



syngenta

# Recent Successes in New Product Innovation: What Works Best?

**Mike Bushell** 30th November 2010

## The challenge of feeding 9 billion people

The world must grow more crops on the currently available land to meet the increasing demand for food, feed and fuel

***Growing more from less***



## The role of crop protection



40% of the world's food would not exist without crop protection products

- Raising Yield Potential
- Protecting Yield
- Increasing Yield Quality

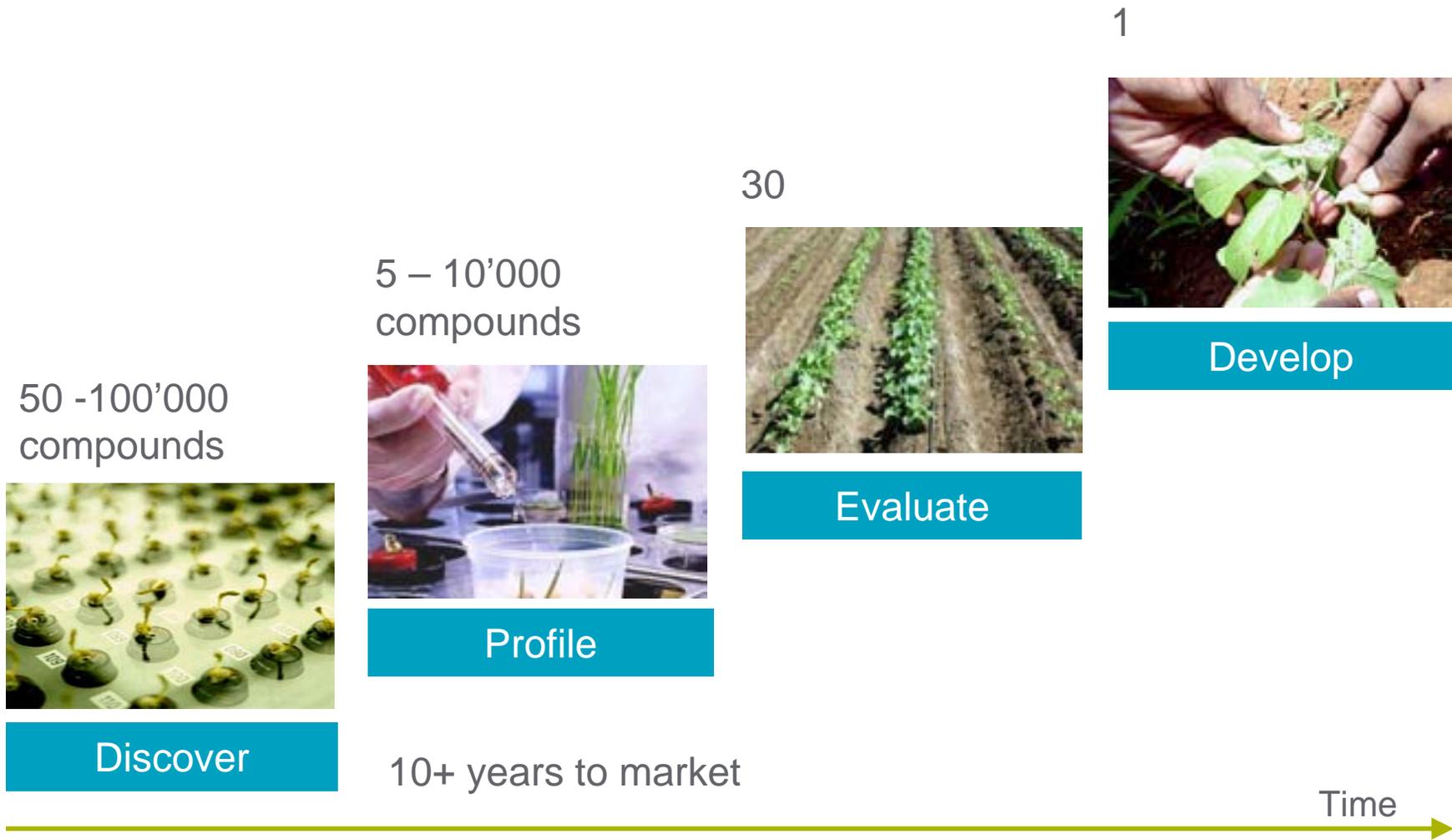
# Technology for Sustainable Ag

- Inventing a new product
  - Breeding new crop varieties
  - **Crop Protection chemicals**
    - New active ingredient, Formulation and process studies
- Product Life Cycle Management
  - Themes – **the importance of underpinning capability and Knowledge based decisions**
- **Integrated technology approaches**
- **Systems approach in fields to improve outcomes**
  - Technology plus Agronomy
    - **Productivity, Biodiversity, Soil and Water protection**
    - **Resource use efficiency**
      - **Water, Land**

## Recent Successes in CPR&D

- Continued growth of blockbuster products
  - Life cycle management - Mesotrione, Amistar, Thiamethoxam
  - Seed Care
  - Crop Enhancement effects
- New ai introduction
  - Revus – potato blight fungicide
  - Bontima – first product launch of new fungicide class
  - Virtako/Durivo broad spectrum insecticide
  - Axial – New Cereal Herbicide (ACCCase inhibitor)
- Expensive business – average industry cost ca \$250m per new ai
  - How is it done and what works best?

# Crop protection compounds: the long road to market

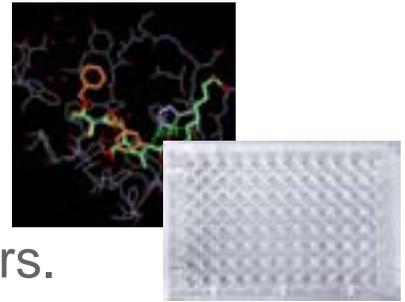


## Improving the success of lead generation

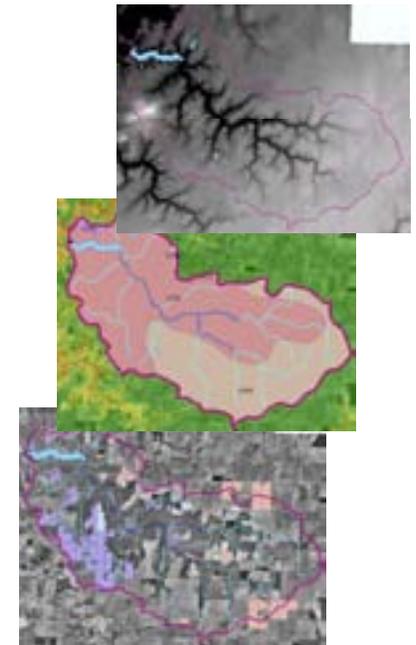
- Make and screen more chemicals
  - Find better chemical sources
- Natural Product derived leads
  - Opportunities for unique “inspiration”
  - Playing the “long game”
- Fast Following
  - Best starting point?
  - How to be faster?
- Innovation by Design
  - Leveraging Bioscience knowledge and modern analytical science



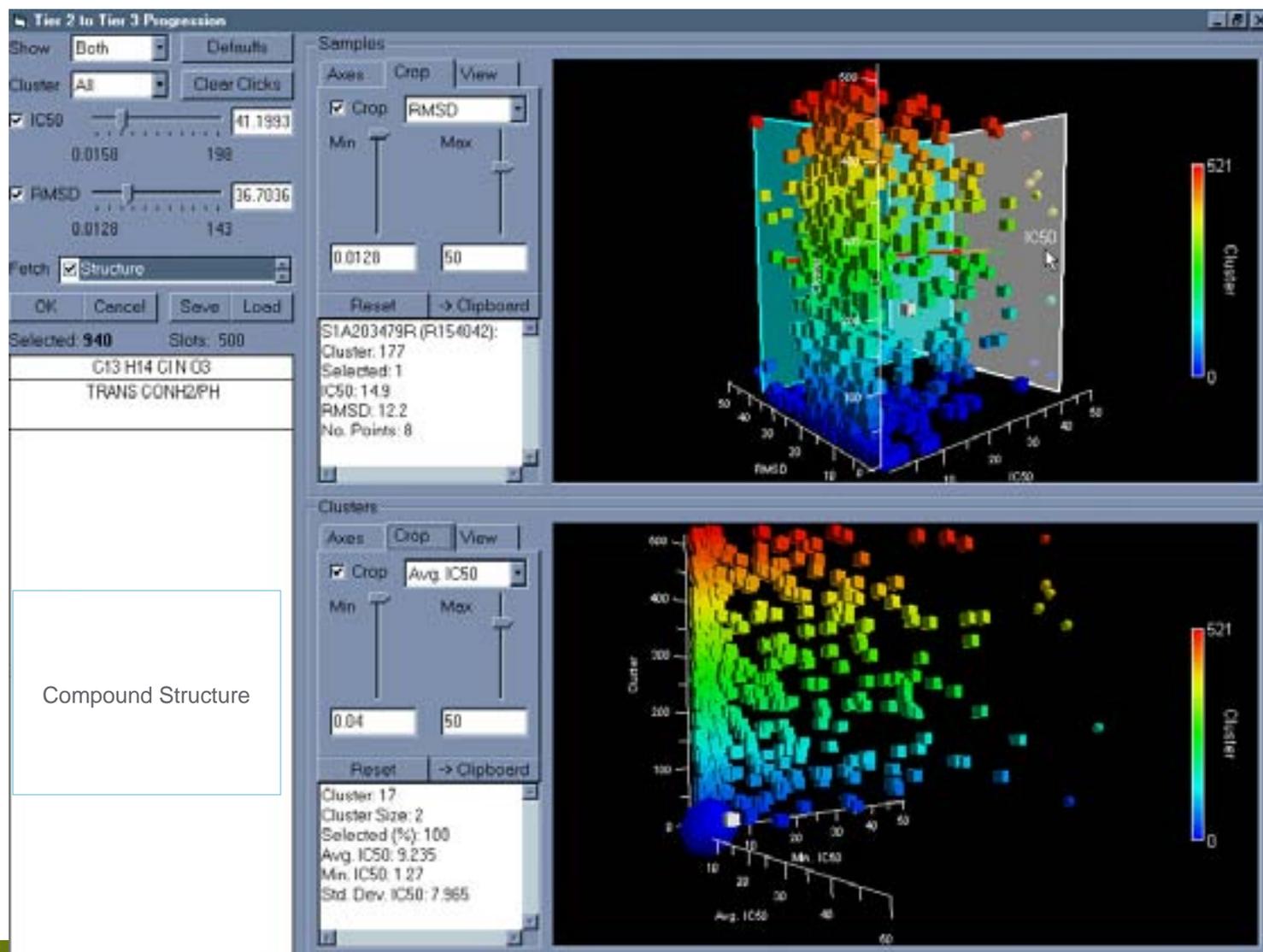
## High throughput technologies let you do more...



- **More Chemistry** – enormous growth in the last 20 years.
  - Combichem libraries - infinite possibilities
  - Purchase; >4 million compounds available for purchase \$10 / 5mg
  - Physical properties – logP, solubility etc.
- **More Biology**
  - Miniaturised biochemical and whole plant assays
  - Model organisms, indicator/smart screens
  - Images – physiology, symptomology
- **More Bioscience** measurements through automation
  - Biochemistry and biokinetics
  - Protein Crystallography and X-ray
  - ‘Omics – metabolite profiling, transcriptomics
- **More modelling** - Molecular to landscape level

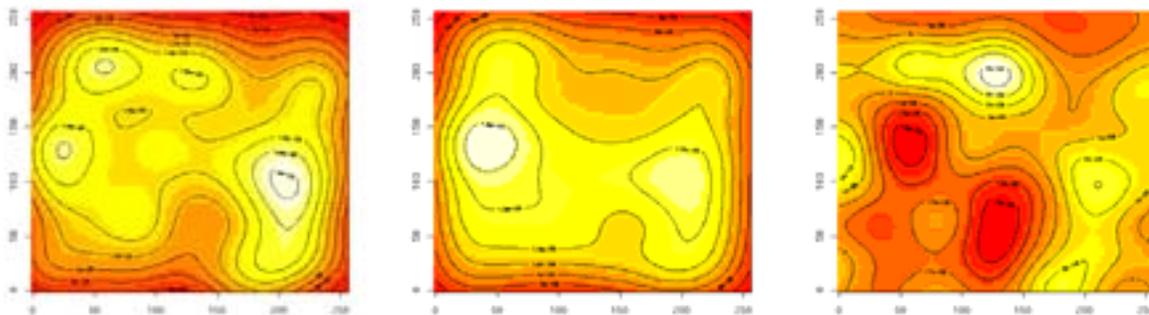
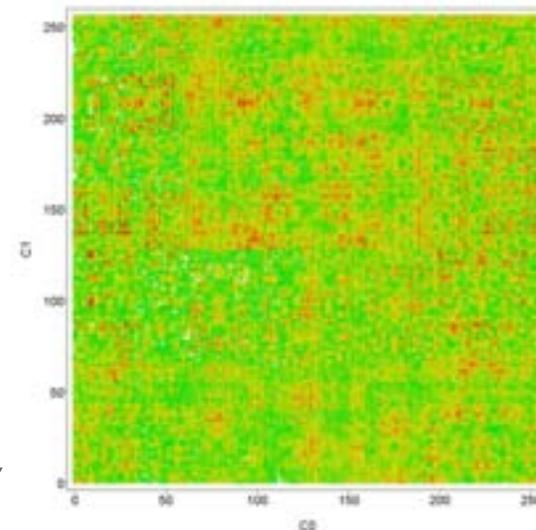


# Making sense of data? - multi dimensional visualisation



## Simplifying multi-parameter space

- It is possible to map the whole of chemical space onto a finite square.
  - Squashing infinite space into a finite area involves compromises.
  - Properties map to neighborhoods
- The maps make sense – similar compounds with similar properties are grouped together
- Maps can be compared with each other – the **key benefit of this technique**.
- **Informs decisions** e.g. Purchase of compounds



J Delaney Syngenta data  
Fingerprinting, similarity  
mapping, neighbourhood  
behaviour, Gray codes, ID  
number line conversion to  
2D Hilbert curve

## Natural Products

- Inspiration for many key product classes
  - Pyrethroids, Strobilurins, HPPD inhibitors
  - VIP trait in GM insect control
- But many problems
  - Slow
  - Rediscovery issue
  - Structural Complexity
  - Cost and resources required for success
- Are there any ways to take a smarter approach?
  - Location for cost, traditional **indigenous knowledge**

## Natural Products Collaboration in China



## Fast Following

- From fast to faster
- How to recognise critical new areas quickly
- Efficient processes, focussed teamwork, indication expertise
  
- Knowledge based approach
- Discriminating data

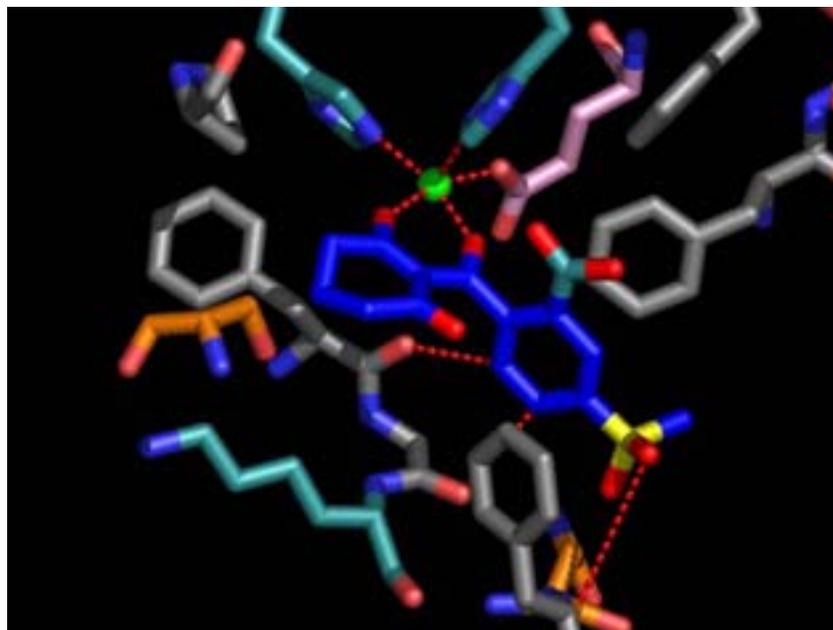
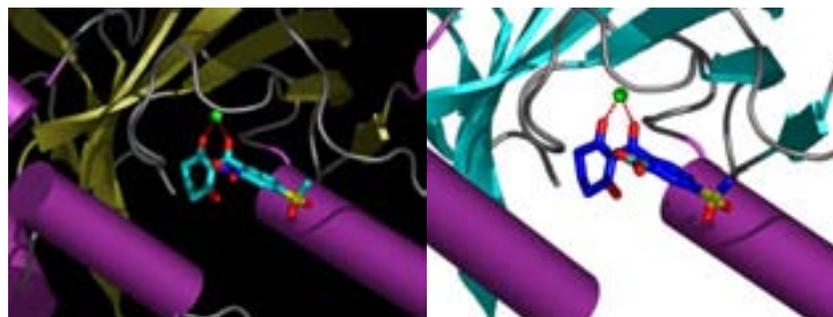
## Innovation by Design

- Biochemical rationale – moa based ideas
- Many tools can help
  - Genetic Modification
  - Protein Science
  - Smart screening
  - Protein crystallisation
- Not exclusively one approach
  - Innovation at intersections
    - i-Zones for cross disciplinary networking
  - Open innovation platforms

## Innovation Capability

- Clarity of the target
  - Linking R&D to the business and customer needs
- Networking
- People
  - Mindset
- Environment
  - Capabilities

## Hi tech approaches to design



- Protein X-ray crystallography and modelling

## Biology screening on target – lab to glasshouse to field



- Robust, routine, reliable screens, representative of field

## Automating the black art of formulation

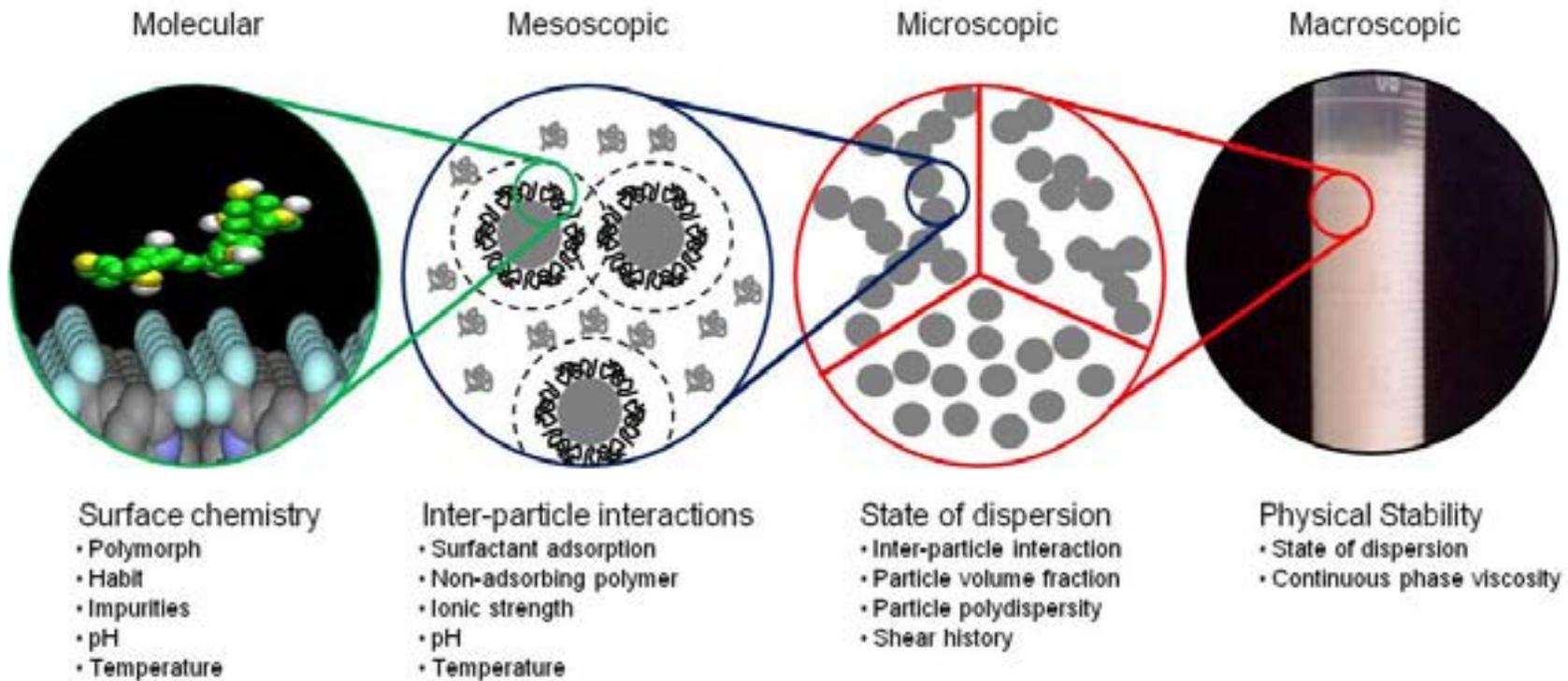
- Formulation Robot - the culmination of a 5 year project to design and build this unique facility
- Bosch – IP sharing for mutual advantage



# Long time to visibly establish instability – sedimentation can be discontinuous



# Stability Needs

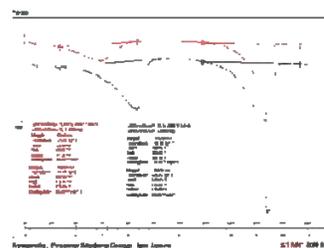
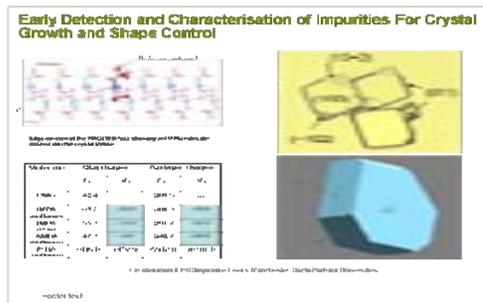
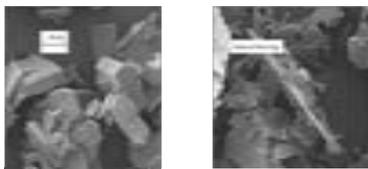


- Phase Mapping/State Behaviour of Real Particle Dispersions and Transient Gels in relation to sedimentation mechanism and rheology
- Measurement of structure and dynamics of structure stability and sedimentation – predictive sedimentation models for dynamic systems
- Extending modelling capability toward molecular scale
- Defining key physical quality attributes for robust window of operations
- Solid state phase stability against growth and modification – opportunities for meta-stable systems

# Particle Science and Technology

## Process and Product Design

Phosphono Methyl Glycine (PMG)  
Impurity Based Shape Modification on Scale-Up Leading to Solid-Liquid Separation Problems



Formulation Instability  
Due to Polymorphism



- HTS crystallisation, X-Ray Diffraction, Calorimetry, Polymorphism studies, crystal growth inhibition, crystal shape modifiers, co-crystallisation, manufacturing support

**IZM**  
THE NEXT GENERATION  
WHEAT FUNGICIDE

Double  
Binding  
Technology

syngenta.

# IZM is the next generation cereal fungicide



IZM is the benz-pyrazole cereal fungicide with unique Double Binding technology

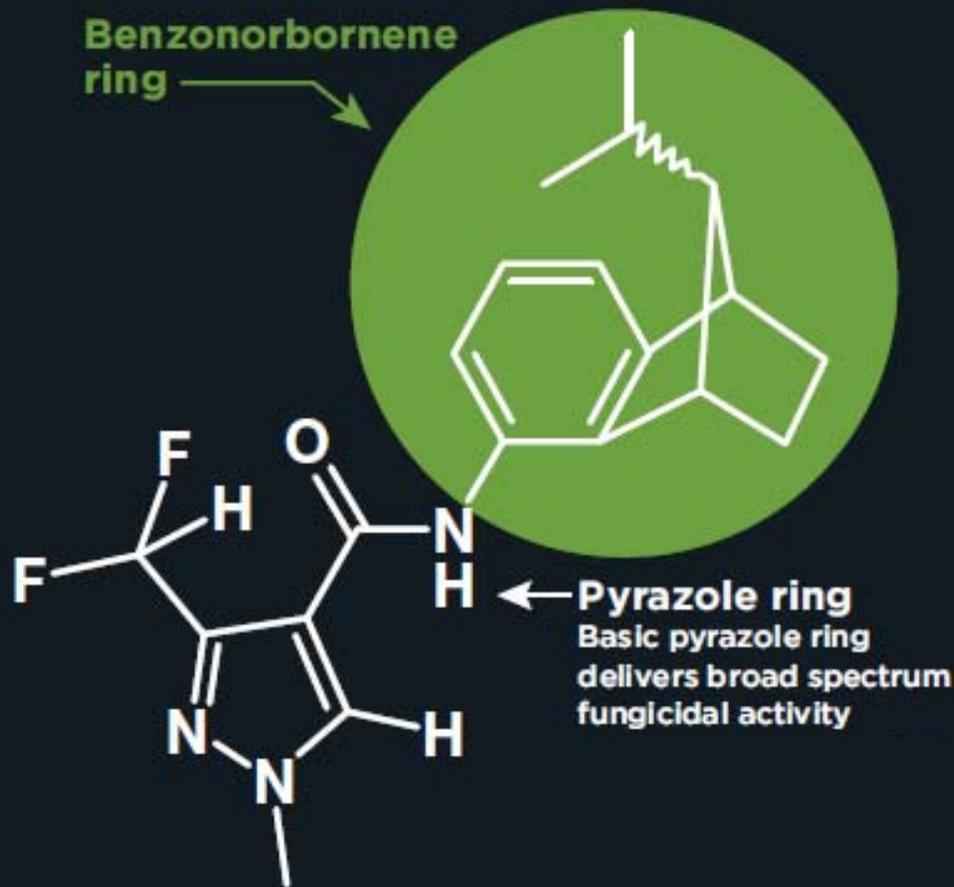
Delivers powerful binding to the pathogen offering greater potency against *Septoria* and rust

Strong and durable binding to the leaf wax delivering long lasting disease control

# IZM is a Benz Pyrazole

Exclusively IZM

Common  
to all new  
SDHI's



More potent  
in cereals

+

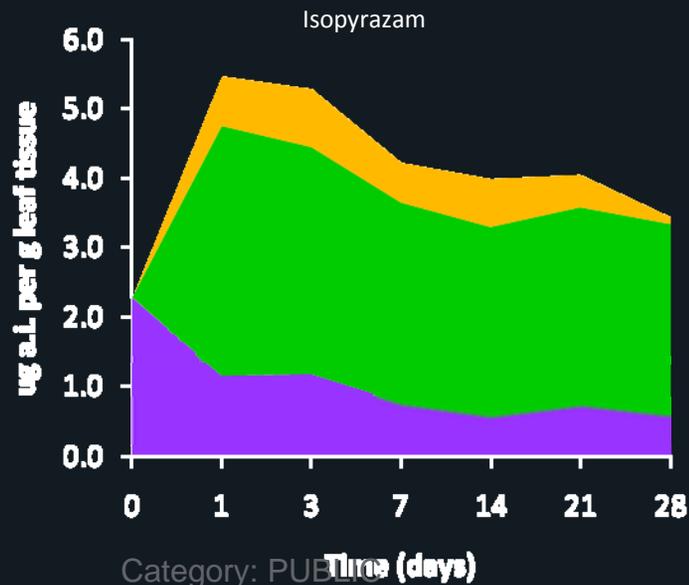
Stable  
binding to  
the wax  
layer

## Double binding 1 – more potent:

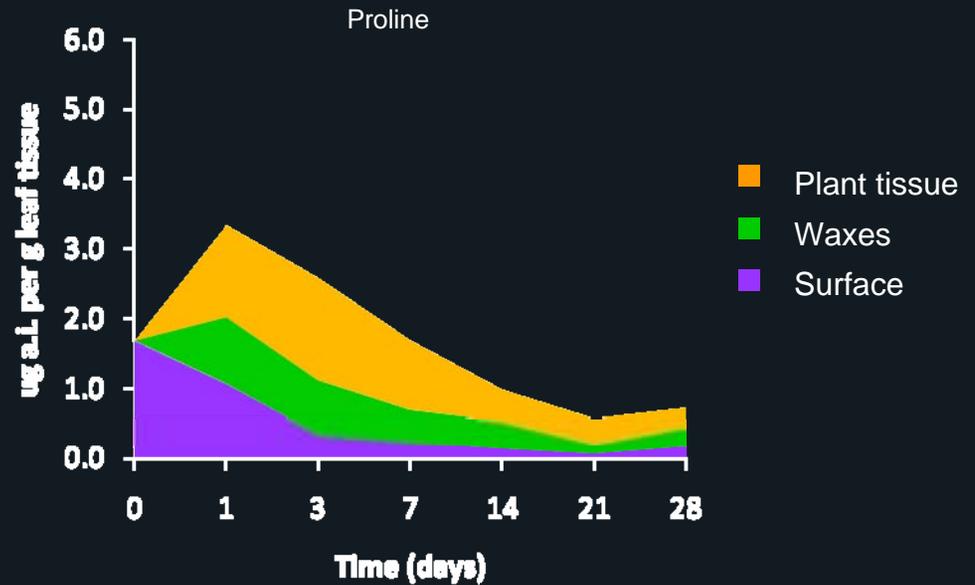
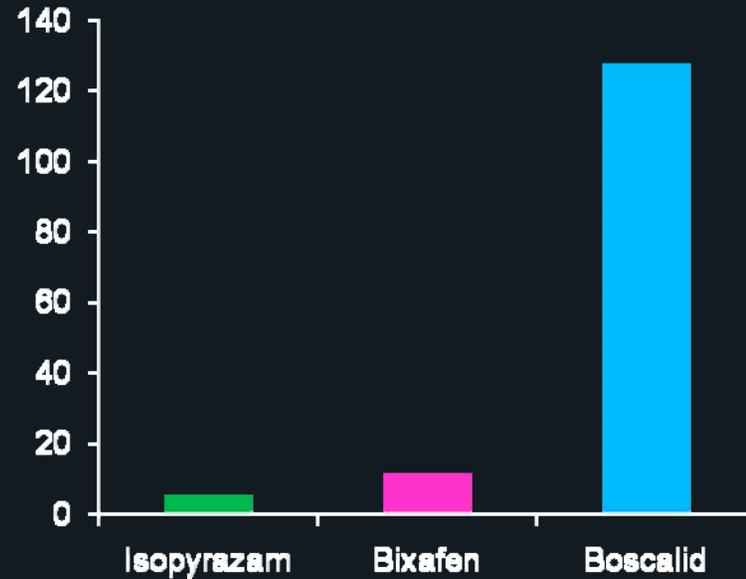
2 x more than Bixafen

25 x more than Boscalid

## Double binding 2 – longer lasting:



IC50 (nM) Septoria – mitochondria binding assay



**IZM**  
THE NEXT GENERATION  
WHEAT FUNGICIDE

Outstanding Septoria and  
Yellow Rust control



**Septoria tritici control - Untreated – Consort (King's Lynn 06/07/2009)**



**IZM 1.0 l/ha EC**



**IZM / EPZ 1.0 l/ha**



**8.50 t/ha**

**Yellow Rust control Untreated – Robigus (Terrington) -6<sup>th</sup> July**

Category: PUBLIC



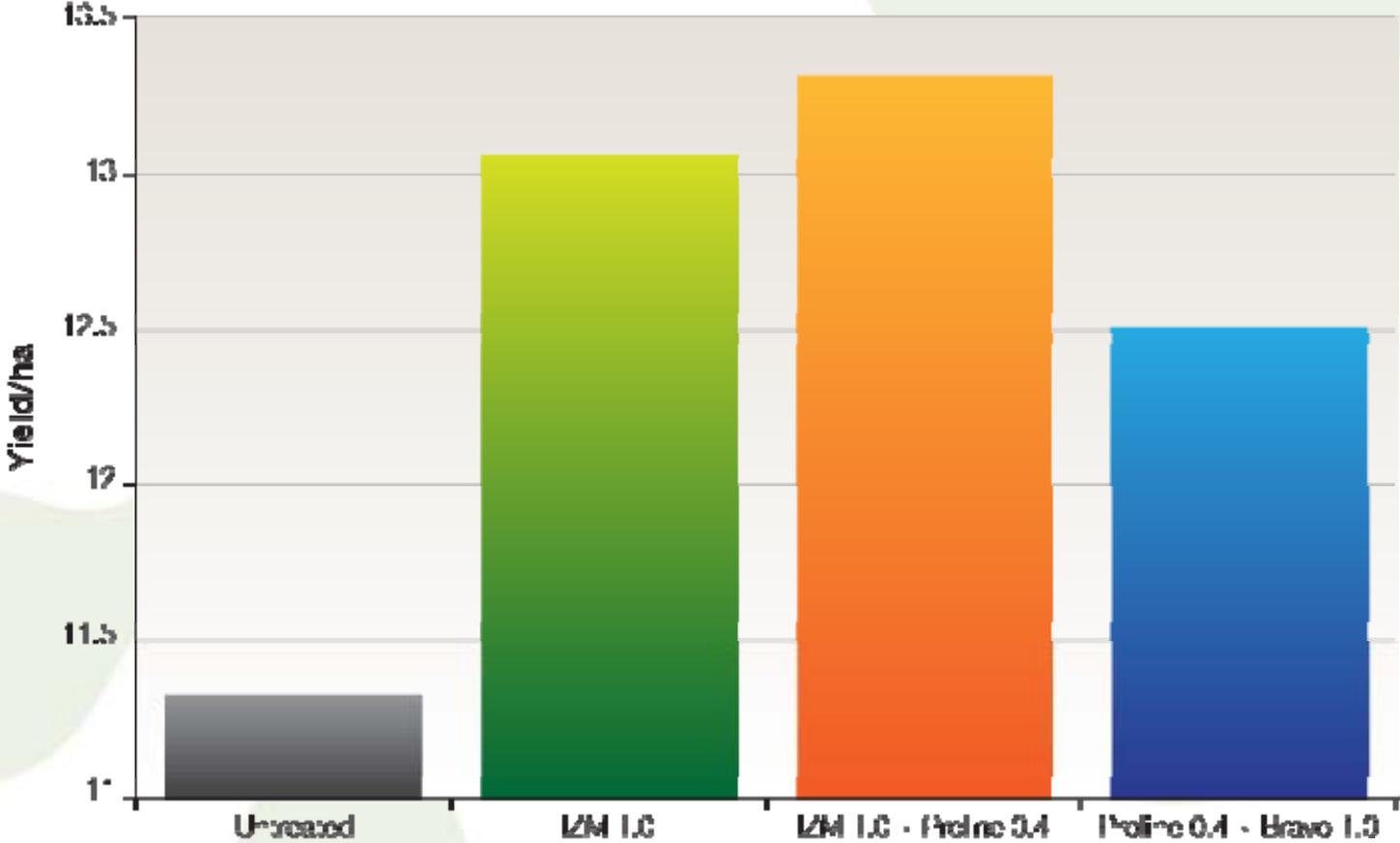
**13.60 t/ha**

**+5.1 t/ha**

**IZM 0.75 + Proline 0.4 fb IZM 0.75 + Proline 0.4**

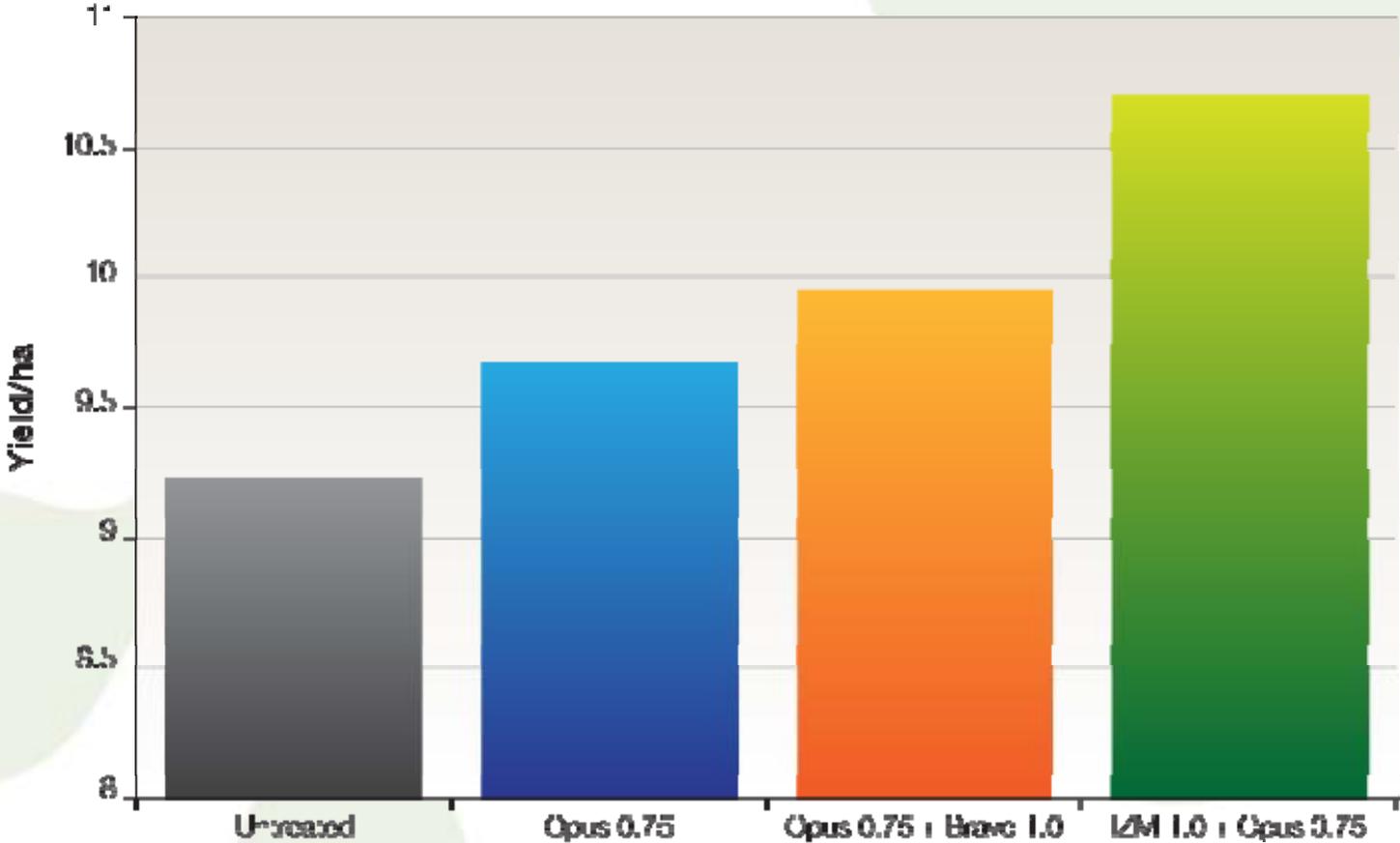
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# IZM takes wheat yields forward – T1



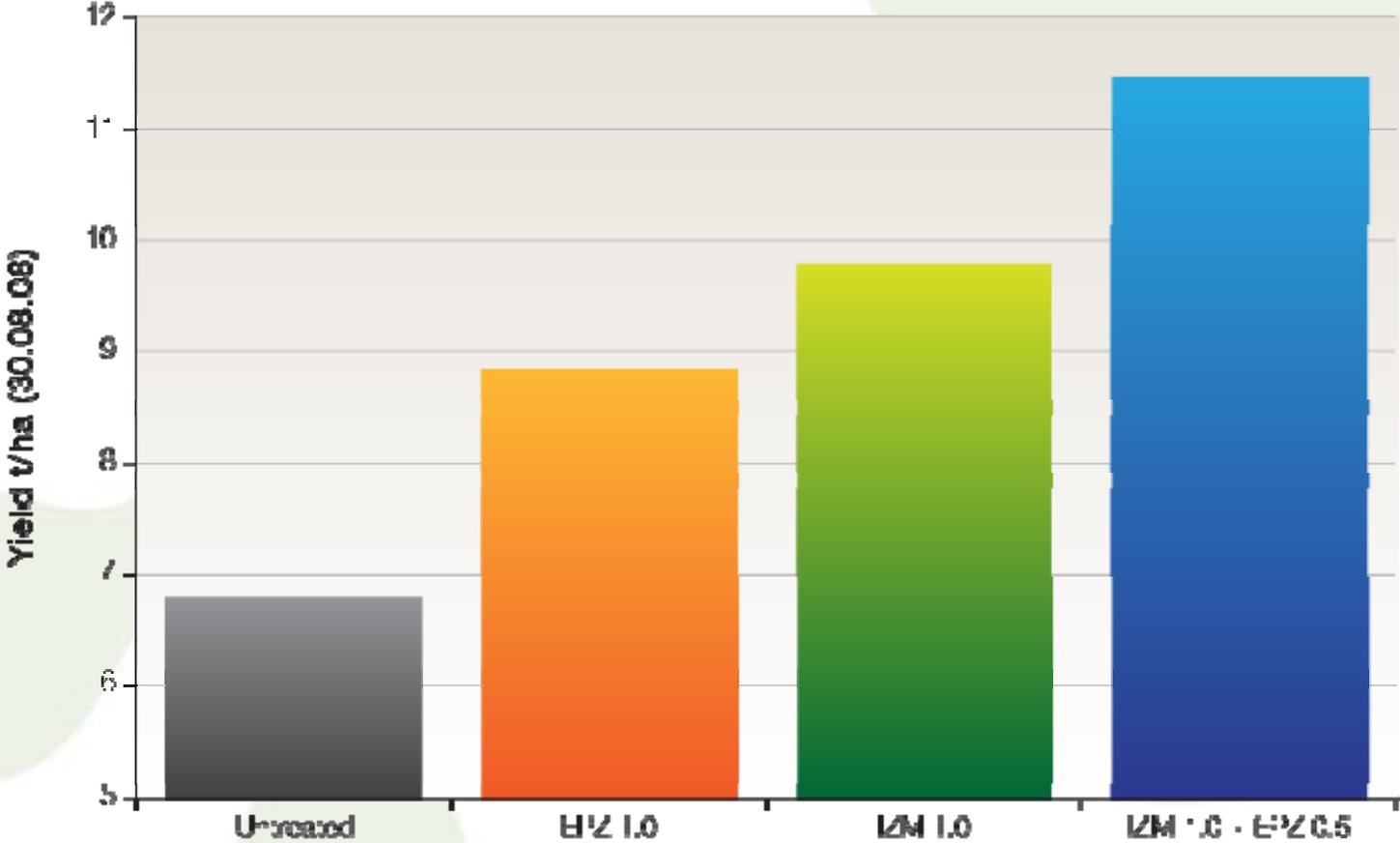
Variety: Consort LSD: 0.62 Application: GS31/32 (20/04) Source: Syngenta 2009

# IZM takes wheat yields forward – T2



**Variety:** Ambrosia **Application:** T2 application only, T1 OPUS 0.5 + BRAVO 1.0 l/ha **Source:** ADAS 2009

# Longer lasting control drives higher yields

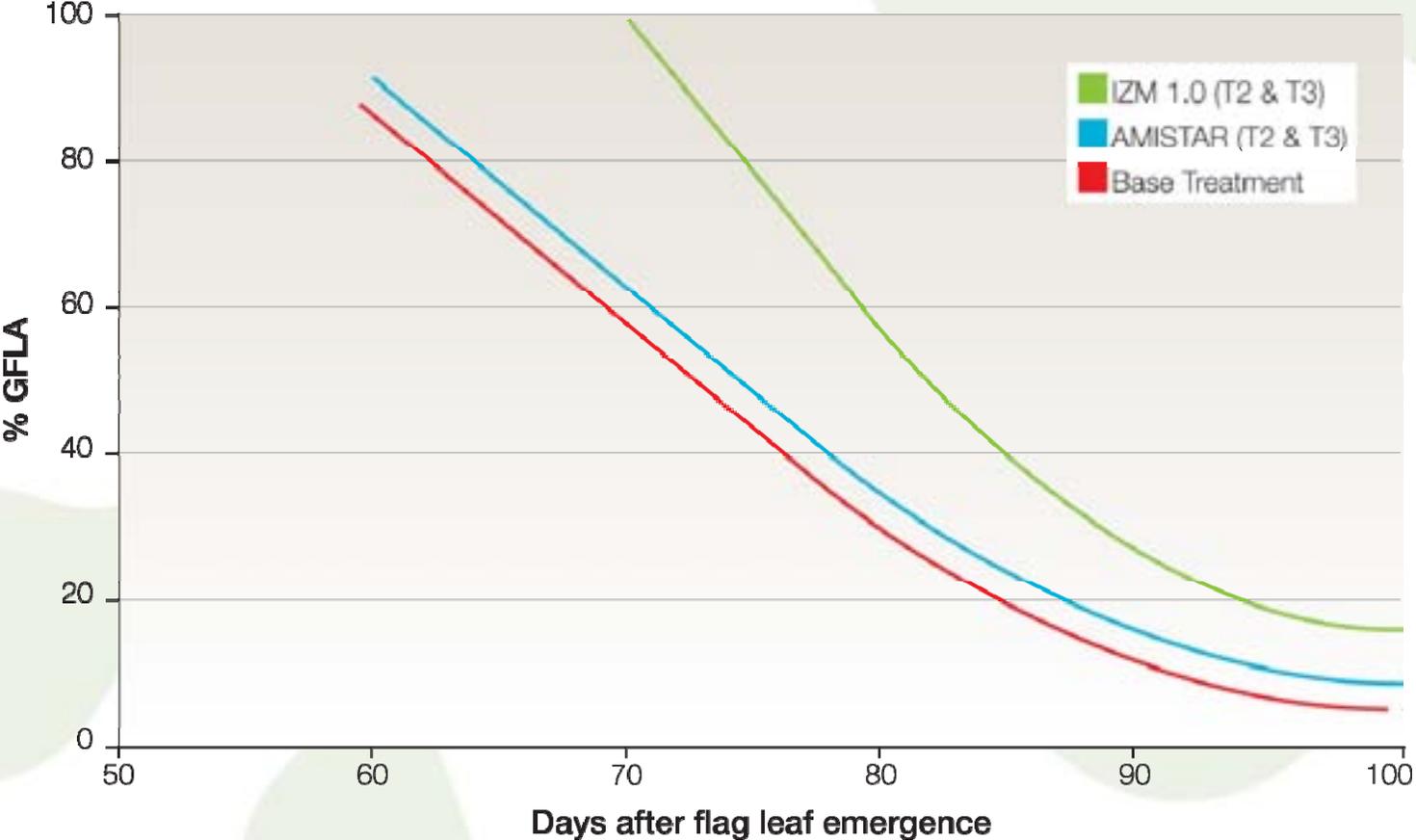


Variety: Duxford LSD: 0.96 Application: GS30-31 (22/04), GS39-41 (14/05) Source: Agrisearch 2008

**IZM**  
THE NEXT GENERATION  
WHEAT FUNGICIDE

Double Binding  
Technology for  
long lasting greening

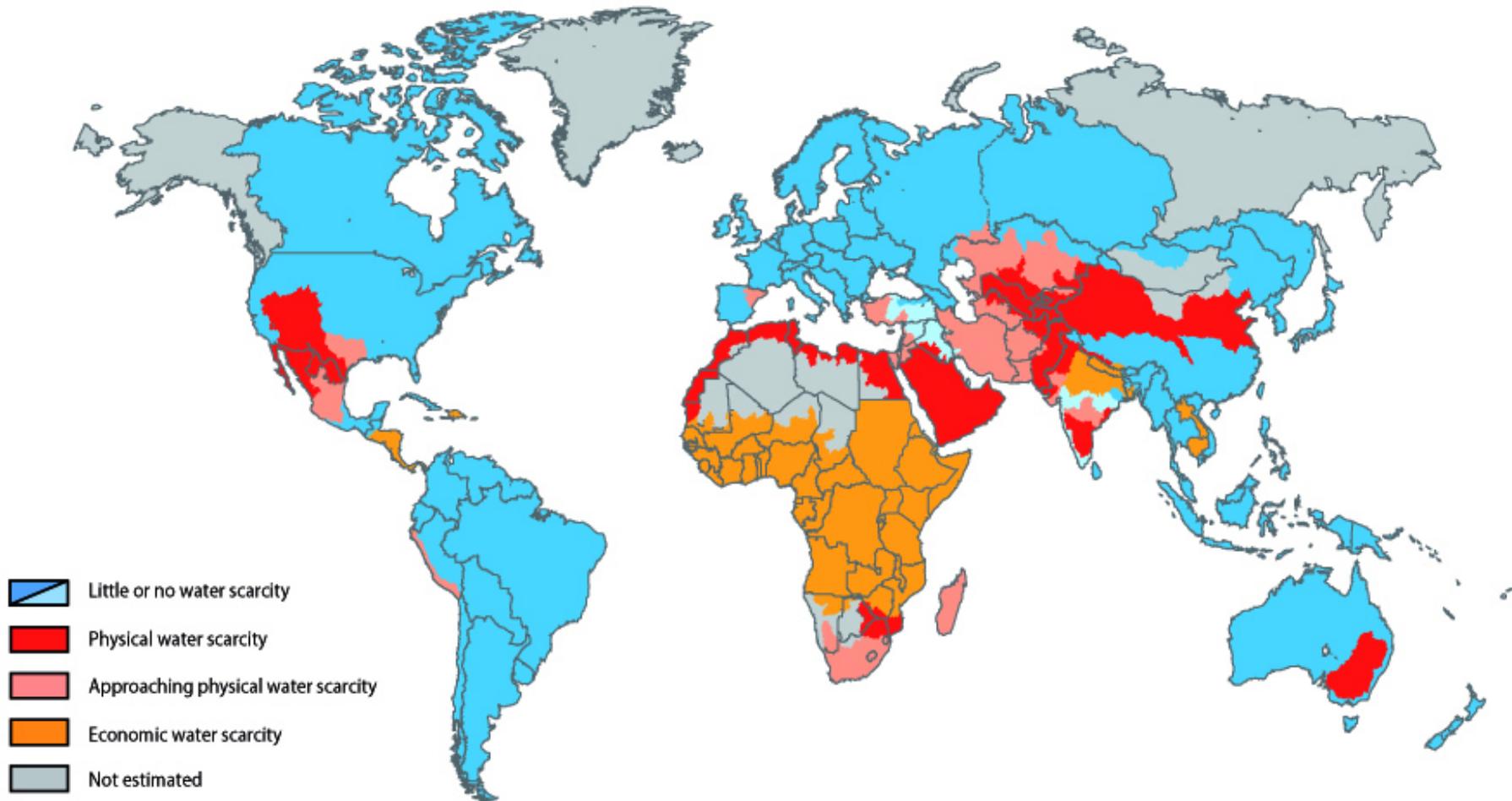
# IZM delivers retention



**Variety:** Glasgow and Ambrosia  $P = <0.001$  **Application:** GS39 and/or GS59  
**Source:** HAUC 2008 Base = 1.0 OPUS T1/T2 fb 0.5 Prosaro. Test products applied at full rate

# Integrated Technology Approaches for Better Outcomes

## Areas of physical and economic water scarcity



Source: IMWI report, Insights from the Comprehensive Assessment of Water Management in Agriculture, 2006 / p8

## Crop Enhancement Chemicals for Water Efficiency



- Programme containing Growth regulator “Moddus” in Wheat
- Yield +15-25%; Reduced irrigation - Water savings 15%
- “Crop per Drop” improvement ca 35%

## Water optimization : Combining GM and non-GM technology

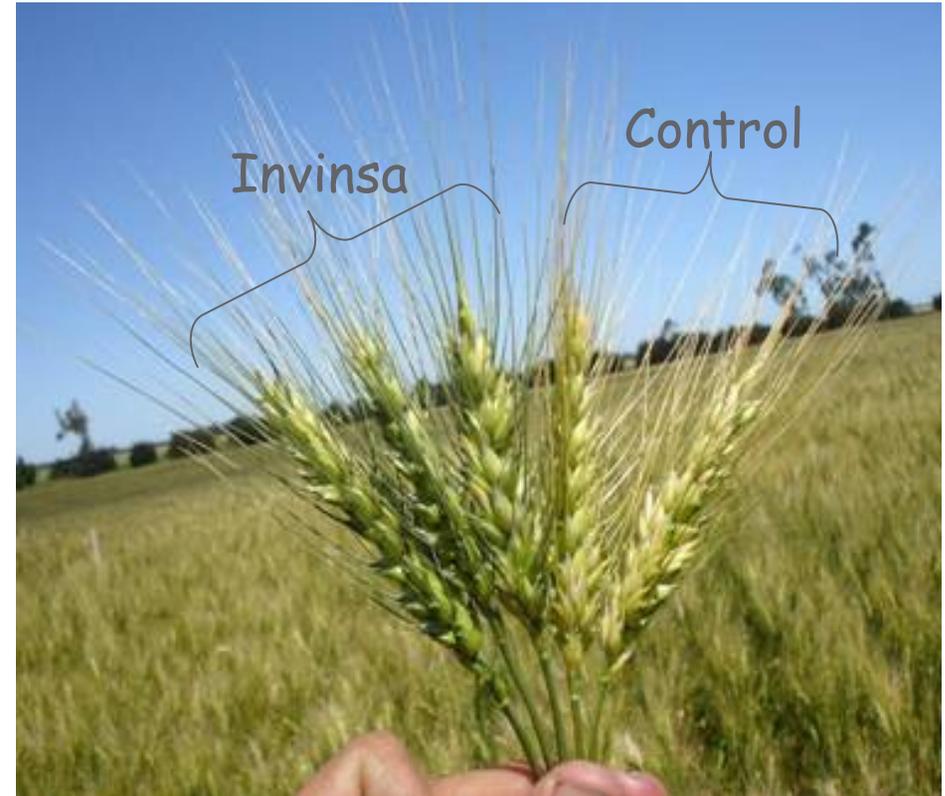
- Drought during pollination leads to poor kernel set
- New technology can protect during drought conditions
- Multiple complementary approaches to new seed varieties: native trait and functional genomics, transgenics
- New trait constructs are currently under evaluation in field trials
- 1<sup>st</sup> Launch US corn, US 2011



Unstressed Plots

Stressed Plots

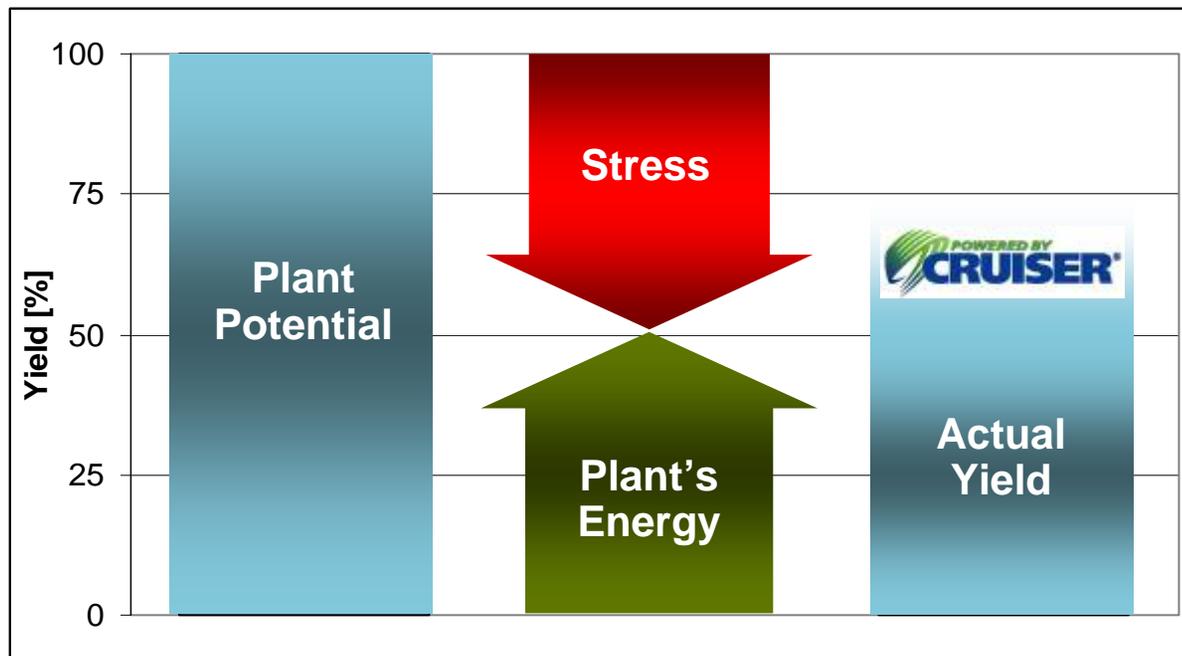
# Chemical approaches to crop enhancement



WHEAT: Invinsa delayed senescence in both stems/leaves and heads when applied at flag leaf and/or heading stage

# Seed Treatment – Chemicals Complementing Genetics

Abiotic stresses are responsible for more than 50% yield reduction. Thiamethoxam shown to activate proteins that protect against stress.



Stress: drought, heat, salinity, UV light, nutrient deficiency etc.



## Agronomic practices for Water Conservation

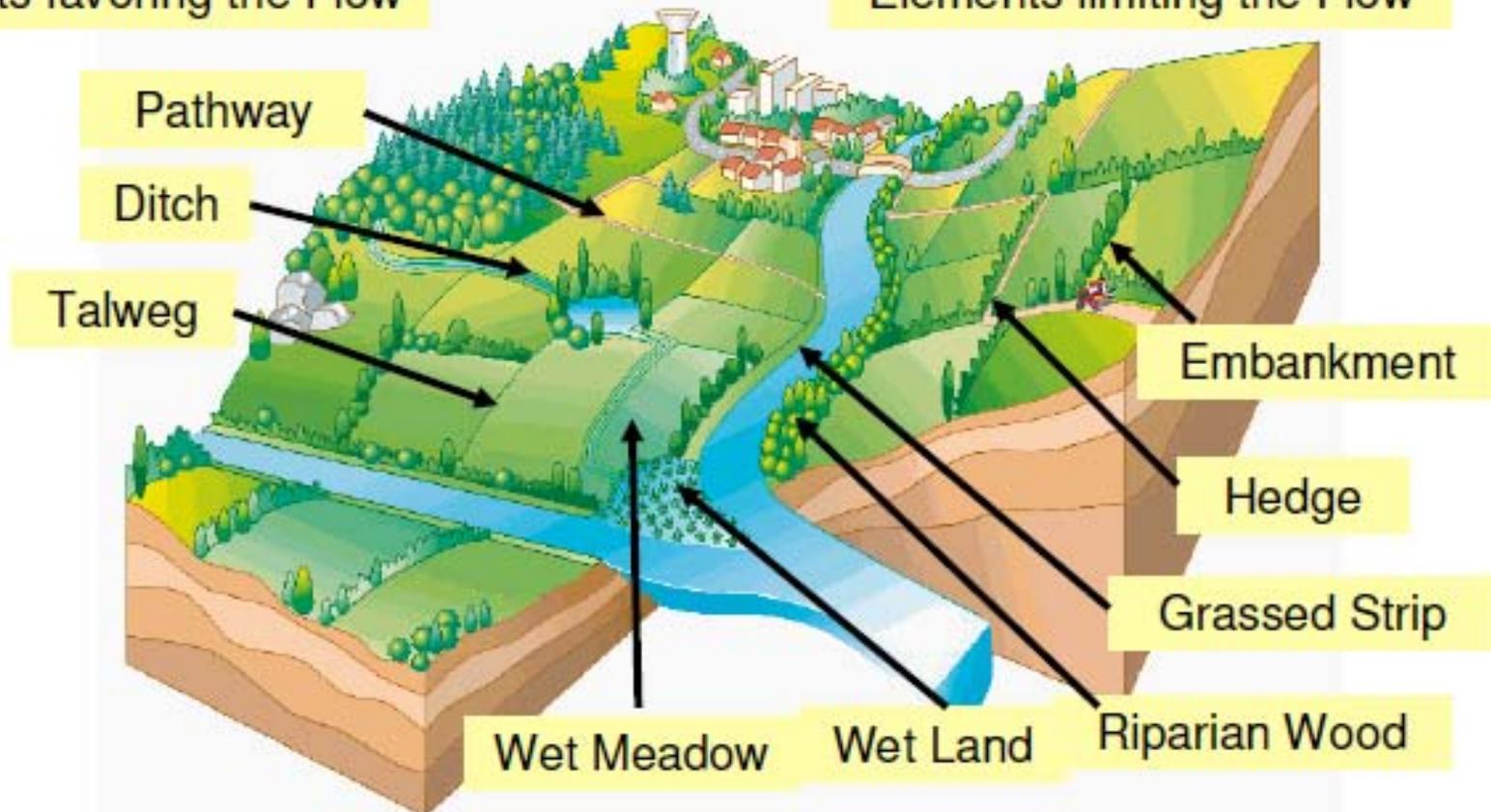


- Useful in water dependent crops like rice...
  - Drip Irrigation
- Pani-Pipe project Bangladesh (50,000 units)
- 46% reduction in water use; 23% cost reduction
- 4-5% yield gain; 27% farmer profit increase

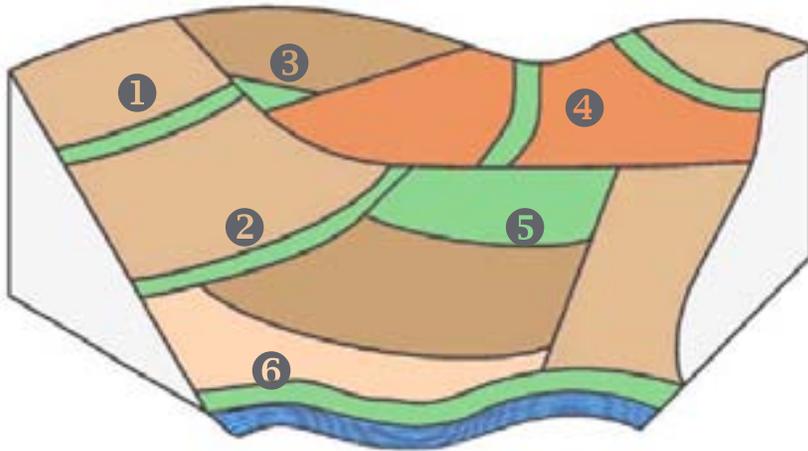
**Water Quality (and aquatic biodiversity) – Best Management Practices**  
Point source – TOPPS, Diffuse pollution – AIM (= work in progress)

Elements favoring the Flow

Elements limiting the Flow



## Describing the correct positioning of vegetative buffer strips...



1. buffer strip inside field
2. buffer zone at the edge of a field This could be a non treated area, and a grassed strip between the field and a road
3. grassed corner of field, where water concentrates before flowing down the catchment
4. grassed pathway to reduce water flow where it concentrates
5. grassed field positioned to intercept concentrated runoff
6. grassed strip along river, to intercept diffuse runoff

# Operation Pollinator: Creating farmland habitats for high biodiversity



Crop

Limited value plants & invertebrates  
Simple structure & composition



Wildflower Mix

Very visual  
Attractive to the widest range of invertebrates & butterflies (8X)



Tussocky Grass

Good for invertebrates (4X bugs & spiders) & small mammals



Pollen & Nectar Mix

Best for Bumblebees & butterflies (13x)  
Pollen & nectar abundant

# A win-win-win Situation for our customers + agriculture: Fulfil environmental obligations + increase of biodiversity + enable efficient farming



## What we do

- Cultivating pollen + nectar margins around fields
- Innovative pesticide use
- Develop targeted seed mix
- Best managmt Practice
- Train farmers + experts
- Educate society



## What we achieve in short term

- Increase of Crop yield
- Simplify field management
- Environmental payment
- Increase habitat for Pollinators
- Increase Pollinator numbers



## What we achieve in long term

- Increase overall biodiversity
- Create habitat for mammals and farmland birds
- Create a more sustainable farming system
- Knowledge on Pollination + Environment
- Grow more food from less land

## From Understanding to Superior Products

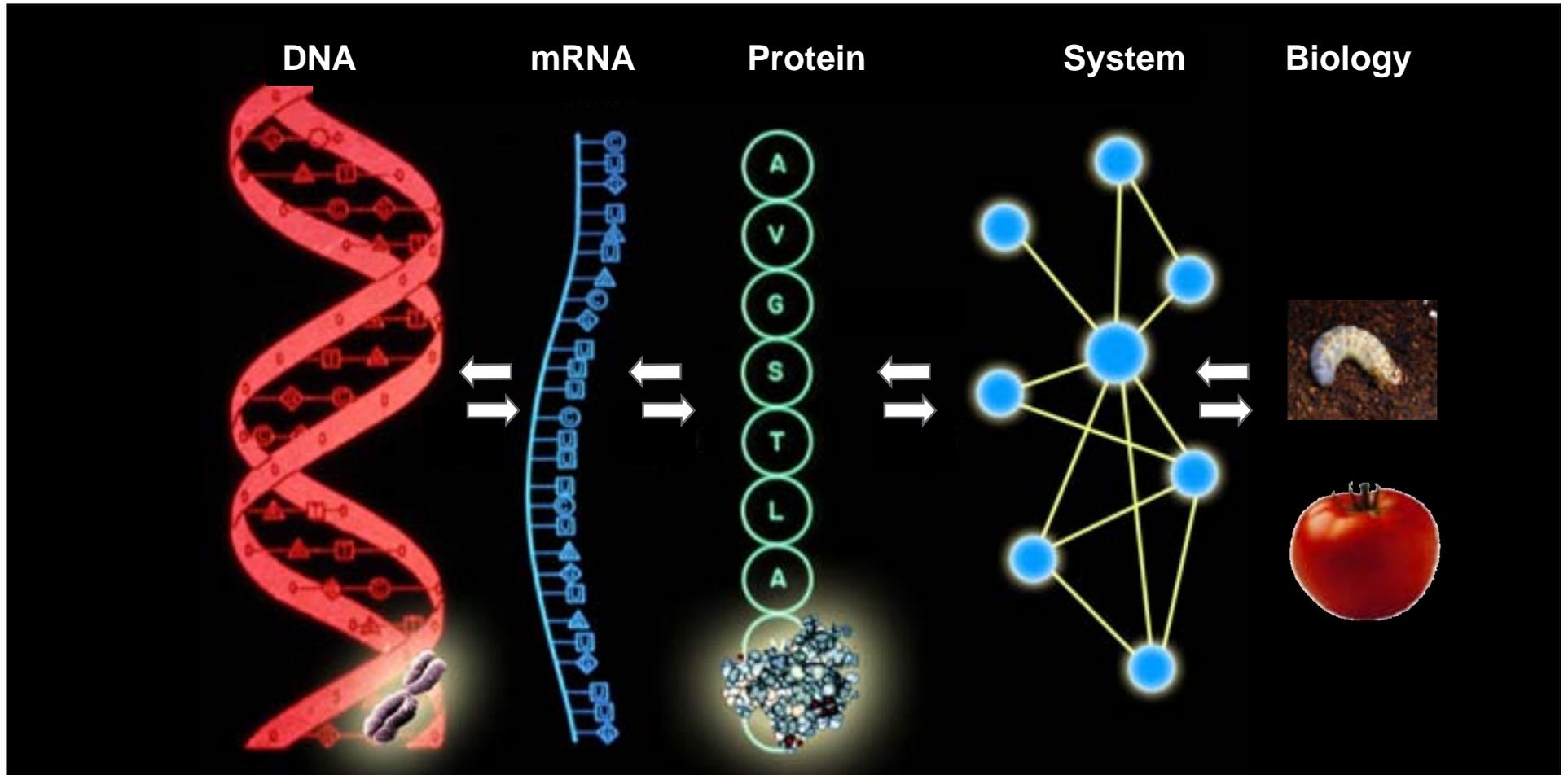
# Translating Scientific Information into Knowledge

From gene data across technologies and crops....



....to trait and marker knowledge within crops

# “Understanding” means - DNA to RNA to Protein to Systems to Organism plus Environment.....



**Predictively linking the genotype to the phenotype.**

## Why an interest in Systems Biology?

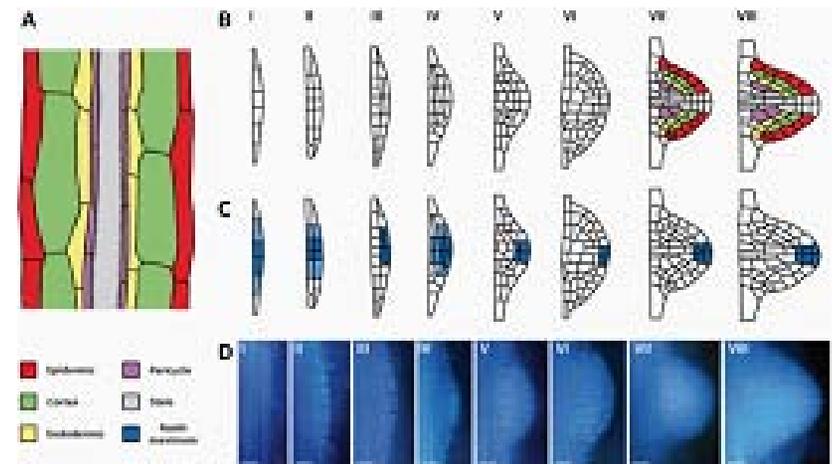
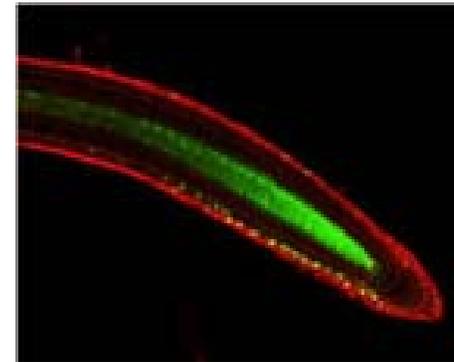
Unprecedented opportunity to understand fundamental biological processes

• Better prediction; from pathway to ecosystem scale

- Translocation and uptake
- Metabolism
- Excretion
- Neurotransmission
- Enzymology
- Multiple gene expression/interactions – stacks
- Epigenetic effects
- Toxicology
- Environment – eg climate
- Plant growth and yield
- Drought
- Ripening
- Heterosis
- Flowering
- Flavour
- Oil content of seeds
- Marker identification
- Prediction of phenotype from genotype

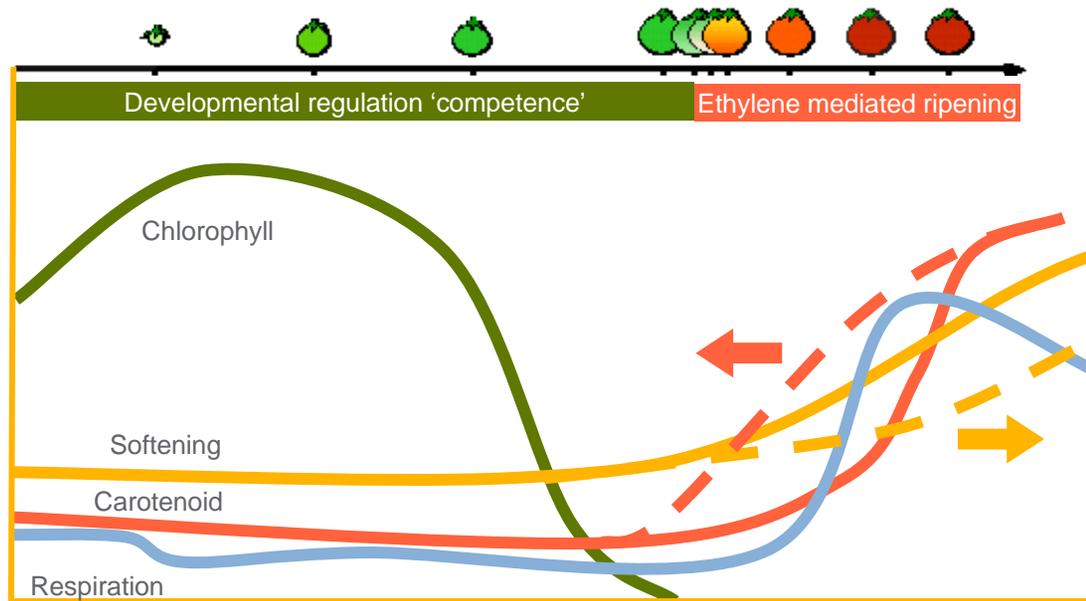
# Understanding fundamental processes through Systems Biology Approaches

- Nottingham CPIB examples
  - (Thanks to M Bennett)
- Multi functional integrated team effort leading to predictive modelling and new understanding and insight
- Imaging arabidopsis root growth
- Tools to visualise intracellular events
- Assymetric Hormone flux in gravitropic response
  - Proves long standing hypothesis
  - Some surprising details!
- Understanding how lateral roots emerge
  - From model to crop...



# Tomato ripening

- **Goal - to understand the genetic and metabolic factors which control fruit ripening**
- Inputs into the model – transcriptomic and metabolomic data sets across tomato fruit ripening for 4 defined genotypes
- Data come from Syngenta platforms in the US & UK and Nottingham University
- **Outputs**
  - **Genetic targets for the manipulation of fruit ripening in conventional breeding programs**
  - **Understanding of tomato fruit metabolism to enhance consumer relevant traits**



## Thinking about farming at a Systems Level



# **plene** transforming sugar cane planting in Brazil



## **SYNGENTA INNOVATION**

- Molecules, active ingredients and formulations
- Coating protectors
- Vigor technology
- Cutting equipments and treatment
- Concept of “Integrated Planting System”

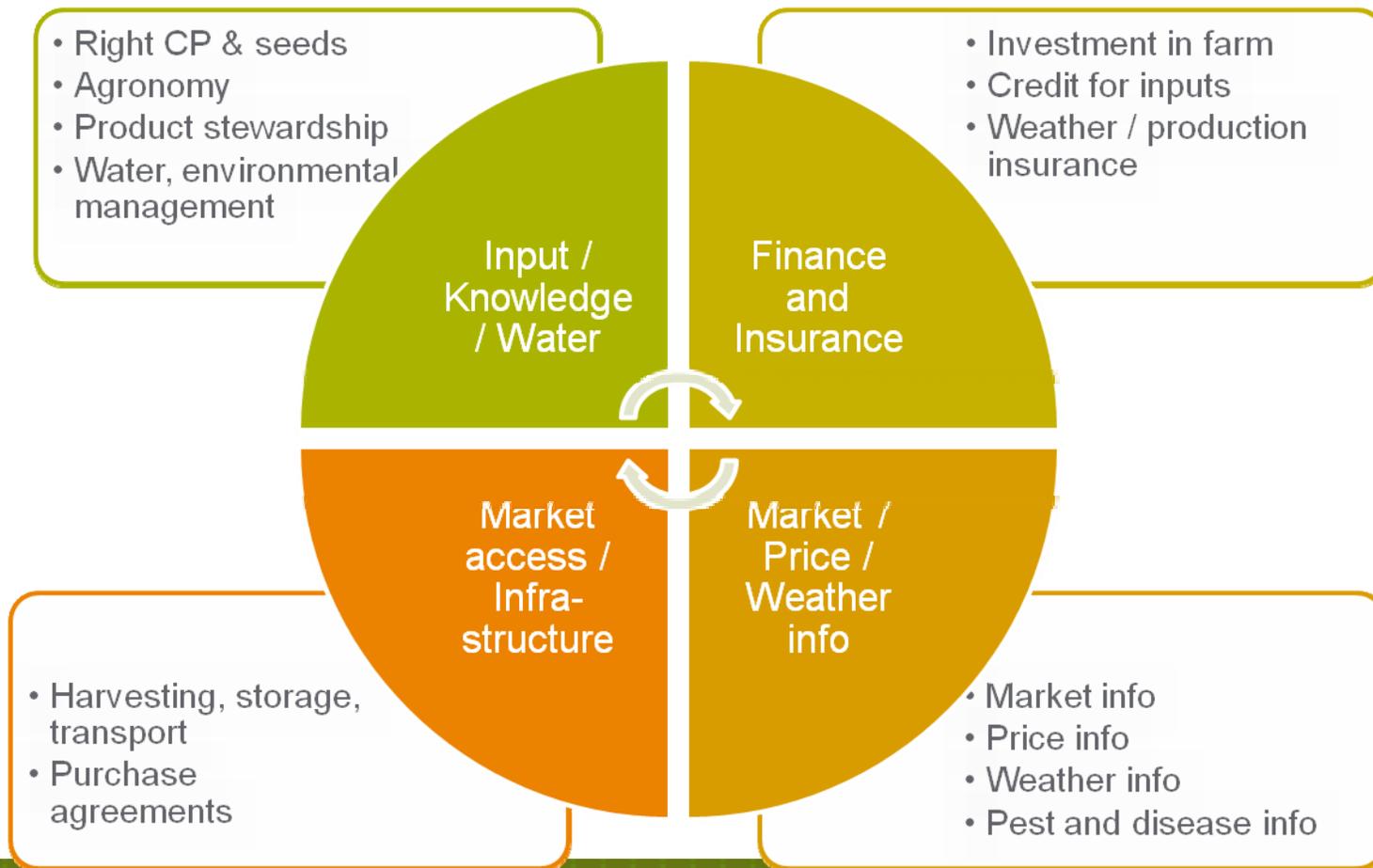
## **TECHNOLOGICAL DEVELOPMENT**

- Planting Equipments
- Treating Equipments

## **GERMPLASM**



# Limitations for smallholders are not just lack of technology



## Kilimo Salama: Insurance scheme





# Integrating technologies for customer benefit

Innovative crop protection  
chemistry and Seed Care



Agronomic  
expertise

Precision breeding  
and plant genomics

## Our view: Grow more from less

### Maintain productivity: Intensive Agriculture

- Competitive, high quality production
- Availability of safe, healthy, affordable food
- Long term contribution to food global security



### Sustainability in practice: Responsible management

- Responsible use of natural resources
- Optimal footprint per unit produced
- Socio-economic, and environmental benefits



### Sound science: Access to technologies

- Continuous improvement and innovation
- Risk based evaluation of new technology

### Knowledge based production: Provision of education

- Coordinated education and knowledge transfer
- Grower training on sustainable farm management and safe practice