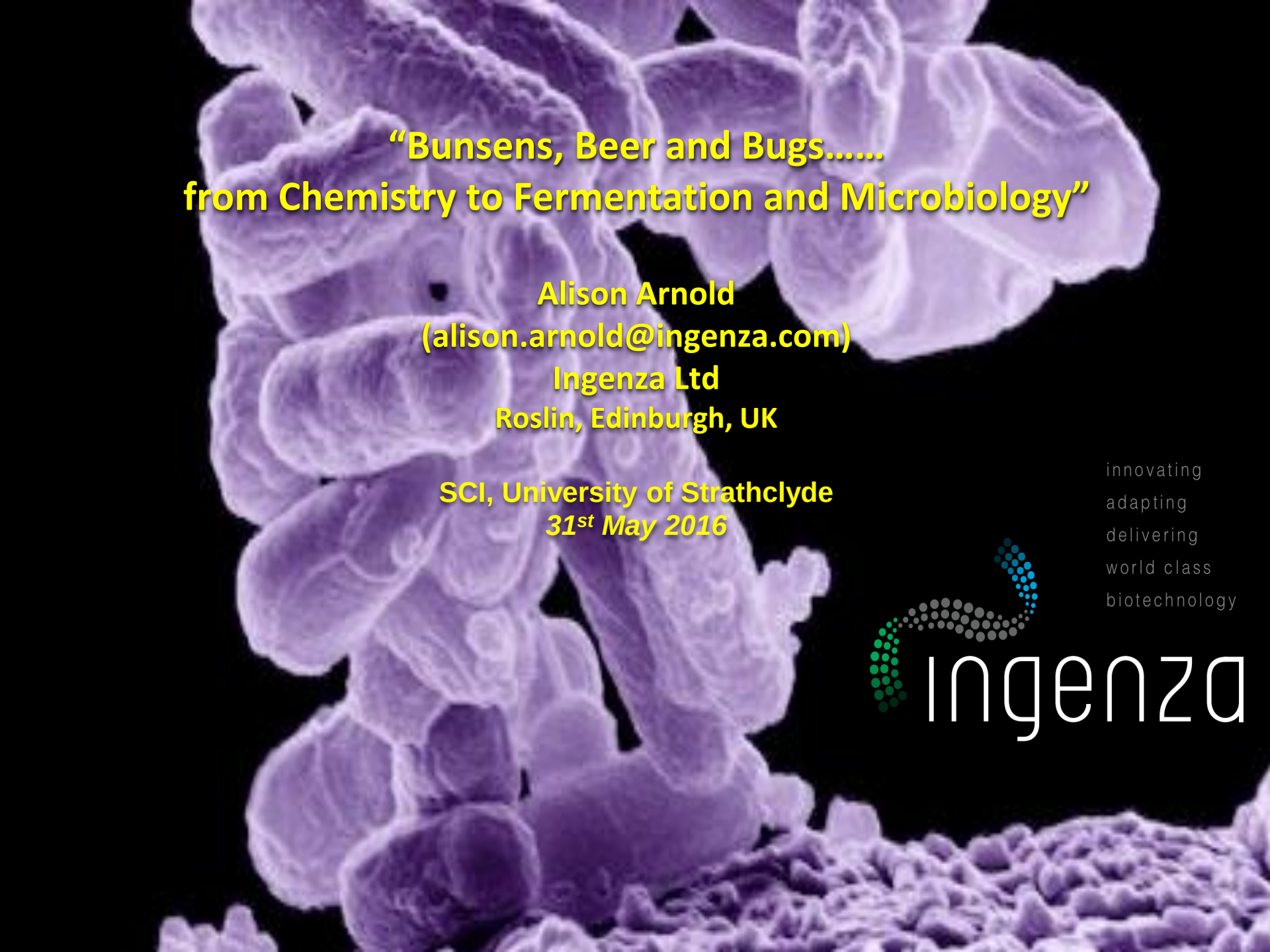


"Bunsens, Beer and Bugs……
from Chemistry to Fermentation and Microbiology"

Alison Arnold
(alison.arnold@ingenza.com)
Ingenza Ltd
Roslin, Edinburgh, UK

SCI, University of Strathclyde
31st May 2016

innovating
adapting
delivering
world class
biotechnology

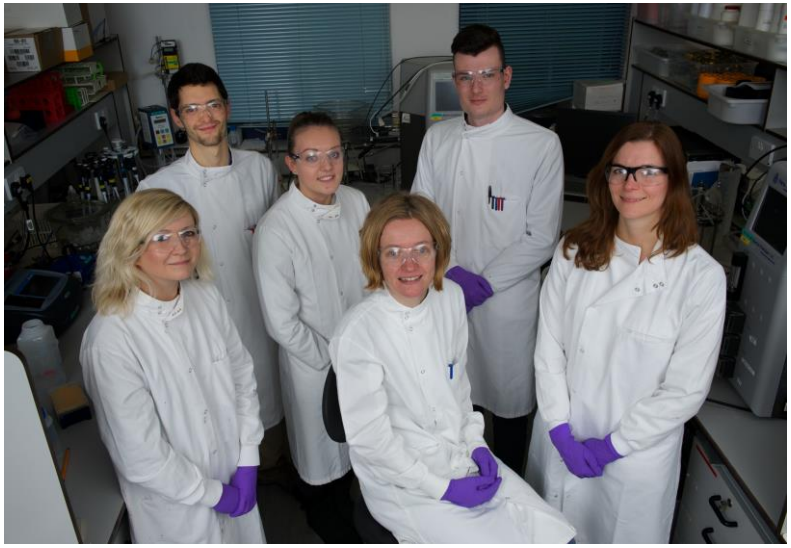
ingenza

Who am I? And how did I get to where I am today?

S. Alison Arnold

Current Role:

- Head of Fermentation Team at Ingenza
- Responsible for all the development of fermentations and scale up of fermentation processes within Ingenza
- Joined Ingenza in 2003 when there was 4 of us
- Now there are 45 of us!



Who am I? And how did I get to where I am today?

Pre Ingenza:

- Post doc at Strathclyde University and DSM, Delft, The Netherlands

→ Continuous culture of *A.niger* for the production of enzymes

- Research Assistant at Strathclyde University working with Eli-Lilly, Speke, UK and British Biotech, Oxford UK.

→ BBSRC, LINK project to use Near Infrared Spectroscopy to monitor Industrial Bioprocesses

E.coli
S.fradiae

P.pastoris
CHO cells

- Combined work as a research assistant with a PhD write up

"*The use of at-line and on-line near infrared spectroscopy to monitor industrial microbial bioprocesses*".

- BSc (Hons) Chemistry from University of Aberdeen

- Bit of working and travelling abroad between degree, PhD and jobs

Daily Life at Ingenza

Current Role:

- Head of Fermentation Team at Ingenza
- Responsible for all the development of fermentations and scale up of fermentation processes within Ingenza
- Joined Ingenza in 2003 when there was 4 of us
- Now there are 45 of us!

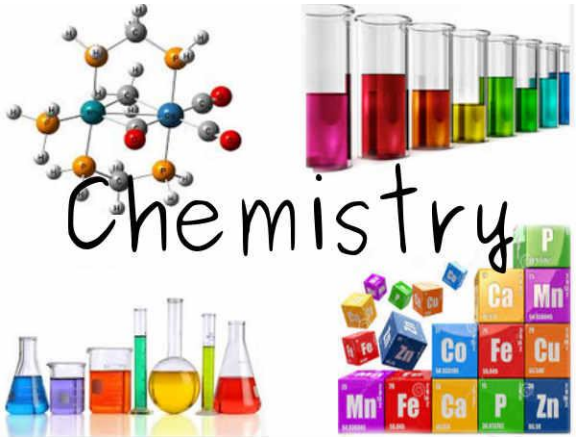
Job Description:

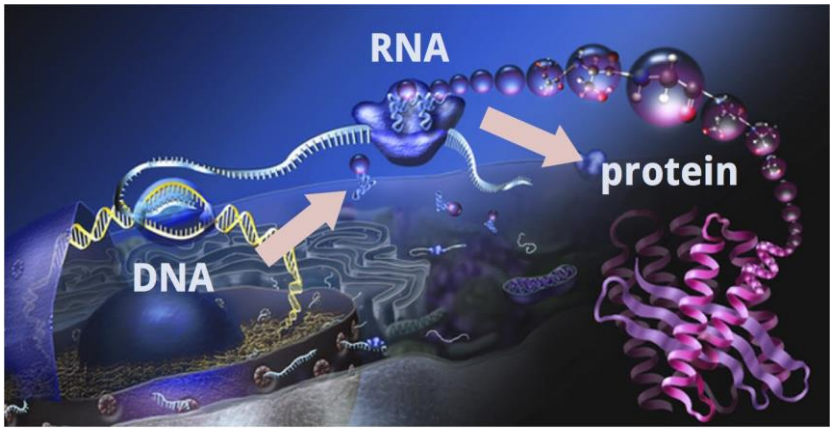
- Varies day to day!
- Meeting potential new customers
- Building relationships with current customers
- Planning and running the fermentations
- Supervising and training other more junior staff
- Working closely with both Molecular Biology and Chemistry Teams at Ingenza – multidisciplinary company
- Industrial PhD supervisor
- Technical Transfer of Processes off-site
- Going on site to assist with running of the process scale up
- Managing Projects and Grants
- Hob nobbing with Politicians !

Who am I? And how did I get to where I am today?

Description of what I was and what I am now…

Former chemist, turned microbiologist….at points an engineer (!) with a touch of molecular biology (!!)

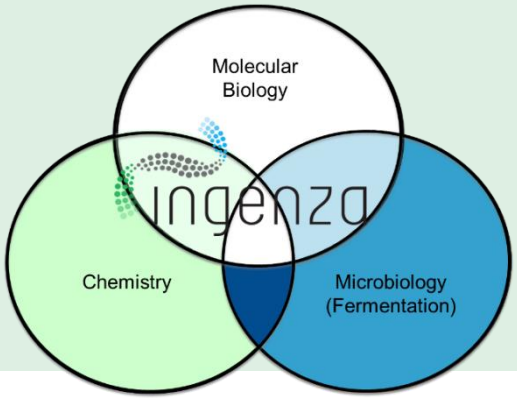




"Bunsens, Beer and Bugs……

from Chemistry to Fermentation and Microbiology"

Ingenza Ltd
Roslin, Edinburgh, UK
Industrial Biotechnology/Synthetic Biology R&D company



Capabilities:

- Strain construction using proprietary synthetic biology /enabling technologies e.g. inABLE®
- Protein expression/enzyme evolution
- Microbial fermentation (2 L) - scale up with partners (2.6 million L!)
- Cell culture
- Bioprocess development, DSP, synthetic chemistry

START

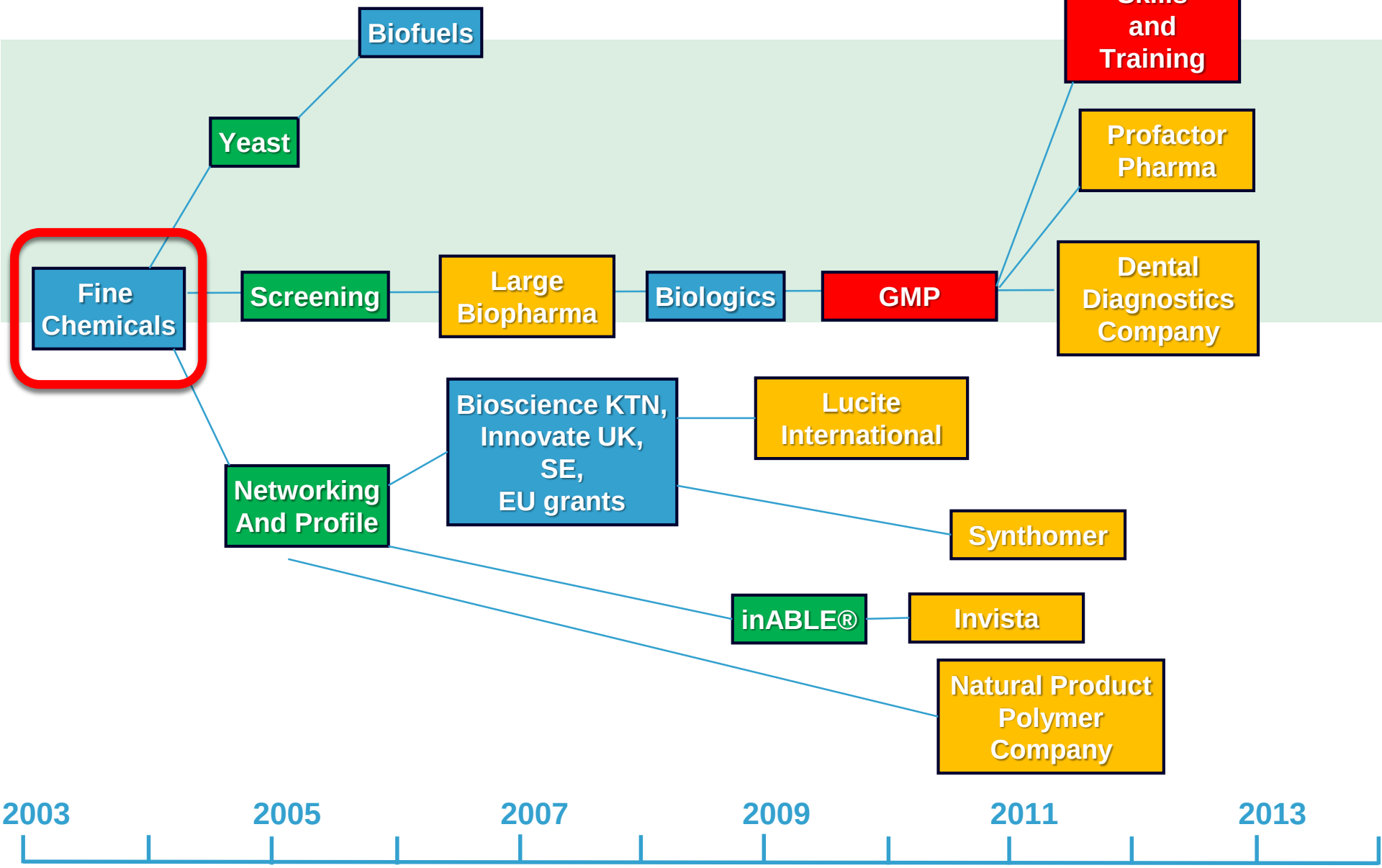
FINISH

Customers:

- **Chemical companies** looking to source capabilities in micro/molecular biology and bioprocess development for the production of biobased chemicals and biofuels
- **Therapeutics companies** looking to outsource application of synthetic biology for natural product pathway and protein engineering/optimization
- **Academics** looking to transition early stage research through proof of concept and on to spinout/startup companies

An Unusual Chemical Company

How we got here…..



The Beginning
Biosynthesis of Chiral Compounds

- **Academic group**

Angew. Chem. Int. Ed. **2003**, *42*, 4807 –4810

Directed Evolution

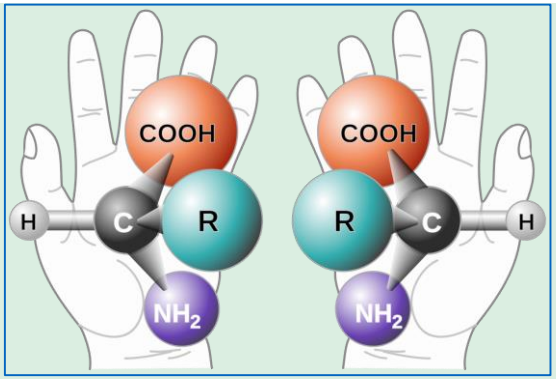
Directed Evolution of an Amine Oxidase Possessing both Broad Substrate Specificity and High Enantioselectivity**

*Reuben Carr, Marina Alexeeva, Alexis Enright, Tom S. C. Eve, Michael J. Dawson, and Nicholas J. Turner**

ChemBioChem **2005**, *6*, 637 –639

Directed Evolution of an Amine Oxidase for the Preparative Deracemisation of Cyclic Secondary Amines

Reuben Carr,[a] Marina Alexeeva,[a] Michael J. Dawson,[b] Vicente Gotor-Fernández,[a] Cara E. Humphrey,[a] and Nicholas J. Turner*[a]



Scientifically successful but the economics needed

Improved for cost effective manufacturing

Enzymes

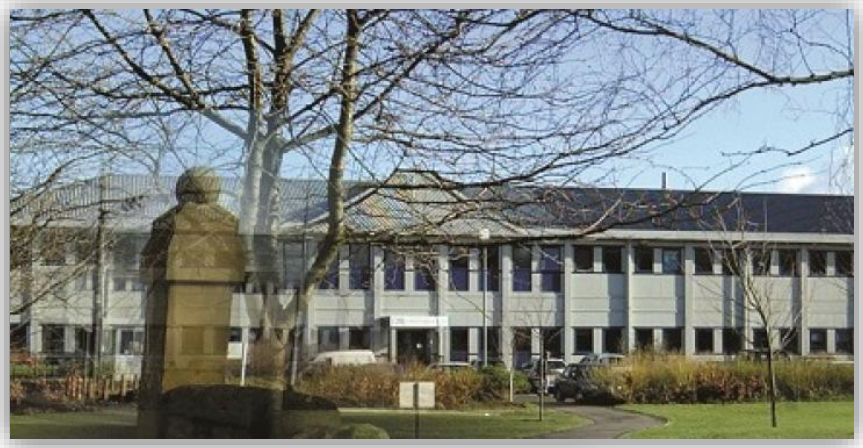
Ingenza spun out of Department of Chemistry, Edinburgh University based on this technology

"INdustrial GENetics and enZymes"….A

The Beginning
Biosynthesis of Chiral Compounds

Chemistry Department
Joseph Black Building
2003-2006

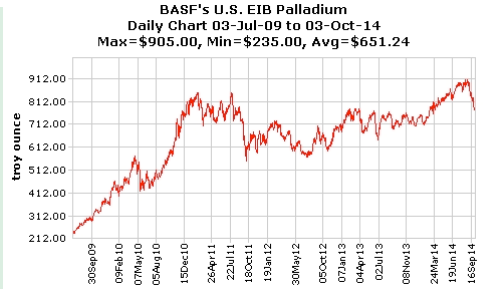
Prof. Nick Turner
Prof. Sabine Flitsch
Dr. John White



The Wallace Building
Roslin BioCentre
2007-2016

Fine Chemical Business
Why it didn't work for Ingenza….

We had a solution looking for a problem to solve…..



Customers

- Large Pharma companies

Costs

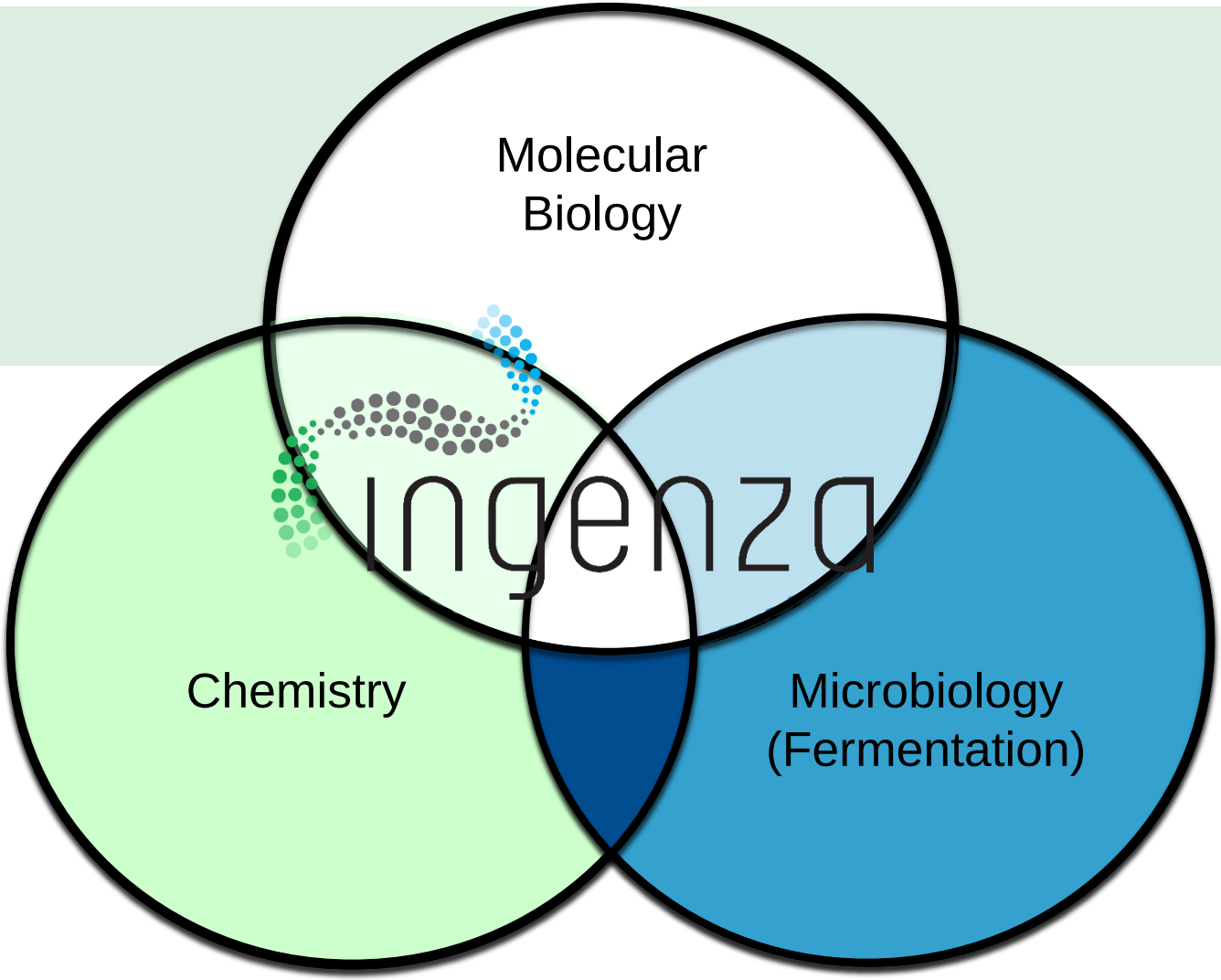
- Raw materials

Route to Market

- Difficult to predict, clinical trial

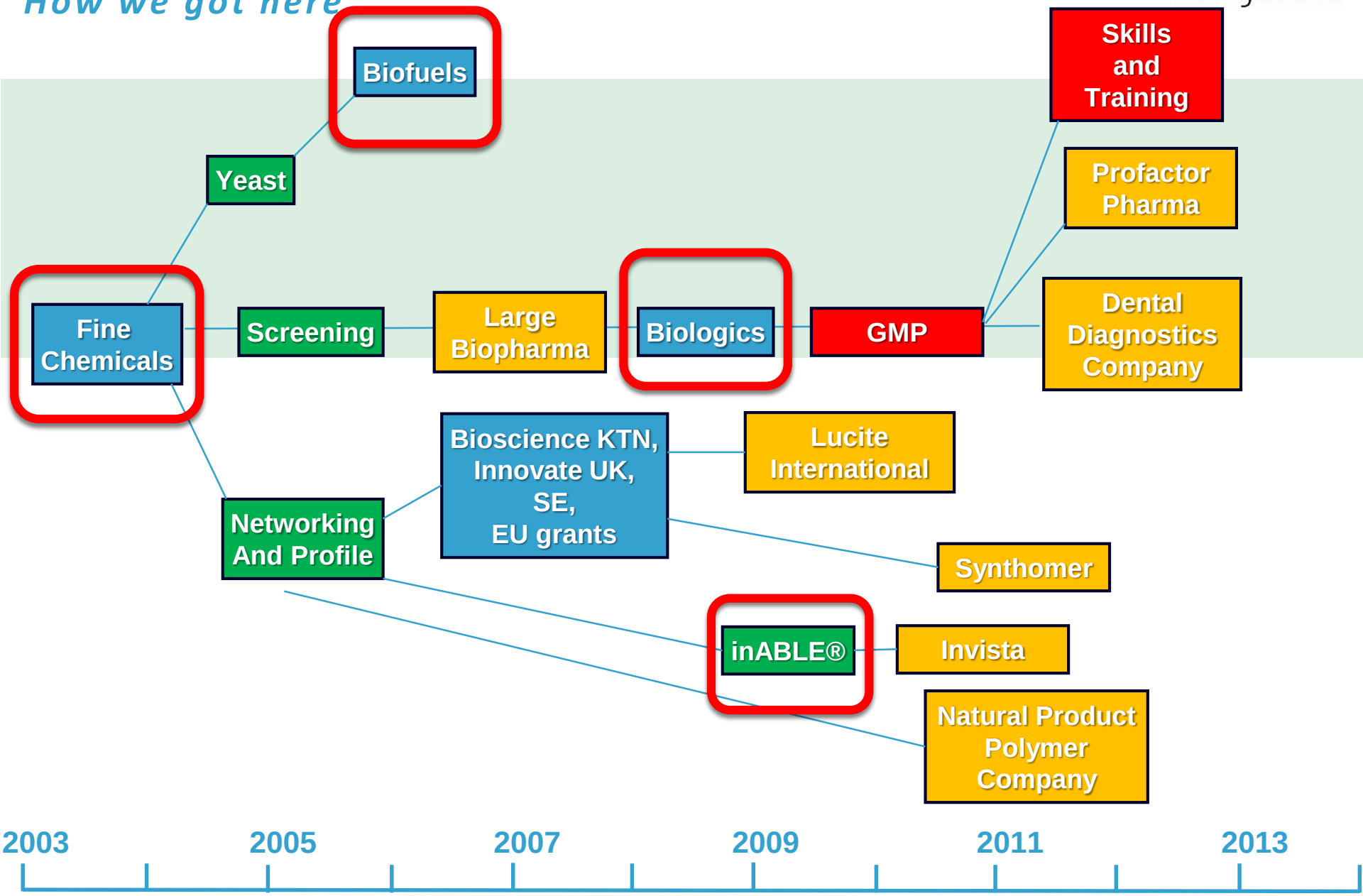
Industrial Biotechnology and Synthetic Biology

Where is the value?



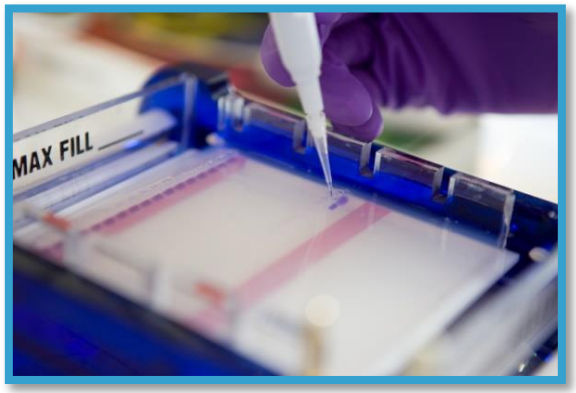
An Unusual Chemical Company

How we got here



Fermentation at Ingenza

Molecular Biology



Bacterial, Yeast, Fungal and Mammalian…

- *E. coli* (1 L to 50 m^3)
- *P. pastoris* (1 L to 1 m^3)
- *S.cerevisiae* (aerobic) (1 L -30 m^3)
- *S.cerevisiae* (anaerobic)
  - 100 mL → 2.6 Million Litres !
- *Corynebacterium*
- *Pseudomonas*
- *Bacillus*
- *Aspergillus*
- *Mammalian*

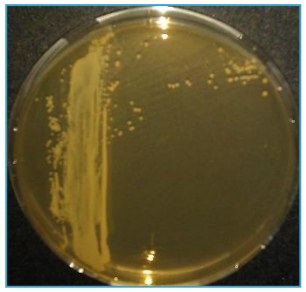
Fermentation

Chemistry

- Broad ranging suite of microorganisms
- Development and application as necessary for a specific project

Overview of Fermentation Scale UP

Scaling fermentations up is easy – isn't it??



Colony on a plate

50m^3 fermentation

Fine chemicals

Biofuels

Step 1- Develop a Fermentation Process

Original Ingenza Process
Shake Flask

- Good for small scale work as proof of concept
- Poor control
- Low growth
- Low product yield
- Not cost effective
- Not Robust

→ Can not scale to 1000's L

Optimise the Process

Optimised Ingenza Process
Fermentation

- Good control
- High growth
- High product yield
- Cost effective
- Robust and reproducible

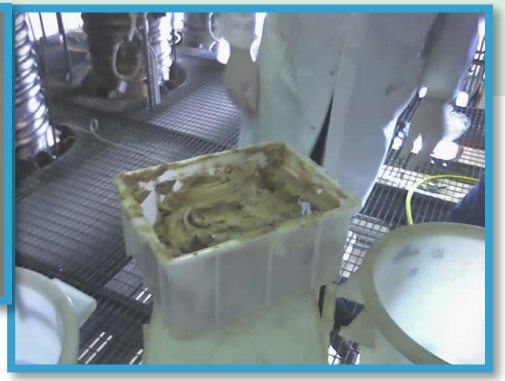
→ Can scale to 1000's L

Step 2- Scale up the Process

Lab Scale vs Scale Up

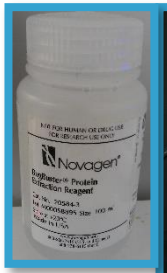
Raw Materials

Cell Harvest



Cells

Fermentors



Lysis

Examples of Ingenza's Fermentation Scale Up

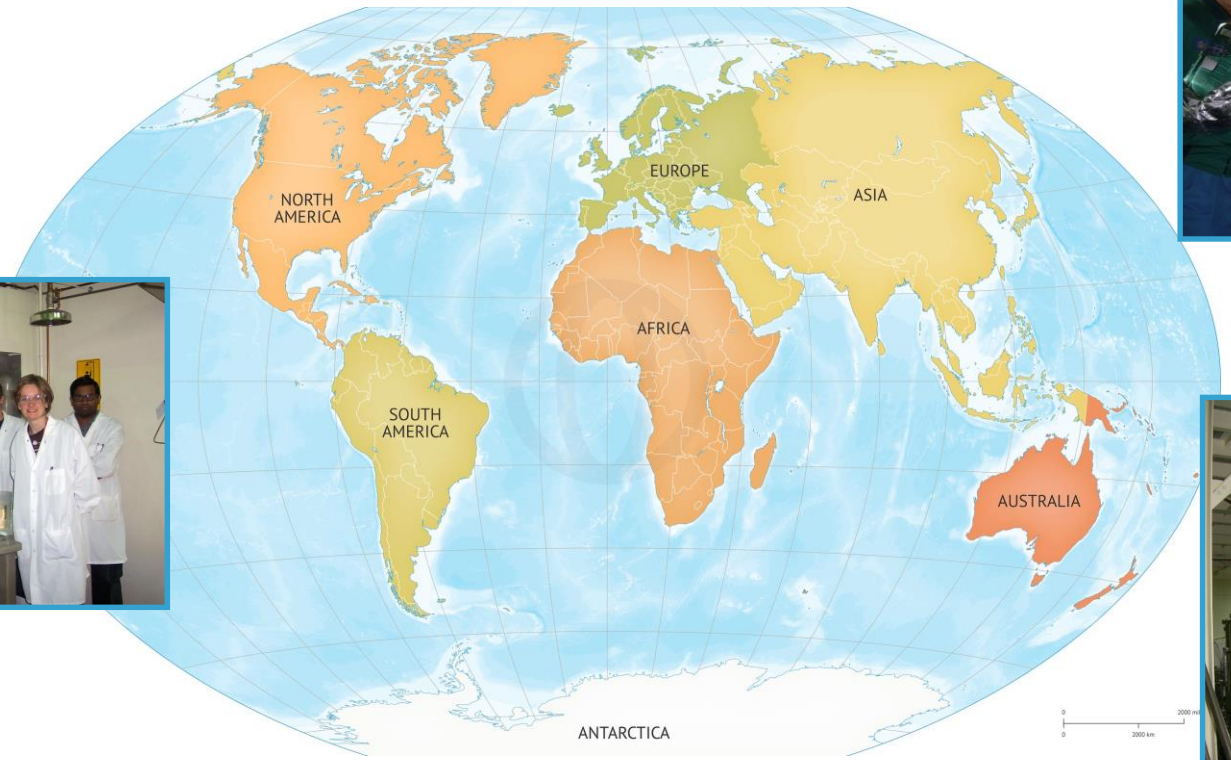
USA
Customer Project
10L Pilot
50m^3 Production

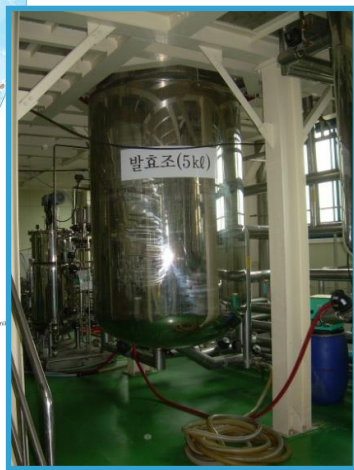
UK
Customer Project 100L
Ingenza Process 1000L

Europe
Customer Project
300L Pilot
12m^3 Production

Asia
Ingenza
Process 5m^3

USA
Ingenza Proce
100L





Step 2- Scale up the Process

Potential Hazards Scaling Up

- Environmental (Weather too hot, too cold, too humid)
  - → cooling / heating capability
  - → storage of raw materials and product
- Contamination (especially in CMO which often operate wide range of microorganisms)
- Safety and Operations
- Communication and language
- Cultural
- Food → illness
- Long hours – making key decisions when tired so better to send a team of people to supervise the first scale up

Industrial Biotechnology Requires "Abilities"
(feasibility, adaptability, predictability, scalability)

How does it fit into our core business?

Leading SME in industrial biotechnology /synthetic biology

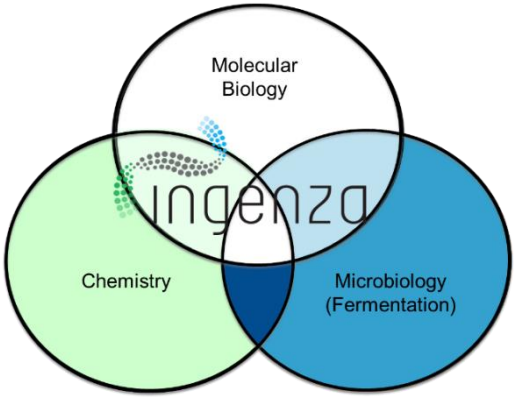
- Partnerships worldwide with major players in chemicals, biologics and natural products
- Adaptability means survivability!

Unusual chemical company

- Started off as a biocatalysis company and we still work in the chemical industry but in a different way
- Have developed many enabling technologies e.g. inABLE®
- Ingenza has many other synthetic biology tools

What does this mean?

- Faster development of customer process from START → FINISH core competencies in



Technology and business focus on:

- Long-term high-value relationships
- Scalable, cost-effective and sustainable bio-manufacturing opportunities
- Cutting edge industrial biotechnology
- Combining synthetic biology design principles with capabilities in industrial biotechnology
- Networking wherever possible

Ingenza's Modern Apprentice Scheme

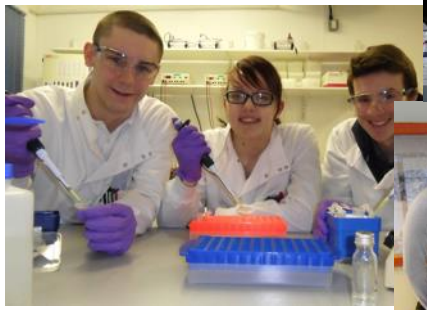
The early days.....

- In November 2009 Ingenza welcomed Kirsty and Ross to the team
- 2016: Fifth modern apprentice

Ingenza employs

- School leavers
- Degree and Masters Qualified staff
- PhD Scientists

IBioIC



Ingenza engages with the community


Ingenza are very much engaged in an open policy when it comes to communicating with the local community with regular visits from MP's, Councillors, School Kids, Universities and Internships.

Ingenza also play an active part in encouraging youngsters to learn more about science as well as active charity work.


www.ingenza.com

Ingenza – Our expanding team

2010

2016

Our team has continued to grow and since 2010 we have doubled in staff size.

Acknowledgements

Ingenzers, our partners and customers

innovating
adapting
delivering
world class
biotechnology

ingenza

alison.arnold@ingenza.com