Synthetic Biology
Opportunities in Agriculture

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Stuart John Dunbar Oxford 2010

Road map of today

- The global challenge that our science needs to address
  - Water and sustainable agriculture
- Synthetic Biology
  - Our definition
  - Opportunities
  - Biocatalysis
  - Production platforms
  - Protein and pathway engineering - Amylase
  - Opportunities and next steps
  - Risk perception
- Conclusions

Caution – we are on a journey

- From an industrial agriscience perspective Synthetic Biology has *potential*
- We don't know how to realise this potential yet - we are on a journey to explore it
- The talk describes where we are on the journey

The Global Challenges

Food

Energy

Climate Change

Water

Raw Materials

- The key questions for policy makers and scientists are these:
  - Can 9 billion people be fed equitably, healthily and sustainably by 2050?
  - Can we cope with the future demands for water?
  - Can we provide enough energy and raw materials to supply the growing population coming out of poverty?
  - Can we preserve biodiversity?
  - Can we do all this whilst mitigating and adapting to climate change?

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Water

- It takes .....
  - 11,000 L to make one hamburger
  - 4000 L to make one litre of milk
- In the west we rely on 100x our body weight in water every day to produce the food we eat - that's 2,500 m^3 each per year.
- BUT there's only 1,400 m^3 available per person
- Agriculture consumes 70% of the world's fresh water

We have a problem NOW

Source Fred Pearce "When the rivers run dry"

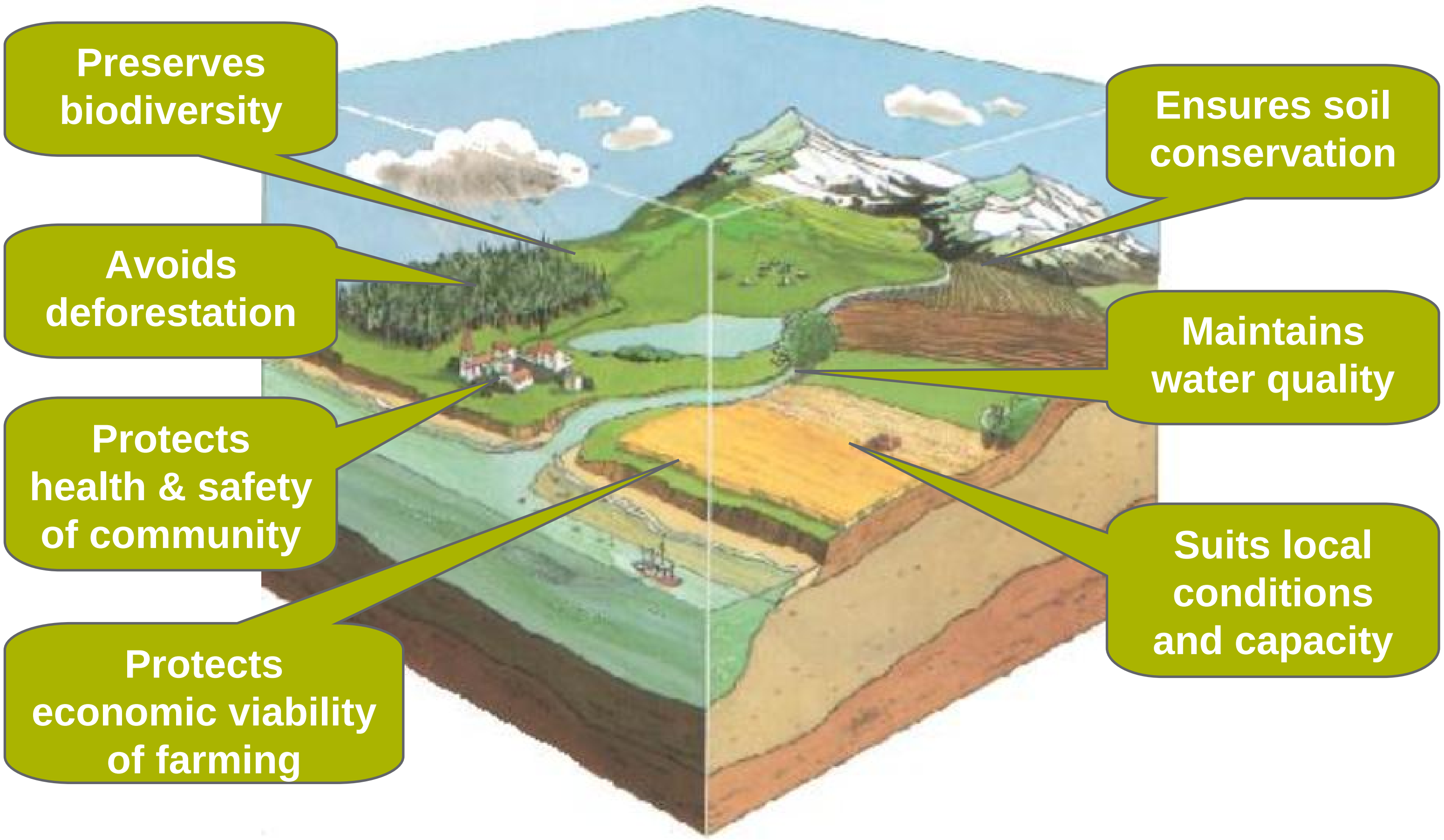
Food

- By 2050 the world's population will rise to 9 billion from 6 billion
- We can not feed the world's population now – poverty is the key issue today but there is a bigger spectre of calorific deficit in 2011
- We have to increase crop yields by 3x to feed the world by 2050
- We have to do this sustainably

Source -Parry *et al.* Global Environmental Change **9** S 521997

Sustainable agriculture

Our commitment: contribute to sustainable agriculture in the production of healthy food and the conservation of biodiversity



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Sustainability factors

- ✓ **Soil**  *Fertility / Moisture / Erosion*
- ✓ **Water** *Quantity & Quality* 
- ✓ **Energy** *Minimise use / Crop Footprint* 
- ✓ **Waste** *Minimise / Valorise as energy*
- ✓ **Productivity**  *Economics / Reduce land use changes*
- ✓ **Environment** 

Preserving ecosystems

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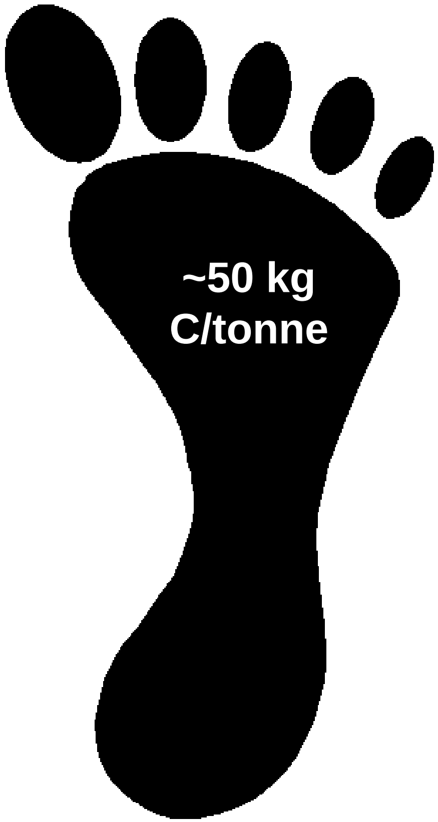
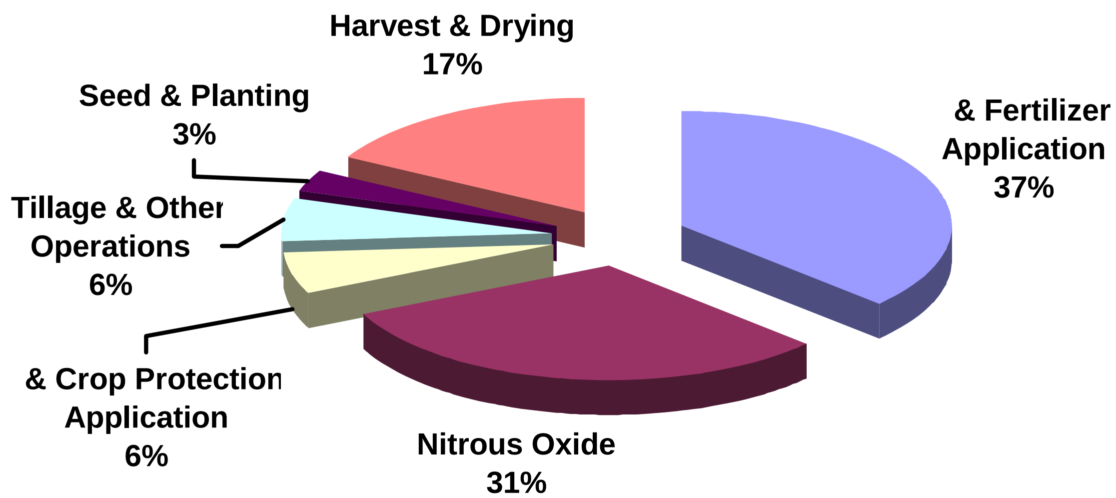
What is in a typical carbon footprint for a crop?



Conventional Wheat



Note: footprints can also be developed for water and other elements of sustainability

Agriculture represents 14% GHG directly

Land Use Changes a further 18% GHG emissions

How does this relate to synthetic biology?

- Integration with Systems Biology and Predictive Sciences
- Water use efficiency – producing crops that use less water
- Nitrogen use efficiency – less fertiliser
- More efficient plants – increasing yield – less CO_2

Our definition

- Whilst there are many different definitions of Synthetic Biology the core of the science involves the application of “engineering approaches” to biology.
- Moving from a reductionist, descriptive approach since the discovery of DNA where small parts of the genome are manipulated to a more engineering approach where large portions of genomes are transferred to do precise roles.

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Synthetic Biology Opportunities

- Biocatalysis – using synthetic biology to optimise production of compounds of interest – particularly a natural product or a compound with many chiral centres
- Engineering safety into a protein or natural product – linking Synthetic Biology to targeted evolution
- Changing feed stocks into production plants to lower costs
- Pathway engineering. This is a big opportunity. It could be used in GM strategies, MOA determination, protein production and chemical production.
- Biosensors

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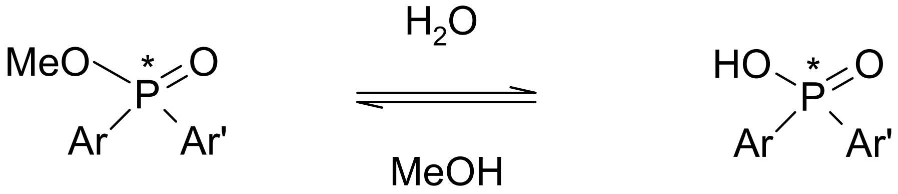
Biocatalysis

- A big opportunity for targeted enantiomeric synthesis using synthetic biology to drive the reactions. For example:-
- Enantiomerically enriched ‘chiral at phosphorus’ compounds
- A kinetic resolution by hydrolysing the unwanted enantiomer is one approach, but the ideal is reverse reaction forming the ester using an alcohol. Since the phosphinic acid racemises, the reaction would be dynamic and could give high yields.



Target Enantioenriched
Phosphinic Ester

Phosphinic acid
(not configurationally
stable)

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Production

- Plants
  - High yielding, pest, disease and drought resistant plants
  - Better quality products, e.g. flavour, aroma, colour, anti-oxidant content, altered oil content, and improved fibre quality
  - Improved processing characteristics, e.g, high solids tomatoes, high cellulose cotton
  - *In planta* production of raw materials, e.g. sugars, cellulose, starch, biofuels
- Other systems
  - Production of natural products in high yielding environments – microbial engineering

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Alpha amylase

- Continue to maximize productivity on the farm
- Innovate *within the existing infrastructure to build upon the success of* corn ethanol and make it more profitable and sustainable
- Unlock the full potential of the corn plant via expression of enzymes and other output traits

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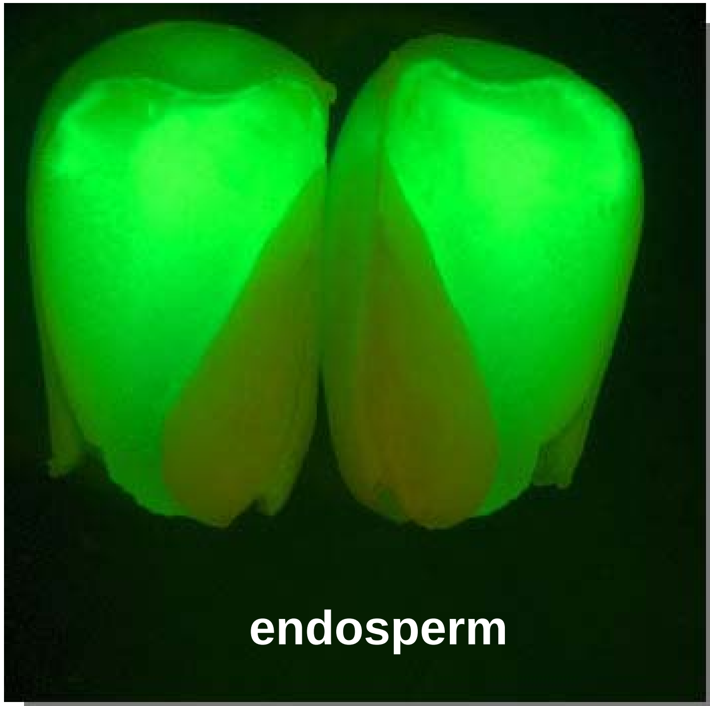
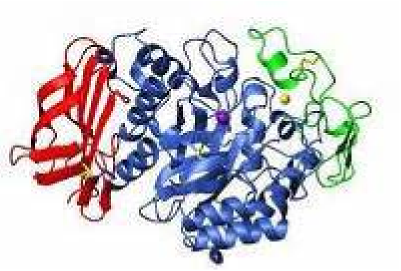
Unlocking the full potential of the corn plant - Today



Corn-expressed amylase

Optimized alpha-amylase enzyme delivered directly in the corn grain

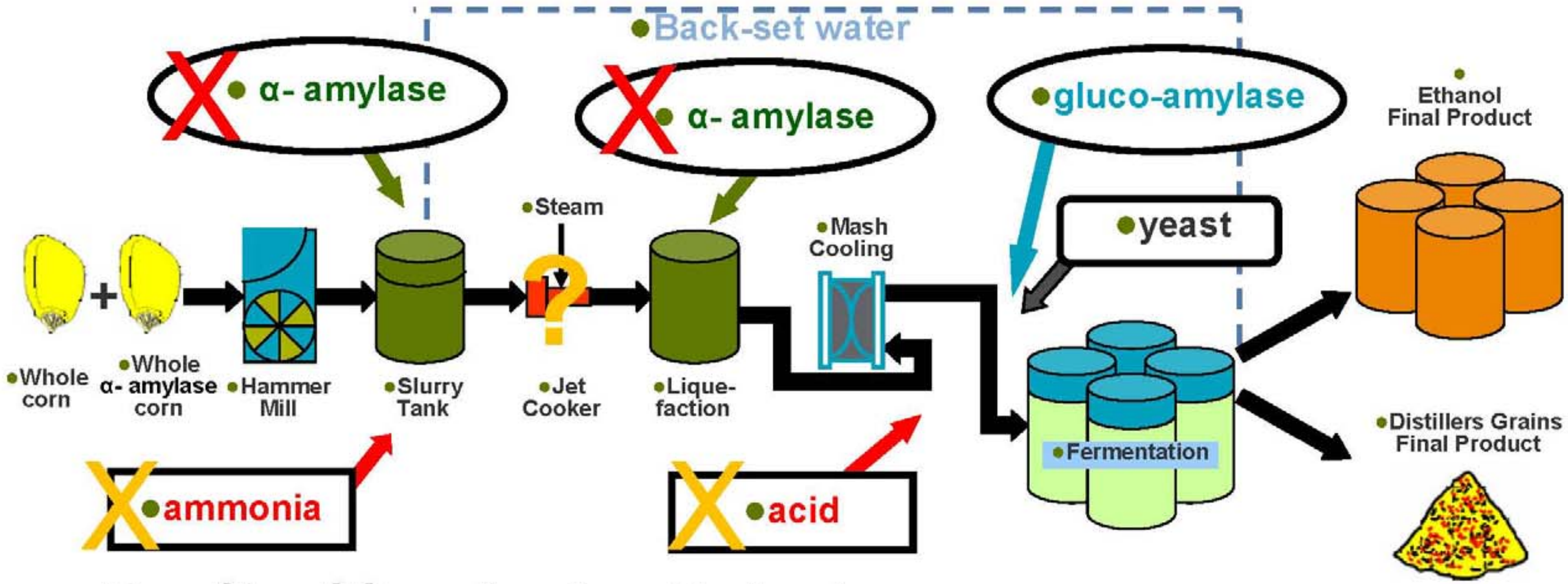


In grain, broad temperature range and pH tolerance

Optimizing the first generation starch-based ethanol process

- Alpha-amylase enzyme delivered directly in grain
- Energy, chemical and water savings
- Greater process flexibility
- Increased throughput
- Greater productivity, profitability and sustainability

Adding value to ethanol production with α-amylase corn



Benefits of Corn Amylase Technology

- Simplicity of α- amylase delivery
- Dramatic "viscosity break" reducing energy consumption
- Reduced equipment "wear & tear" and less maintenance
- Higher solids throughput and lower water requirements
- Greater plant output and efficiency
- Faster, more efficient, more profitable ethanol production

Optimizing the first generation starch-based process: Potential industry wide sustainability impact

By increasing the efficiency of production Corn Amylase/Enogen reduces energy and water needs as well as carbon emissions. In a 100 million gallon ethanol plant this could translate to:

Save 450K gallons of water:

- Equivalent to 6,900,000 8 oz cups of water

Save 1.3 million KWh of electricity and 244 billion BTUs of natural gas:

- enough to light 1,200 homes for a year
- enough to heat 3,889 homes for a year
- Save $1,684,000 in operational costs

Reduce the emission of 106 million pounds of CO2e:

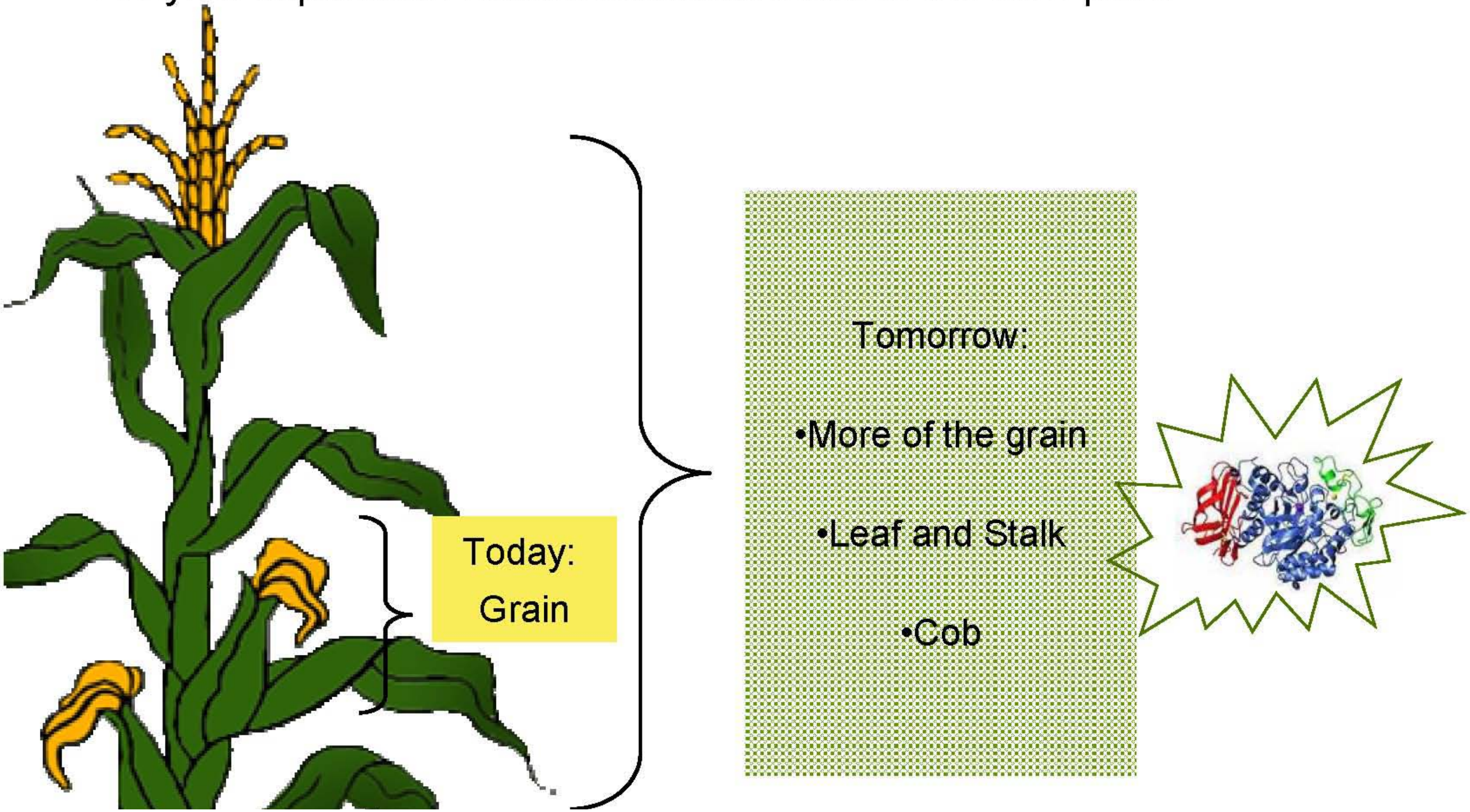
- Equivalent to removing 4,604 passenger cars from the road each year

Urbanchuk et al 2009 AgBioforum 12 2009

http://www.agbioforum.org/v12n2/v12n2a01-stone.htm

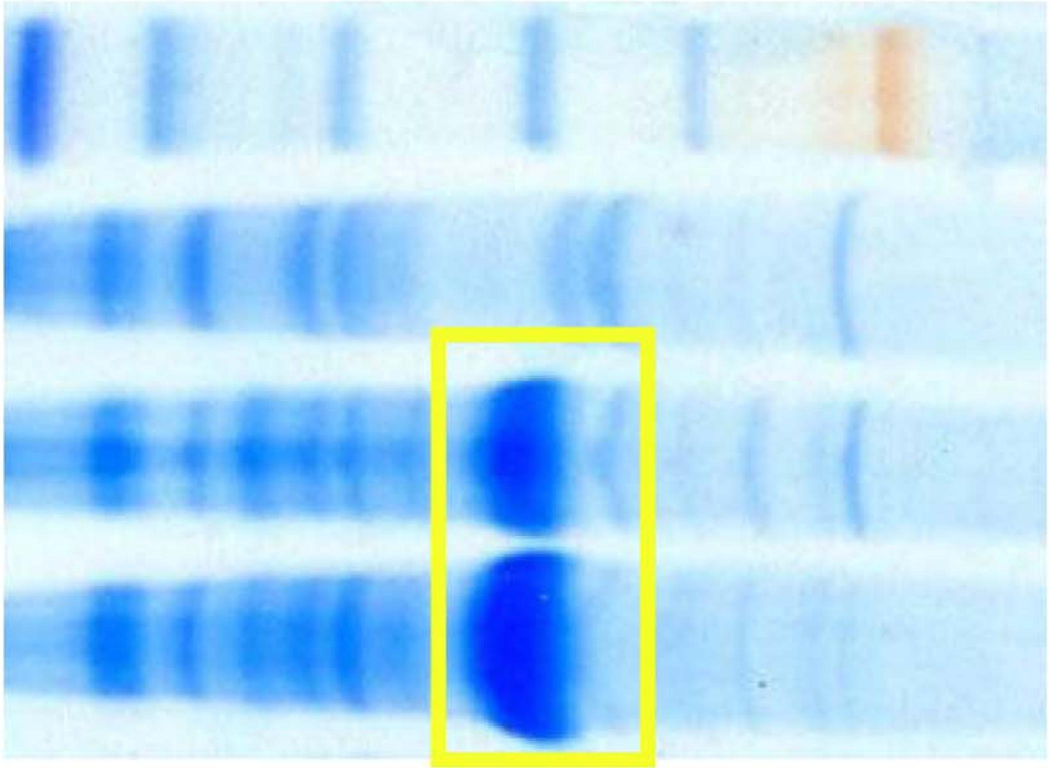
Unlocking the full potential of the corn plant - Tomorrow

Enzyme expression makes available more of the corn plant



Unlocking the full potential of the corn plant - Tomorrow

Capability to express robust, best-in-class enzymes at high levels and right location opens up more of the corn plant for conversion



Molecular Weight Marker

Non GM Corn Leaf

Cellulase Corn Leaf - plant 1

Cellulase Corn Leaf - plant 2

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Unlocking the potential of the plant – The Day After Tomorrow

- Moving what we can do in bugs to plants
- We need more tools for industrial application
  - Position dependent expression, more promoters, organelle specific.
  - Knowledge of fluxes through systems "fluxomics"
  - How different systems interact
  - Control mechanisms – eg cell signalling
  - Plant specific components/cassettes
  - Non invasive measurements – more reporter systems
  - Extraction procedures – cost efficient – eg compartmentalisation, secretion
  - Crop and weed knowledge

Protein and metabolic engineering

- Low lignin plants
- High lycopene/vitamin levels
- N_2 Efficiency
- Water efficiency
- Controlling flowering time
- Flower colour
- Heterosis – vigour
- Metal deficiency
- Starch production

Risk perception

- Integrating risk perception and mitigation will be critical to the implementation of industrial aspects of Synthetic Biology
- This is especially so in Europe where the GM debate has been challenging

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Risk perception

Synthetic Biology Dialogue

Opportunities and Next Steps?

- Integration of Systems and Synthetic Biology
- Further development of existing crops to improve, yield, quality and stress resistance
- Plant processes transferred into microbes
- Microbial processes transferred into plants
- Improved consumer characteristics – tastier tomatoes

Future science...

- Develop carbon dioxide further as a chemical feedstock, e.g. Plants capture it slowly, algae are 10x faster. Could we develop a system which is 1000x or even 1,000,000x faster?

Conclusions

- The knowledge and technology with which we can start to engineer multiple changes into plants using Synthetic Biology is developing rapidly – we are on a path of understanding them
- Pathway engineering is a key opportunity

Thank you

BRINGING PLANT POTENTIAL TO LIFE

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