVERAGE

Platform development
(enzyme-centered research)

VersaTile technology

patented

1. VERSATILE CLONING
2. TILE REPOSITORY
3. VERSATILE SHUFFLING



**High-throughput
Screening** (microdroplet
platform)

**Design
Rules** (machine
learning)

**Lead
characterization**

Case study: fast attrition rate for neofunctional class biopharmaceuticals (antimicrobials)

7 active variants (~2%)

1 variant inhibits 4 strains
3 variants inhibit 3 strains
3 variants inhibit 1-2 strains

389 variants

+ 10.000 possible variants
General configuration

$40 \cdot 2 \cdot 6 \cdot 21$

50 active variants (~26%)

22 variants inhibit 4 strains
17 variants inhibit 3-4 strains
11 variants inhibit 1-2 strains

189 variants

336 possible variants
Design rules for peptide conformation
and subdomain

$4 \cdot 2 \cdot 2 \cdot 21$

13 active variants
in human serum

10 variants inhibit 1 strain
3 variants inhibit 2 strains

29 variants

29 most active variants
A general structure is defined

3 variants inhibit
tested strains in 50% human serum

CASE STUDY: LEAD CHARACTERIZATION

- Low minimum inhibitory concentrations on multidrug-resistant strains (4-14 $\mu\text{g/ml}$).
- High bactericidal effect in human serum (>5 log).
- High thermoresistance (2 hours at 90°C).

➔ VersaTile Technology stands for molecular engineering for rapid functional optimization

VERSATILE TECHNOLOGY: CONCLUSIONS

- VersaTile technology is a highly efficient method for the rapid assembly of libraries of modular variants with easy re-use of the building blocks
- Other assembly methods do not allow the combinatorial assembly of non-homologous building blocks
- VersaTile technology outcompetes commercial gene synthesis for library construction in terms of costs, especially when a higher complexity is envisioned and iterative improvements are planned
- Implementation of an iterative engineering approach for modular enzymatics, similar to the hit-to-lead development of small molecule drugs
- Validation ongoing in (single domain) antibody field (Ghent cluster), mycology (crop protection), biopolymers

VALUE CREATION

- Feasibility/evaluation study together with research group
- Strategic collaboration or service-type agreement
- Licensing (Ghent University Tech Transfer)

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