

BRAIN Biotech AG

Creating a #BiobasedFuture

Capital Markets Day 2023

Zwingenberg, February 27, 2023

WE SUPPORT



Since 2021 we have been committed to the UN Global Compact corporate responsibility initiative and its principles in the areas of human rights, labor, the environment and anti-corruption.



The Engine for a #Biobased Future: BioScience Zwingenberg
Dr. Alexander Pelzer, Head R&D

Introduction – Dr. Alexander Pelzer

Head of R&D

- 2005: Biology at Heinrich Heine University in Duesseldorf
 - 2010: PhD at Juelich Research Center
 - Institute for Molecular Enzyme Technology (IMET)
 - Scholarship CLIB-Graduate Cluster Industrial Biotechnology
 - BRAIN Biotech job evolution:
 - 2014: Research scientist and project manager in the Enzymes & Biocatalysts Unit
 - 2017: Head of the technology platform Tailor-Made Biocatalysts
 - 2018: Head of Enzymes & Biocatalysts Unit
 - 2023: Head of Research and Development
-
- ▶ 13 years in enzyme technology
 - ▶ Specialized on the development of industrial enzymes
 - ▶ Broad education in diverse fields of molecular- and microbiology



Future Nutrition will be Produced Differently

cornerstones of sustainable food production



Why?

- Industrial livestock farming has a significant GHG footprint
- Fishing grounds are being depleted
- May be considered unethical and contributes to the global antibiotics crisis
- Energy, water and land use is threatening biodiversity and the global climate

► **Industrialized countries will move away from meat and dairy towards alternative sources**

Future Nutrition will be Produced Differently

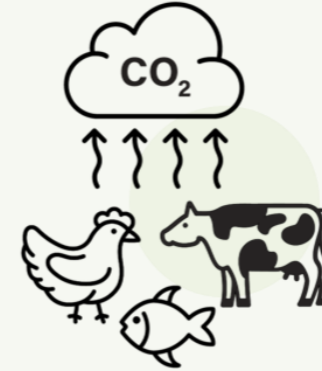
cornerstones of sustainable food production



9.8 billion by 2050



More people
More protein



Industrial livestock farming
Ethical issues and footprints



Precision fermentation
Alternative proteins



Enzymes
Processing of plant-based protein

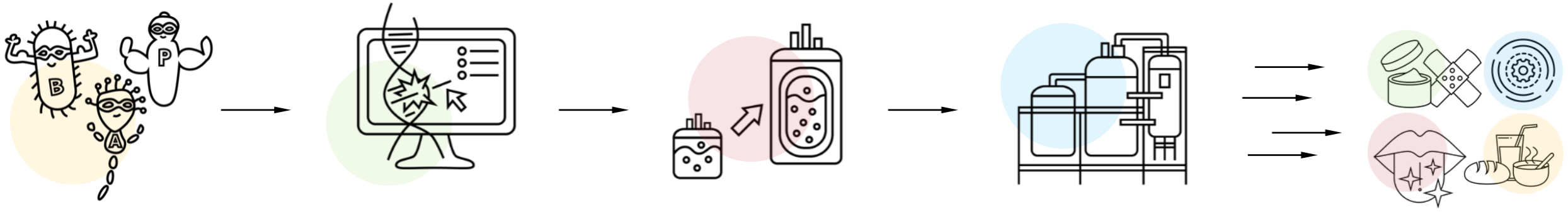


Microorganisms
Fermented food

► **Industrialized countries will move away from meat and dairy towards alternative sources**

Biotechnology will be **The Key Enabler**

future nutrition and materials will be more sustainable

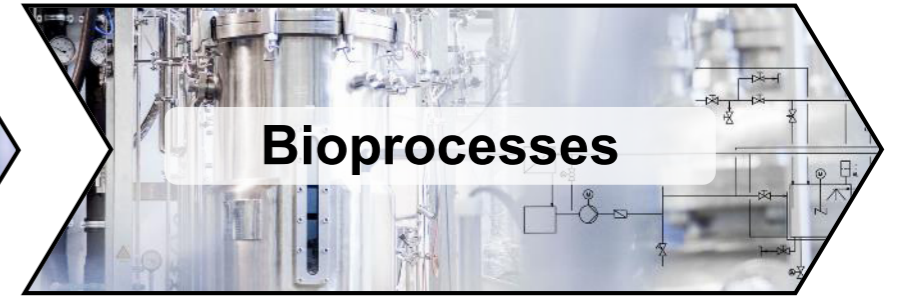


- ▶ Future nutrition will be produced differently
 - **Alternative proteins** as protein source via precision fermentation
 - **Enzymes** are versatile helpers for processing and optimizing food sources
 - **Microorganisms** specialized on fermenting food
- ▶ Materials of the future will be different and sustainable
 - **Performance and functional proteins**
- ▶ Strong microbes are set to take centre stage to provide suitable quantities
- ▶ BRAIN Biotech's core expertise comes into play and will support the transformation to a sustainable industry
 - Established methods can be applied to these emerging fields
 - All the prerequisites are in place to also break new ground

BRAIN R&D – An Integrated Solutions Provider

superior bio-based solutions for our customers

Creativity and diversity of nature



Technology units



Enzymes & Biocatalysts



Strain Development



Bioprocess Development

Technology fields

Function-driven discovery
Sequence-driven discovery
Rational enzyme engineering

Microorganism discovery
Genetic & metabolic engineering
Production strains

Process development & optimization
Process transfer & scale up
Analytics

BRAIN BioArchive: Valuable Resource for Microorganisms, Proteins & Enzymes

access biodiversity and use nature's solutions for our challenges

Creativity and diversity of nature



BRAIN BioArchive



High-performance Microorganisms

~ **53,000** Characterized microorganisms

~ **2000** Strains in Green-Mining-Toolbox

~ **600** Strains from Food Sources

450 Habitat collections and environmental samples

~ **15** Different expression hosts



Enzymes Proteins

> **130** Enzyme products

~ **600** Characterized enzymes from EC1-5

> **230** Giga-bp DNA

54 Metagenome libraries

~ **60 Mio** Digitalized meta-genomic open reading frames



High-performance Microorganisms

Value culture collection including

- Food collection (~ 600 strains)
- Mining collection (~2000 strains)

- ▶ Digitalization of selected sections of BioArchive via next generation sequencing (NGS)
 - ▶ Strong bioinformatics guided approach for characterization & discovery



Enzymes Proteins

Powerful discovery pipelines

- Function-driven discovery
- Sequence-driven discovery

▶ **Fast accessibility via specialized subsets and digitalization of biological data**

Microorganisms for Future Nutrition

discovery & development of microorganisms



Starter cultures (single & co-cultures)

- *Non alcoholic beverages*
 - Fermented grape leaves to produce non alcoholic wine alternatives
- *Alternative protein*
 - Fermented brewer's grains to enrich amino acid profile as optimized protein source
- *Alternative sweetener*
 - Fermented stevia leaves to produce a stevia sweetener product with superior taste
- *Alternative dairy*
 - Fermented plant protein with optimized taste and functionality

Nutritional biomass

- Meat replacement using mycelial growth of fungi

Production strains

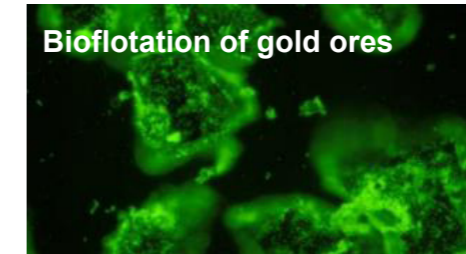
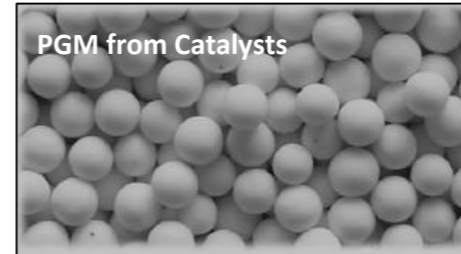
- Production strain producing the sweet tasting plant protein brazzein
- Production strains producing microbial fats to substitute animal derived fats (e.g. from milk)

► **Microorganisms ready to improve and replace conventional food**

Microorganisms are Versatile All-Rounders

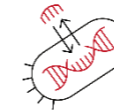
discovery & development of microorganisms

CleanTech BioSolutions – Waste to value



Further application of microorganisms

- New and improved base strains (e.g. AMR marker free)
- Production strains (e.g. acids, vitamins, biological dyes)
- Pro- & Postbiotics (e.g. gut health, technical)



Development of microorganisms

- Microorganism discovery
- Genetic engineering
- Metabolic engineering
- Genome editing nucleases

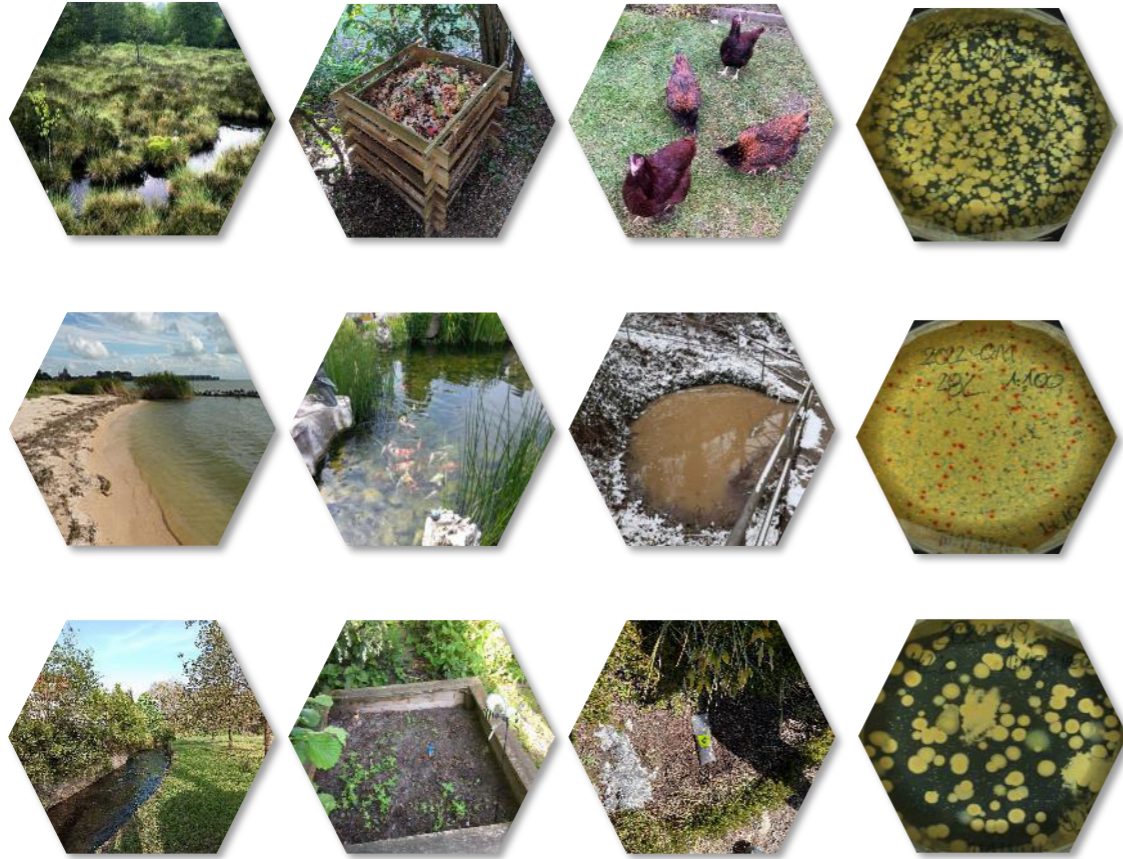


► **Our microorganisms platform enables access to diverse fields of application**

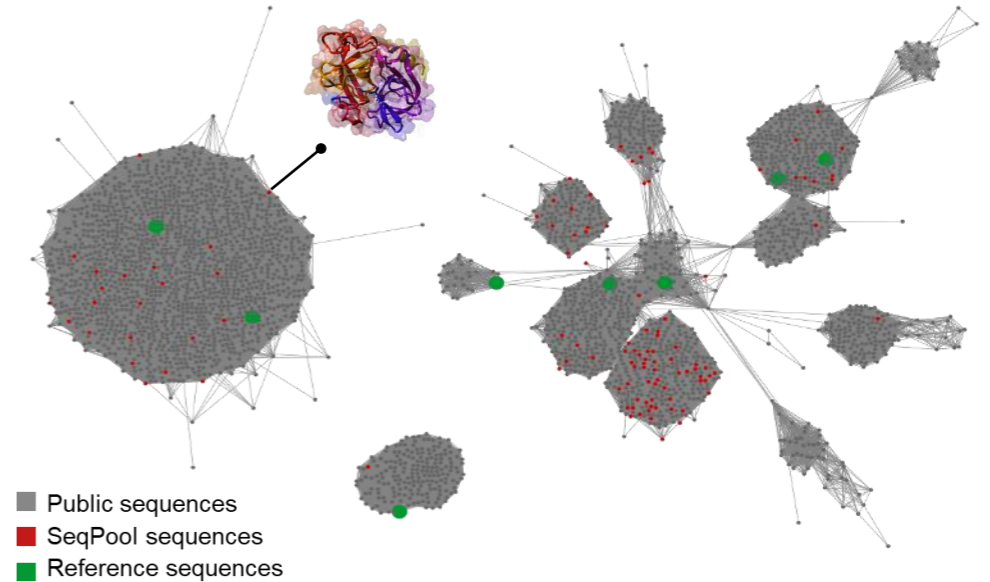
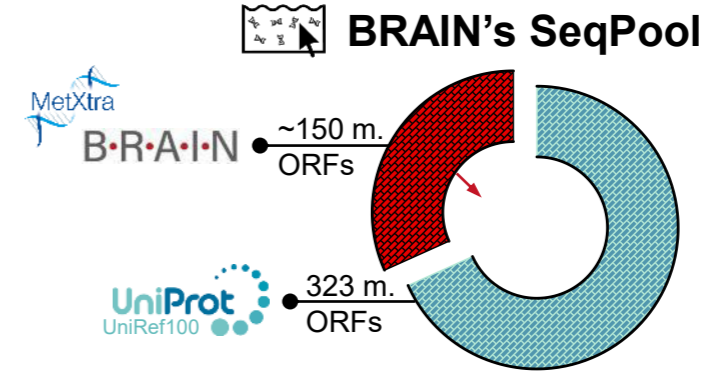
SeqPool: A Digital Sequence Database

proprietary database for fast enzyme & protein discovery

🔍 Rational bioprospecting



> 50 metagenomes, selected & enriched organisms



► **Fast discovery of new enzymes & proteins in SeqPool or in custom made data sets**

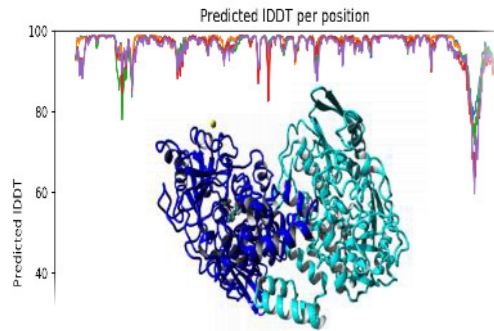
Designed and Tailor-made For Application

rational engineering of enzymes & proteins

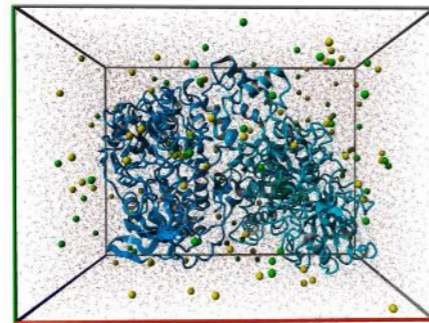
Sequence-/structure-based engineering

Bioinformatics guided rational approach

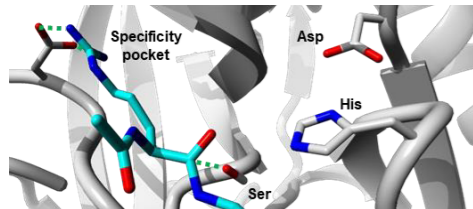
Structure modelling



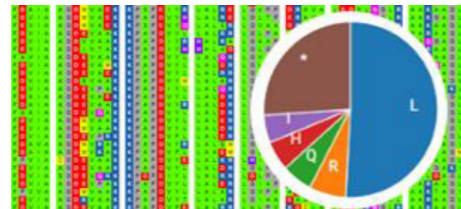
MD simulations



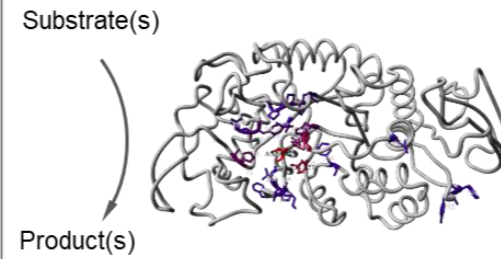
Docking studies



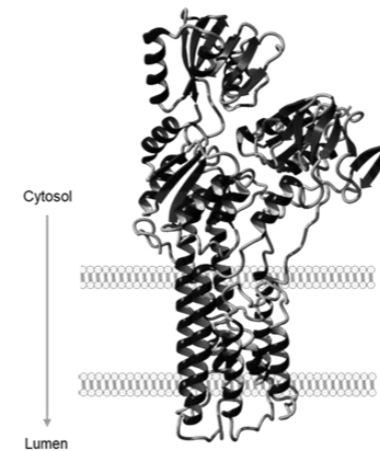
Multiple sequence alignments



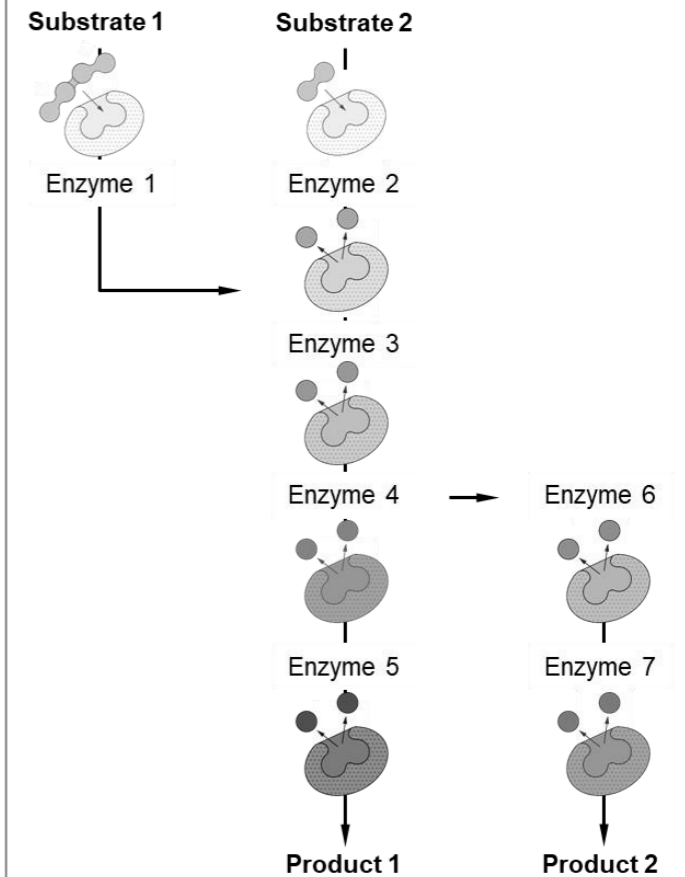
“Classical” enzyme reactions



Difficult proteins



Enzyme cascade optimisation



► Efficient combination of different disciplines enables the reliable engineering of various targets

Designed and Tailor-made For Application

rational engineering of enzymes & proteins

Bio-based performance materials

8 February 2023, Zwingenberg/Neuried, Germany

Structural proteins for the development of sustainable materials: BRAIN Biotech and AMSilk cooperate to develop high-performance bio-based protein fibers

Creating a better future with biotechnology – this vision is shared by BRAIN Biotech AG (BRAIN Biotech), a leader in the development and manufacture of bio-based solutions and products for industry, and AMSilk GmbH (AMSilk), the world's first industrial supplier of innovative biomaterials for more sustainable applications in the textile, medical and consumer goods industries. As part of a strategic collaboration, BRAIN Biotech and AMSilk are combining their expertise to drive the development of high-performance fibers for the performance materials market.

Bio-fabricated products hold enormous potential as sustainable material solutions for the future. New developments, such as those currently being developed by BRAIN Biotech and AMSilk, could revolutionize the performance materials market. Petroleum-based textile fibers made of polyethylene or

8 February 2023

Collaborative Press Release



Enzymes for glucose alternative synthesis

25 October 2022, Zwingenberg, Germany and Charlottesville, VA, USA

BRAIN Biotech and Bonumose collaborate on enzymes for the production of rare monosaccharides

BRAIN Biotech AG, a leading European industrial biotechnology specialist, and rare sugars expert Bonumose, announced today that they have reached initial project milestones as part of their strategic collaboration. The companies aim to improve the performance of several enzymes that catalyze cascade reactions in the continuous production of low-calorie, ultra low-glycemic, naturally occurring sweeteners.

Bonumose has developed a patented process for producing tagatose and allulose which eliminates several processing steps and significantly increases yields during the production process. The company uses multiple enzymes within the synthesis cascades and BRAIN Biotech is optimizing several of these enzymes using enzyme engineering.

25 October 2022

Collaborative Press Release



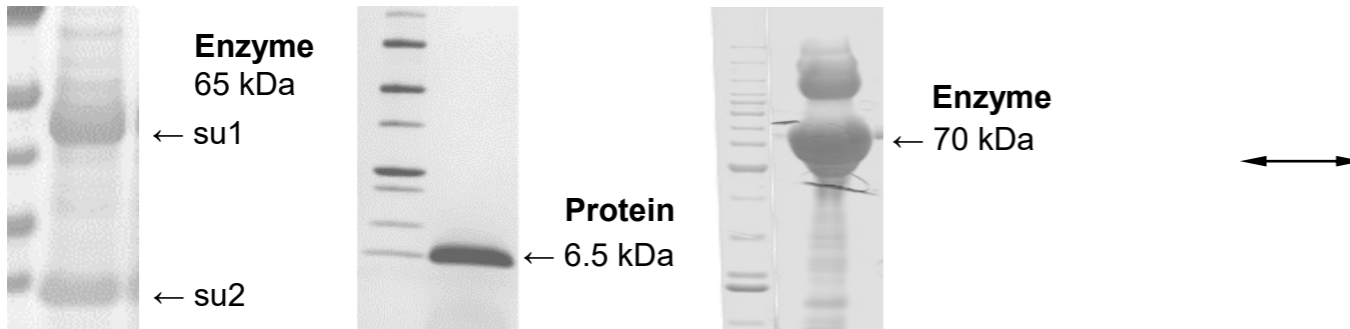
Focus on Developing Strong Protein & Enzyme Producers

production strain development and bioprocess development go hand in hand

 Production strains: *Escherichia coli*, *Bacillus subtilis*, *Pichia pastoris*, *Yarrowia lipolytica*, *Aspergillus niger*




Good starting situations to build on



- Yields in g/L scale possible

Development of production strains

- Relevant industrial strains available
- Expression technology
- Metabolic engineering
- Random mutagenesis approach
- Genome editing nucleases 

► **Good starting situations to build on & required tools available**

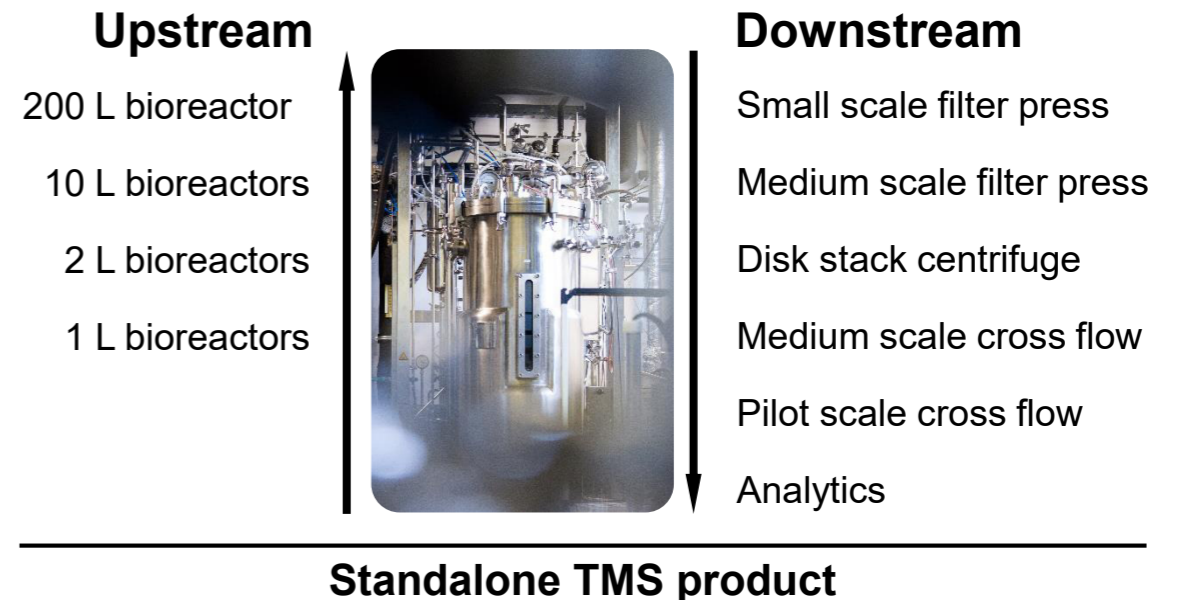
Focus on Developing Strong Protein & Enzyme Producers

production strain development and bioprocess development go hand in hand

Goal: Development of a portfolio of fermentation processes with an “out of the box” g/L yield for the production strains



- Implementation started and ongoing:
 - Removal of 3 m³ bioreactor
 - Enlarge the laboratory space
 - Expand capacity of small bioreactors
 - Improving the predictive power of development candidates
- Joint development of bioprocesses with the colleagues from Biocatalysts



► **Robust development of bioprocesses delivering high protein and enzyme quantities**

Focus on Developing Strong Protein & Enzyme Producers

production strain development and bioprocess development go hand in hand

Nutritional alternative protein

10 February 2022

NUTRITION

Cooperation for the production of animal-free milk protein

BRAIN Biotech AG and Formo Bio GmbH are launching a strategic collaboration to further advance the production of animal-free milk proteins.

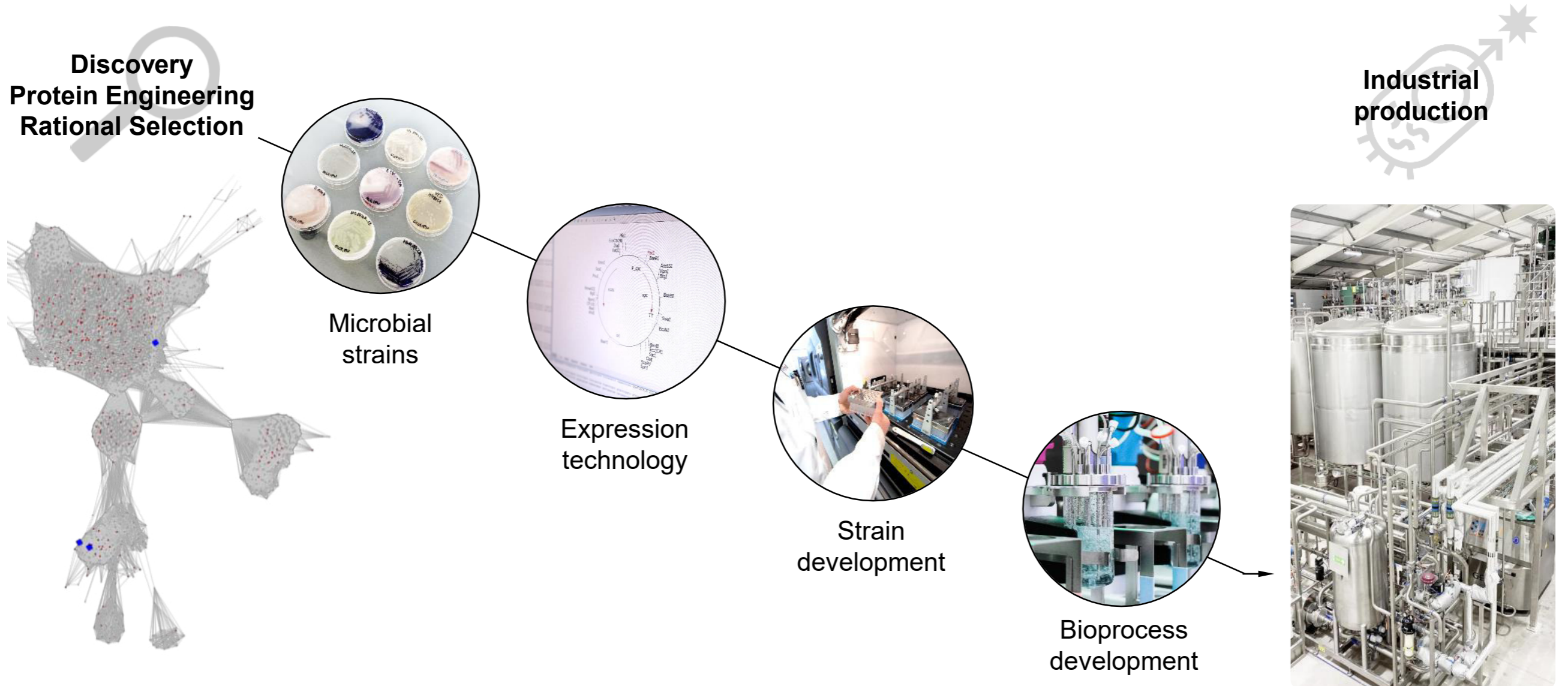
Biotech companies BRAIN Biotech AG and Formo Bio GmbH want to drive forward the animal-free production of milk proteins as part of their strategic cooperation. Formo will scale up their bioidentical milk protein production with a genome editing technology, leveraging BRAIN Biotech's expertise and its proprietary BEC platform. The alliance aims to optimize the microorganisms to further expand novel and sustainable protein production for commercial use through precision fermentation

10 February 2022

Formo

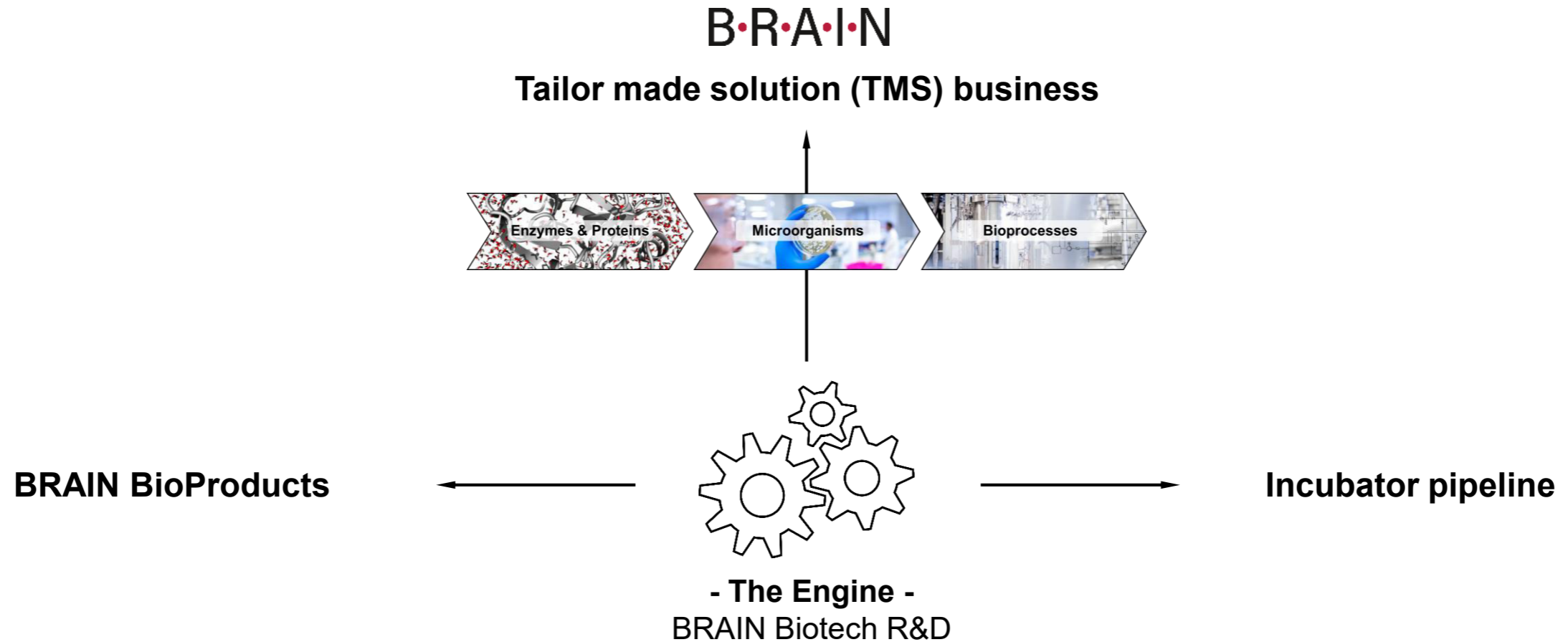
From Candidates to Industrial Production Processes

all the technologies available to deliver the complete process



The Engine of a #Biobased Future

fueled by passion for science and the motivation to create sustainable industries



- ▶ **BRAIN offers extensive experience and technical capabilities**
- ▶ **BRAIN customers benefit by finding all options within the BRAIN Group**
- ▶ **Discovery, development, production of enzymes, proteins and microorganisms**