Revolutionising biology through digitalisation

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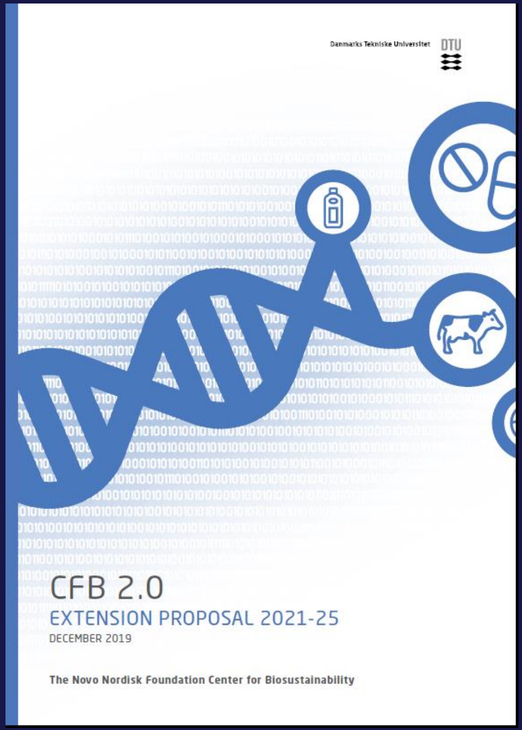
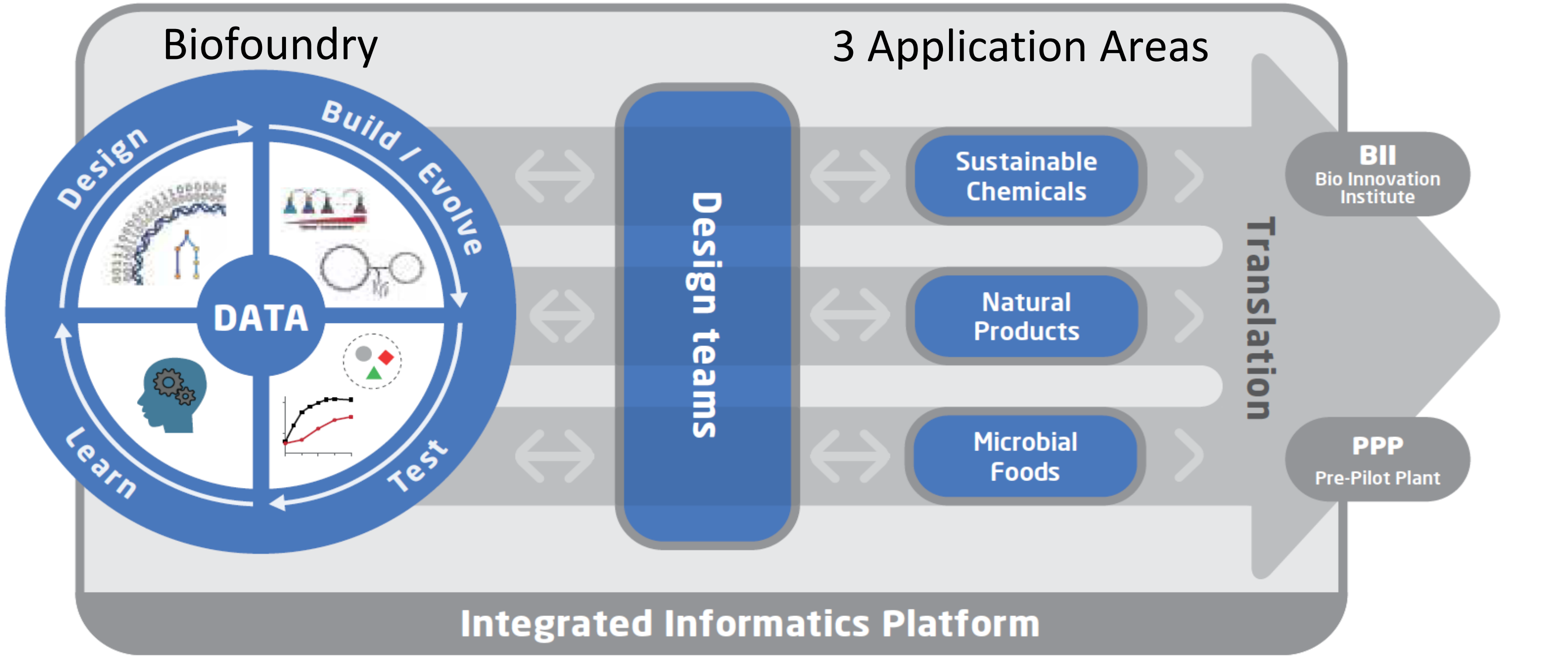
Mission & vision



Vision:	**The development of sustainable lifestyles requires efficient big-data generation and analysis of biological processes fundamental to all aspects of human life.**
Mission:	CFB will be a **world leader in developing and perfecting big data generation and analytics for developing microbial genome-scale science and applying it to production strain design** and to address other fundamental issues of biosustainability.

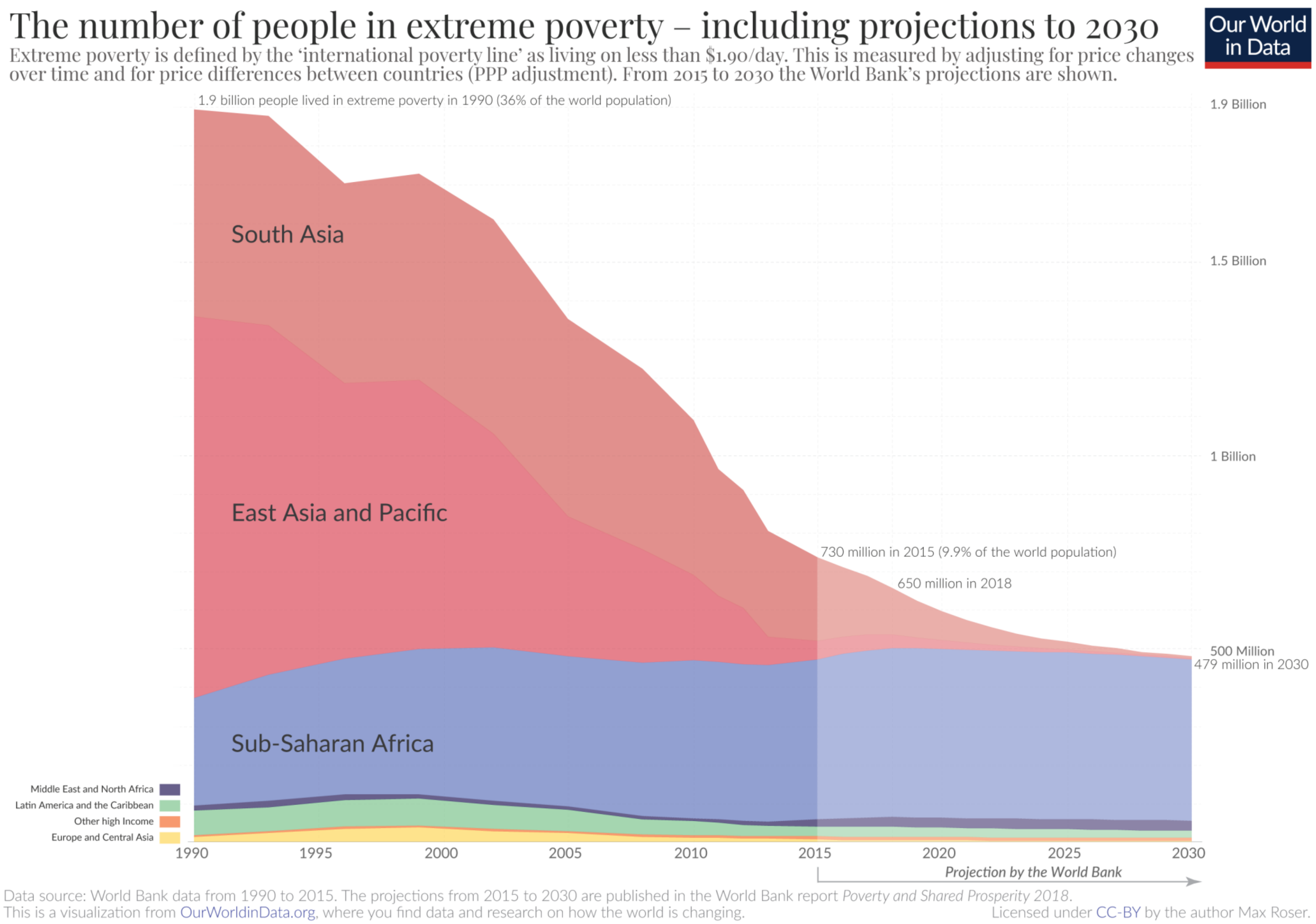
CFB 2.0 Workflow



The triple challenge: People, Planet, Prosperity

"… to end poverty, protect the planet and improve the lives and prospects of everyone, everywhere"

United Nations 2030 Agenda for Sustainable Development


The number of people in extreme poverty – including projections to 2030
Extreme poverty is defined by the 'international poverty line' as living on less than $1.90/day. This is measured by adjusting for price changes over time and for price differences between countries (PPP adjustment). From 2015 to 2030 the World Bank's projections are shown.
Our World in Data
1.9 billion people lived in extreme poverty in 1990 (36% of the world population)
1.9 Billion
1.5 Billion
1 Billion
500 Million
479 million in 2030
South Asia
East Asia and Pacific
Sub-Saharan Africa
730 million in 2015 (9.9% of the world population)
650 million in 2018
Middle East and North Africa
Latin America and the Caribbean
Other high Income
Europe and Central Asia
1990
1995
2000
2005
2010
2015
2020
2025
2030
Projection by the World Bank
Data source: World Bank data from 1990 to 2015. The projections from 2015 to 2030 are published in the World Bank report Poverty and Shared Prosperity 2018.
This is a visualization from OurWorldinData.org, where you find data and research on how the world is changing.
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“How … e on the
ecos… resources
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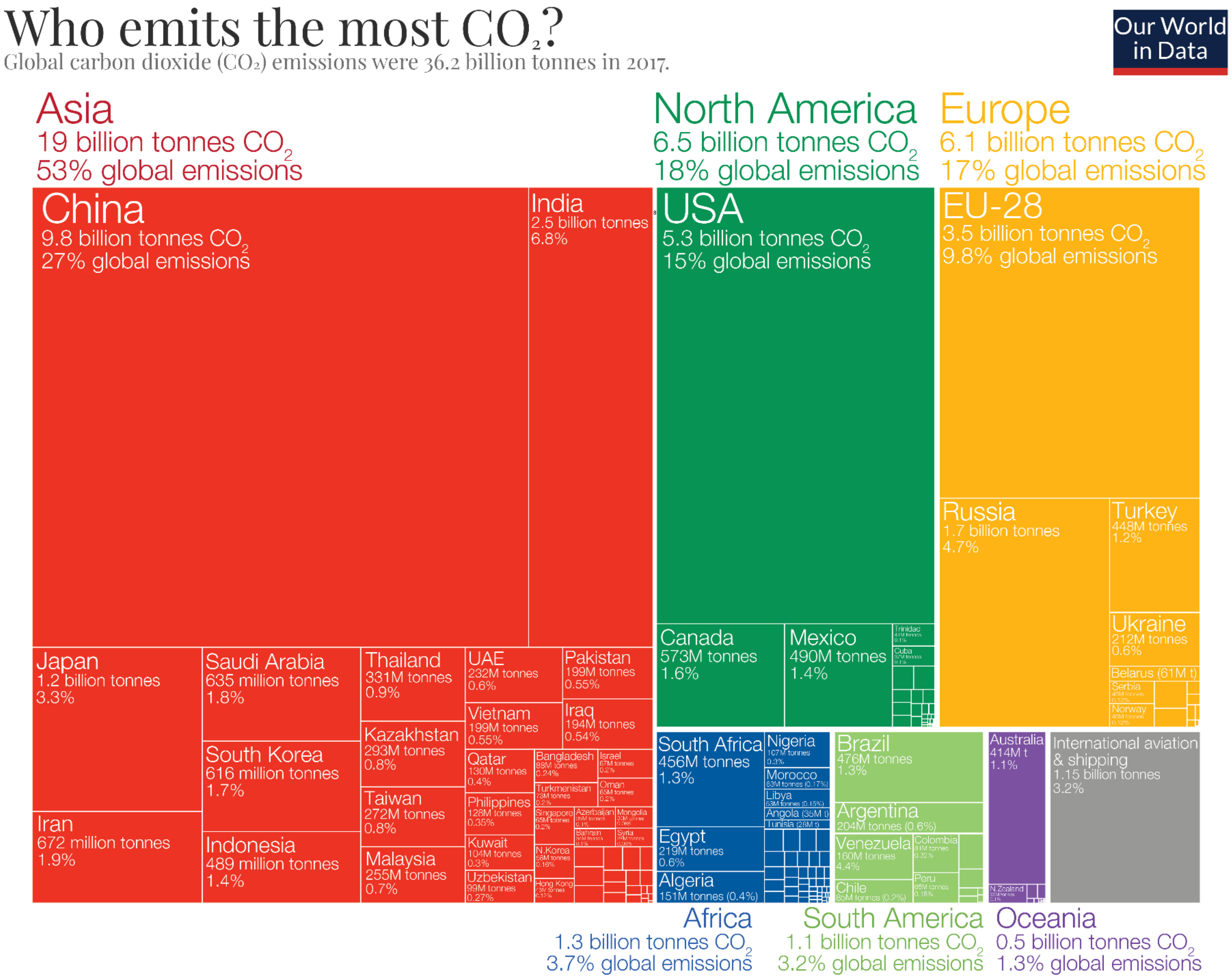
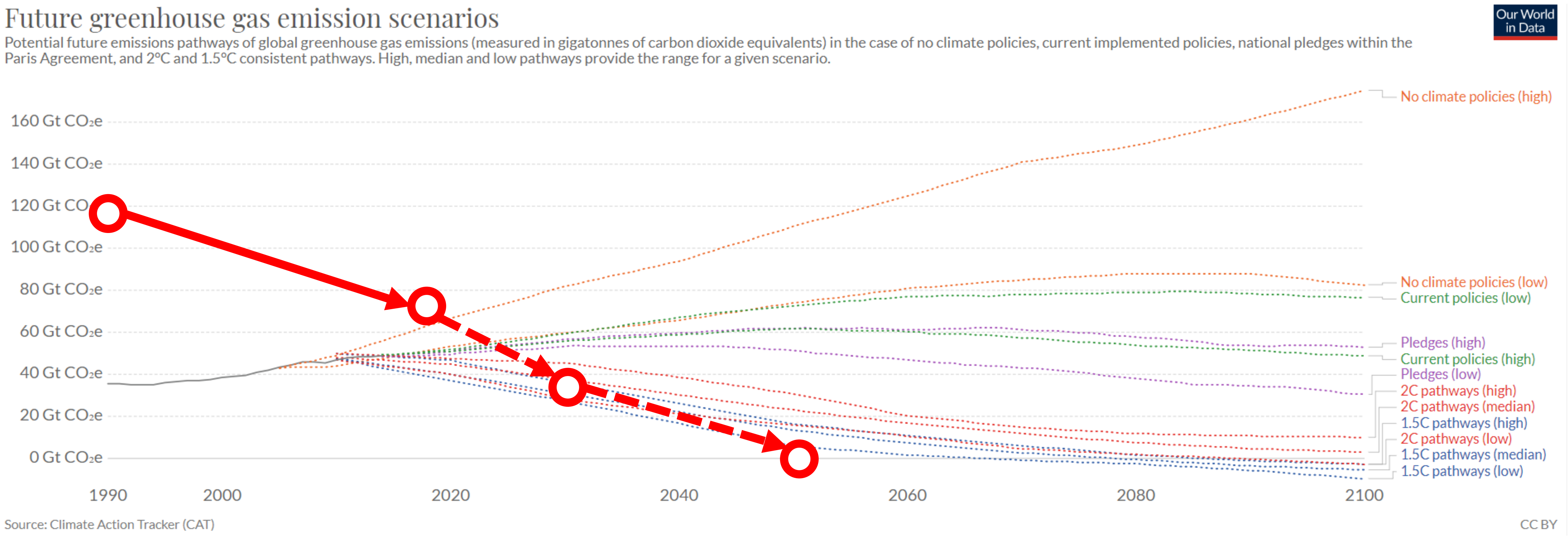
2.0 proposal



What the world needs now …



Creating a renewable carbon economy: Fuel, Food, Fibre

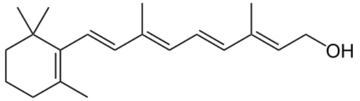
Our ultimate ambition must be to completely replace our reliance on fossil fuels and other non-renewable resources for the production of food, fibre and transportation fuel with a sustainable alternative.

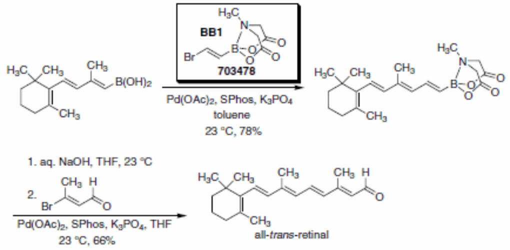
World production	Million tonnes per annum	Million TOE	
Cereal	2600		
Corn	1000		37%*
Sugar	174		
Wood	1600		**
Total biomass	**5374**	**1750**	
Olefin		250	
Liquid fuels		4000	20%***

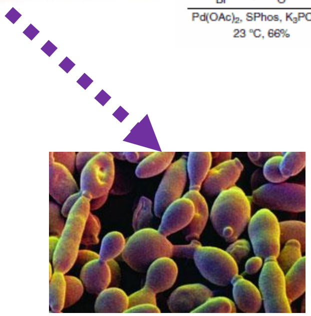
* Food production accounts for 37% of world GHG emissions (57% animal-based accounting for 35% protein)

** Only 11.3% of global wood production is FSC certified

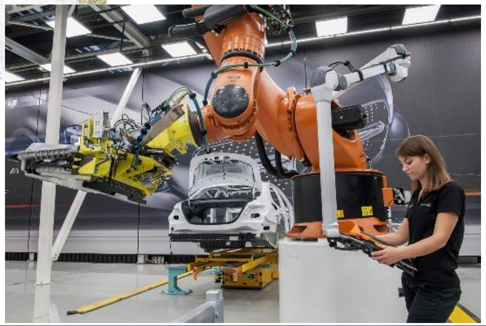
*** 50% readily replaced with electricity



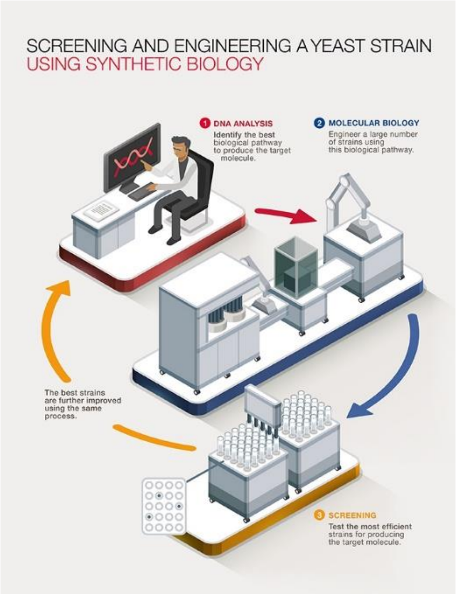




BioIndustry 4.0



Automated Strain Engineering



The Age of Digital Biology

- Established companies
  - Genomatica (2002)
  - Amyris (2006)
  - LanzaTech (2007)

- 2015-: B2B technology companies
  - Ginkgo Bioworks
  - Zymergen

- Naïve model of R&D
  - Zymergen: We take a systematic test-everything, data-driven approach, letting the data speak for itself.

Galanie S, Thodey K, Trenchard IJ, Filsinger Interrante M, Smolke CD (2015) *Science* **349**:1095

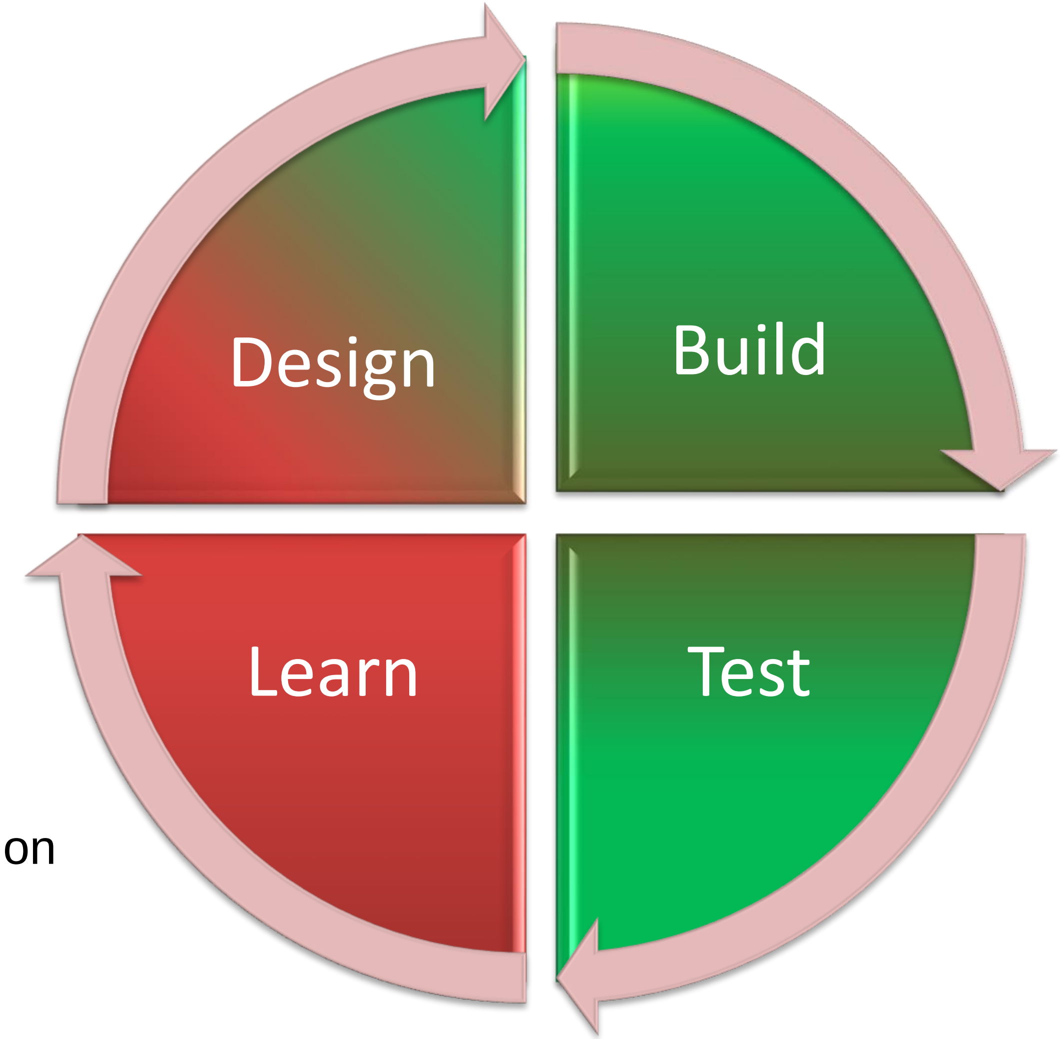
Example: morphine in yeast

Antheia

Possible designs
20 genes, 5 levels:
- 5^{20} = 6.6 billion years

2000 candidates/gene
- $(5)^{20}(2000)^{20} = 10^{80}$

Enzyme engineering
- 20^{400} sequences



Rational
- 20 genes
- 1200 strains/month

Robotics
- Accurate growth & titre

Low cost HT Chemistry
- Transcriptomics
- Proteomics
- Metabolomics

Naïve statistical design
- Complex response function
- Poor performance

Biofoundry fundamentals

- Inexpensive, base-perfect genome editing in combination with automation, analytics and data integration enables Biofoundries

- A biofoundry is a computer peripheral
- Efficient data integration remains a major challenge; data volume, heterogeneity, time scales make this a Big Data problem

- Biofoundries do not accelerate strain engineering, they escalate strain engineering
- Designing informative experiments remains a challenge (*Design to Learn, Learn to Design duality*)

DTU

ACKNOWLEDGEMENTS TO

novo nordisk fonden

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United Nations 2030 Agenda for Sustainable Development

Merton’s Law of Unanticipated Consequences

Three types:
1. Unexpected benefits
2. Unexpected drawbacks
3. Perverse results

Five principle causes:
1. Ignorance
2. Error
3. Short-termism
4. Basic value bias
5. Inertia

EU biodiesel mandate
- 2003: 5.75% by 2010
- 2009: 10% by 2020, demand for palm oil ↑
- 2015: EU report demonstrates tropical biodiesel production cause 3X <u>more</u> emmisions than diesel
- 2021-2031: expected decline in palm oil import from 6.5 to 4 million tonnes as palm oil phase out 2023-2030

“Running on Orangutan blood”

Application Areas

- Sustainable Chemicals
- Natural Products
- Food

Sustainable chemicals

Sustainable potential

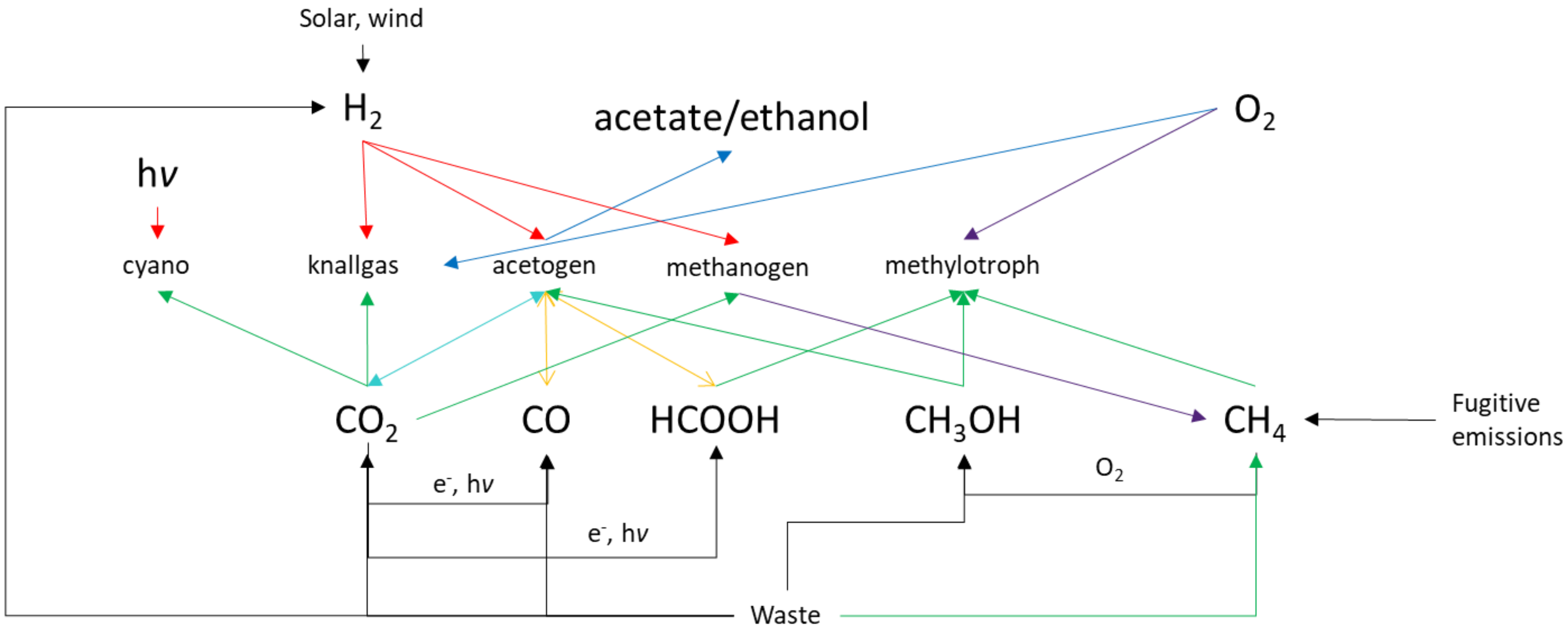
- Chemicals from renewable feedstock
- Reduced pollution from process and disposal
- Access to novel chemistry with better function

Focus

- Sustainable carbon through C1 metabolism
- High Density Physiology - addressing scale-up challenge
- New chemistry and materials, e.g., organic LED, electronics

C1 Global Metabolic Atlas

The Global Metabolic Atlas will describe core and auxiliary metabolism across the known range of bacterial C1 metabolism, while providing in-depth information on regulation and thermokinetics for deeply characterized strains. The Global Metabolic Atlas will be used to guide the design of heterologous C1 hosts. Additionally, techno-economic and life cycle analysis models will be developed for all major production strategies using a common set of assumptions to aid comparison.



Natural products

Sustainable potential

- Access to novel, sustainable chemistry

Focus

- Access to full streptomyces complement of natural products for use in e.g. control agents, including biopesticides
- Yeast platform for heterologous production of sustainable products from plants and fungi

Biopesticides

Insecticides

- Insect pheromones
- Spinosyn

Fungicides

- 10-16% food lost in field
  - Rice blast causing losses of food for 60 million people and catastrophic loss for farmers
  - Fusarium (ie soil based) such as Panama disease in banana; cost the near loss of Gros Michel (used to be main production variety) and now causing loss of Cavendish
- No new pesticides due to high cost and risk; managed by rotation and broad spectrum e.g. copper
- Pesticides being withdrawn due to human and eco-toxicity further reducing management

CFB approach: finding new products and synthons

- Crispr based BASE editor for actinomycetes
- Genome reduced streptomycete hosts for heterologous production
- Large cluster capture strategies and transfer
- Novel biopesticides from various DTU programs and 1000 danish strain library

Transformation of the Food Sector

Data for New Foods

- Fully sequenced and characterized lactobacillus library
- Yarrowia genomes
- Fungal genomes

Alternative Dairy

- Plant-based cheese
- LAB analysis for new starter cultures
- Plant-based yogurt. Recombinant production of milk proteins
- In situ fermentation of milk proteins to enrich plant-based dairy
- Sustainability assessment of recombinant milk

Alternative Meat

- Yummowia – enhanced yeast based meat alternative
- Fungal mycelium as meat alternative
- Fungal seafood alternative
- Exploration of rapeseed protein as alt protein source
- In situ TF production and co-culture for sustainable lab grown meat

Feed stock

- Protein (Feed for Fish, Cattle, Pigs and Poultry, based on underutilized C1-based feedstock)

Flavor formation by microorganisms

- Potential of LABs to generate flavor
- Understanding of flavor (especially kokumi/umami) formation in plant-based ferments

Impact Assessment

- Assessment of the impact of microbial foods on planetary health
- Recombinant protein production on waste streams
- Plant-based dairy from waste streams
- Upcycling of different waste streams including CO_2, endive root, orange peel, cascava, BSG and bran