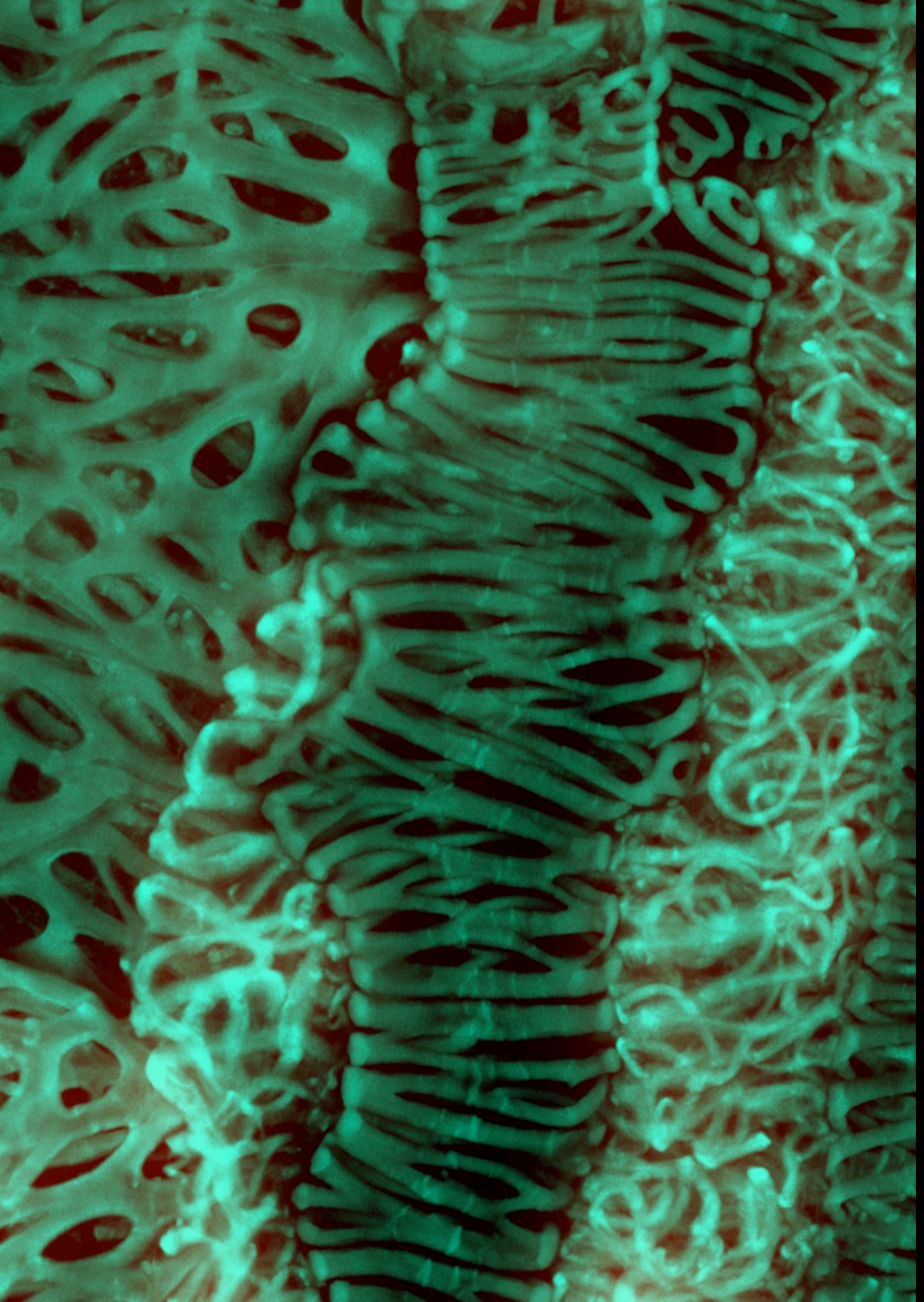


Software for plant Synthetic Biology

Jim Haseloff

University of Cambridge

www.haseloff-lab.org

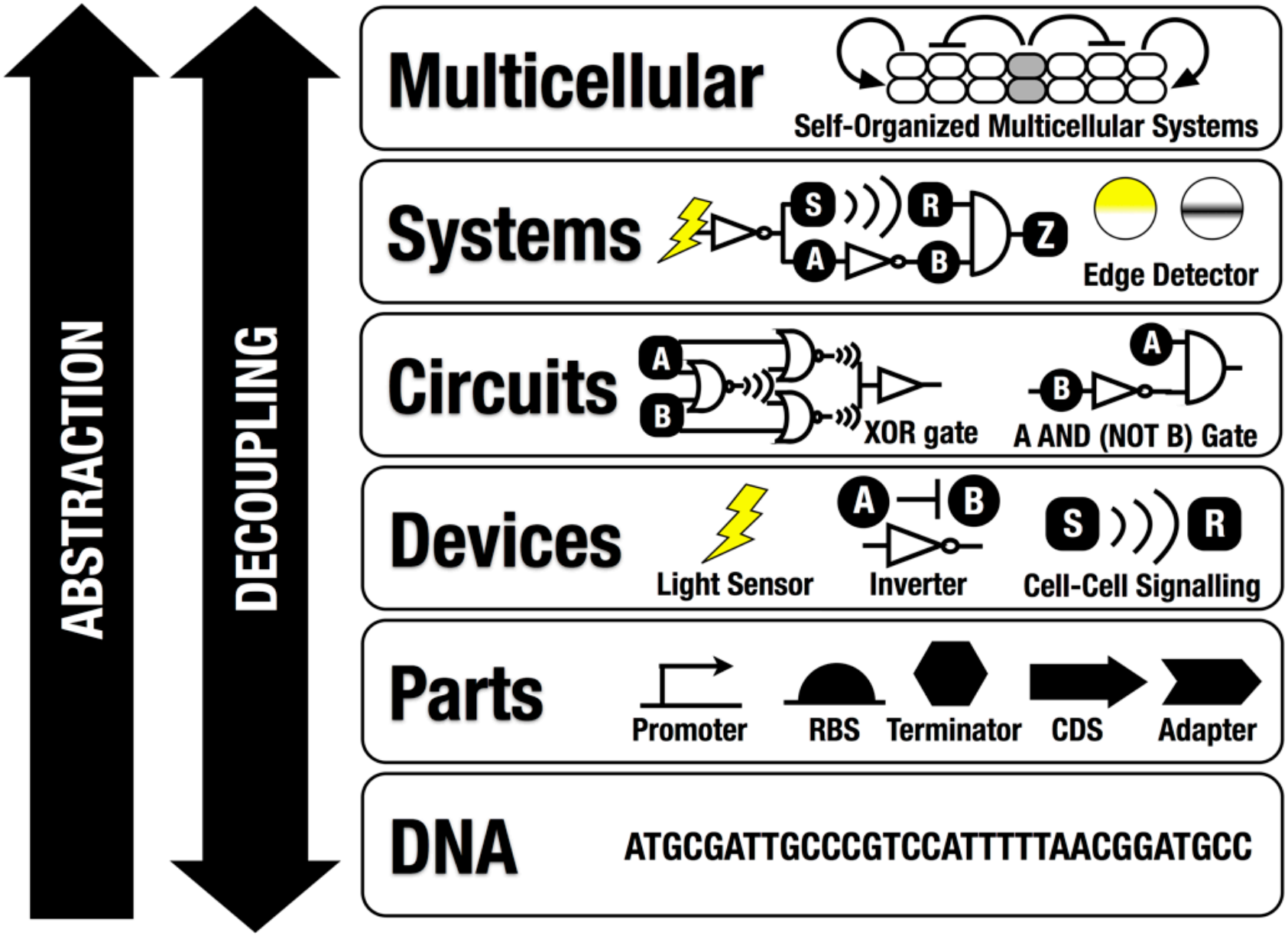
www.synbio.org.uk

What is *Synthetic* Biology?

syn·thet·ic [sin-**thet**-ik] –adjective

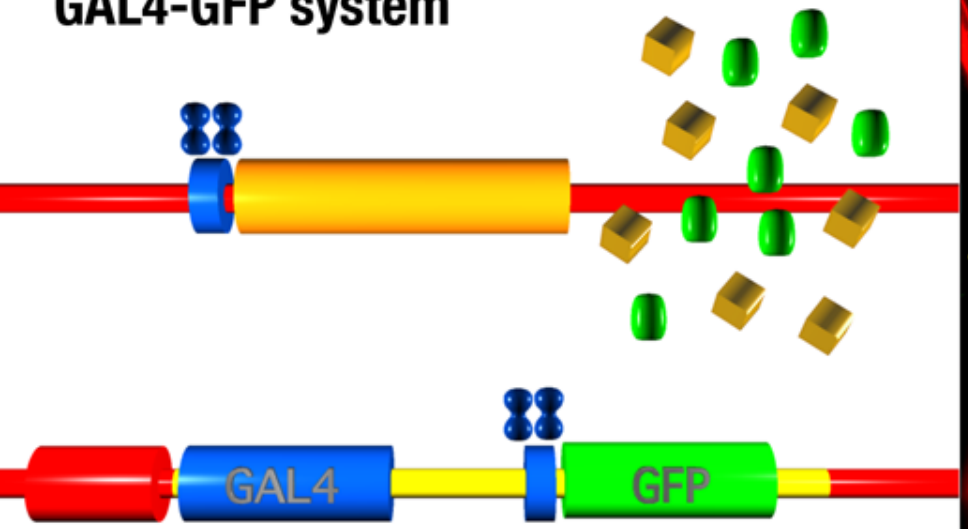
1. Prepared or made artificially, not of natural origin.

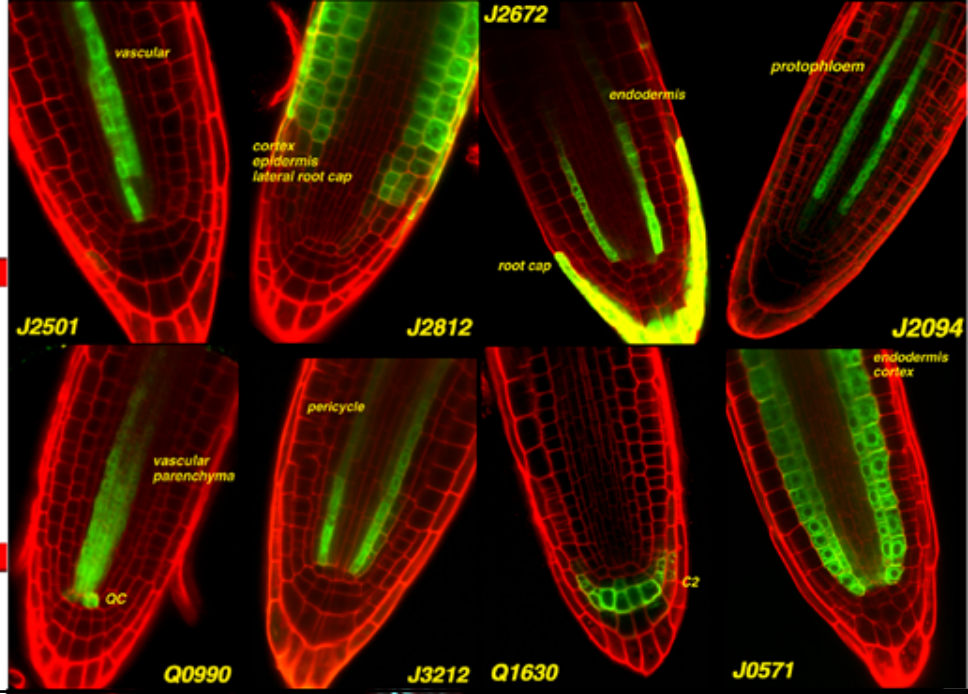
2. Relating to, or involving synthesis (construction of a coherent whole from separate elements)



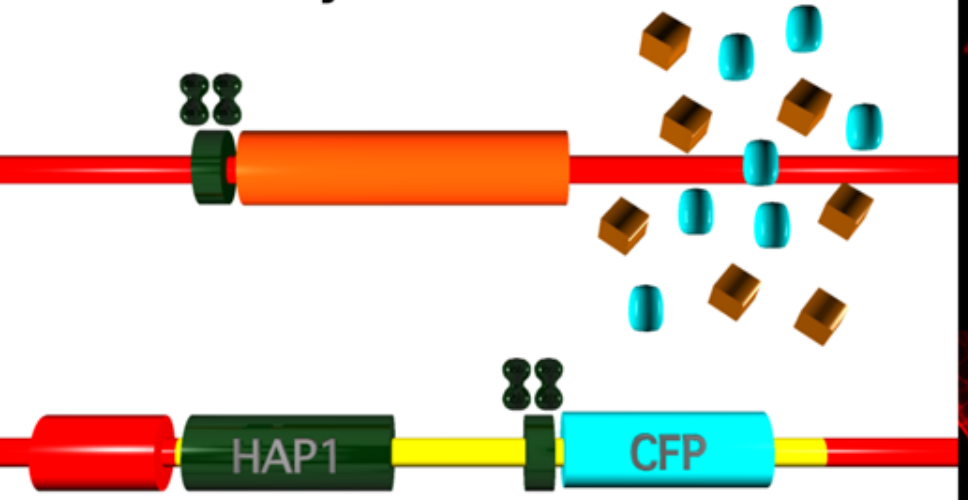
Federici, Rudge, Pollak, Haseloff, Gutierrez, 2013

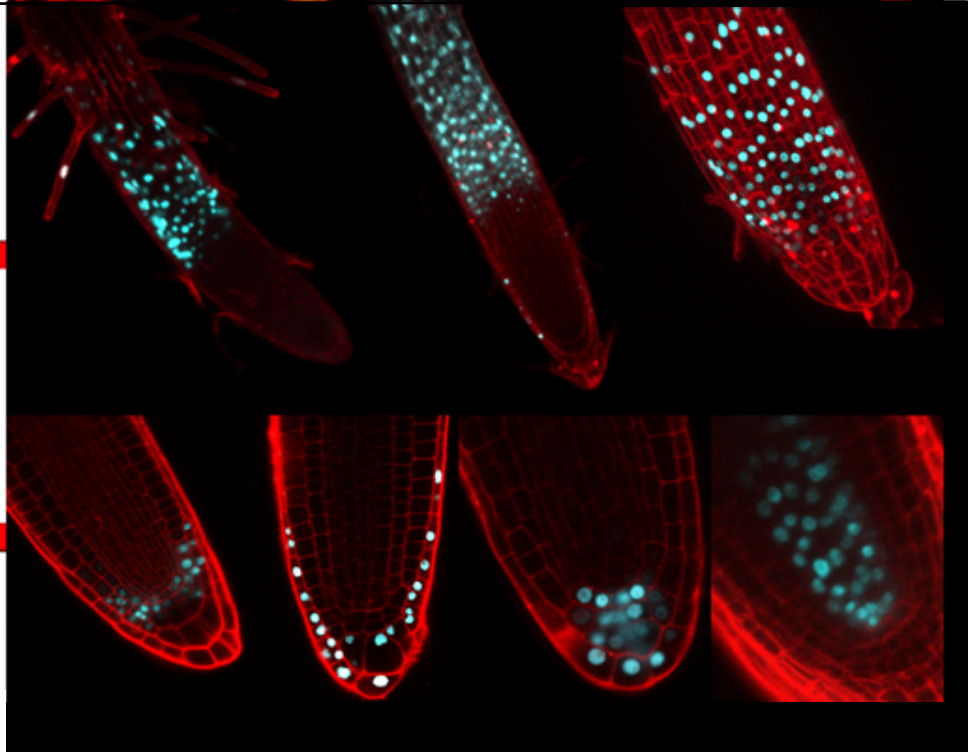
GAL4-GFP system





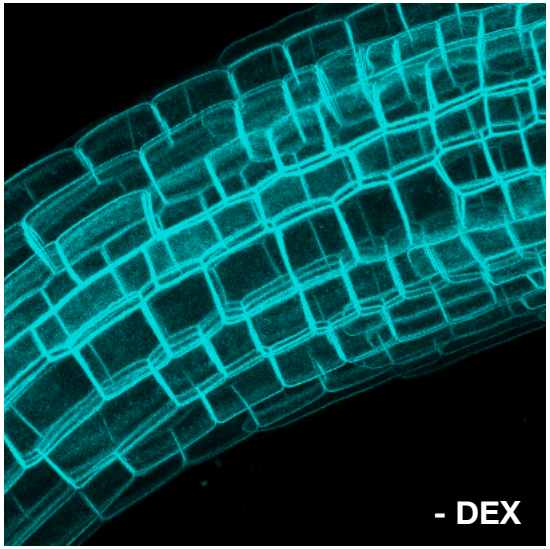
HAP1-CFP system

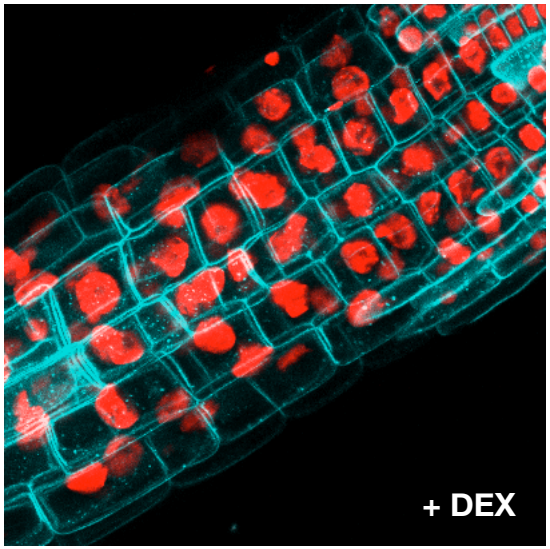




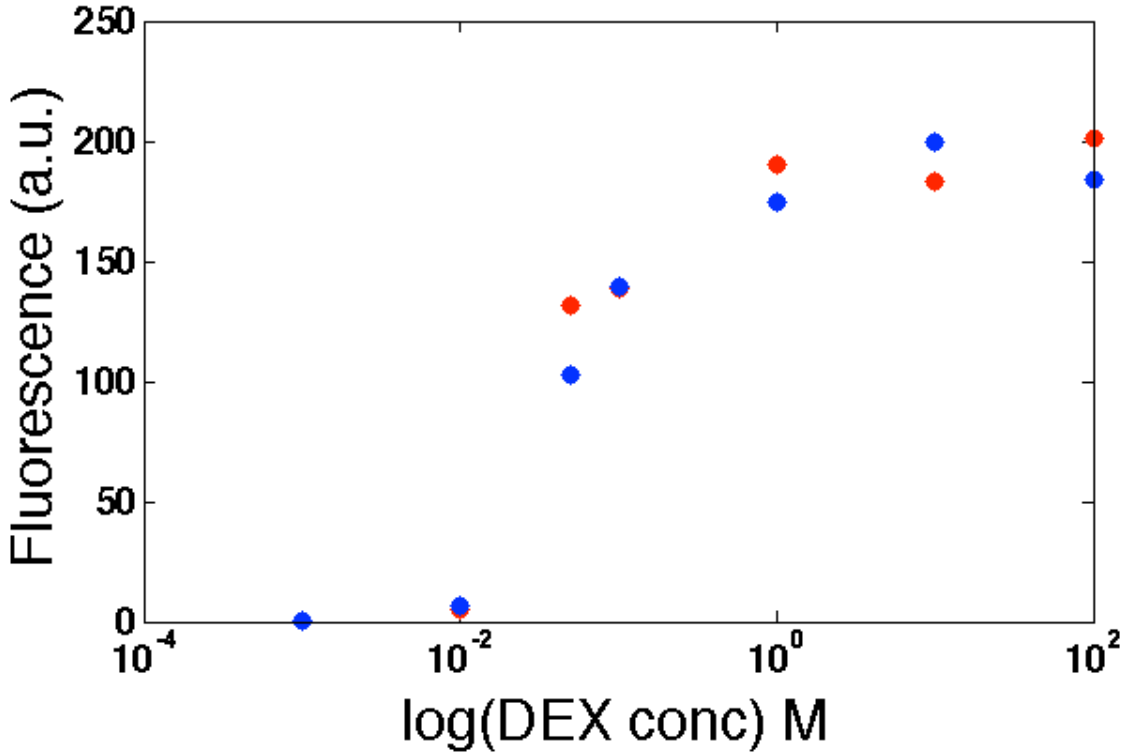
Triggers for gene expression

Temporal switching





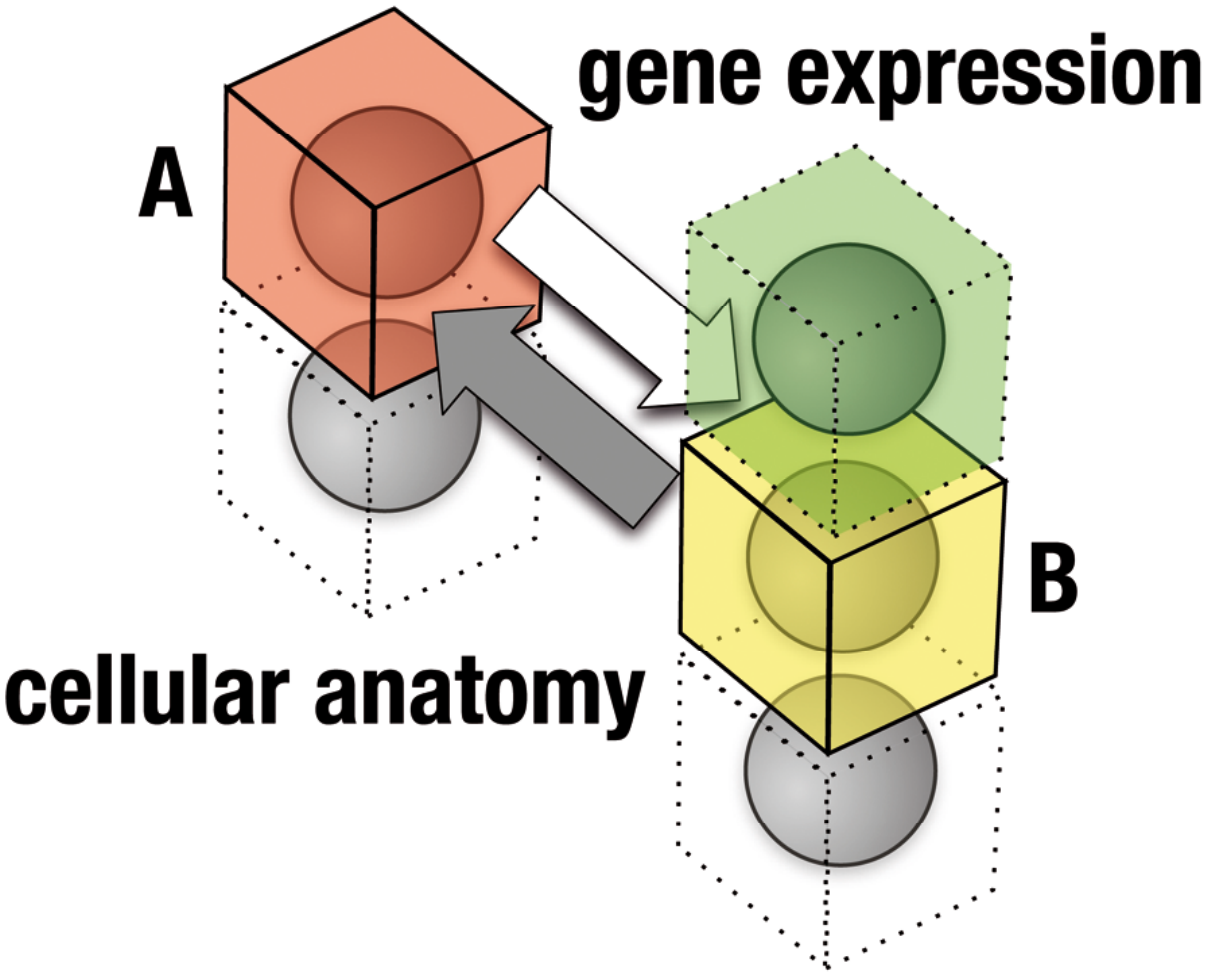
Inducible control of HAP1-mediated gene expression



Federici, Rudge, Robertson & Haseloff

Testbed for synthetic biology in plants

The properties of living systems are governed by parallelism and feedback

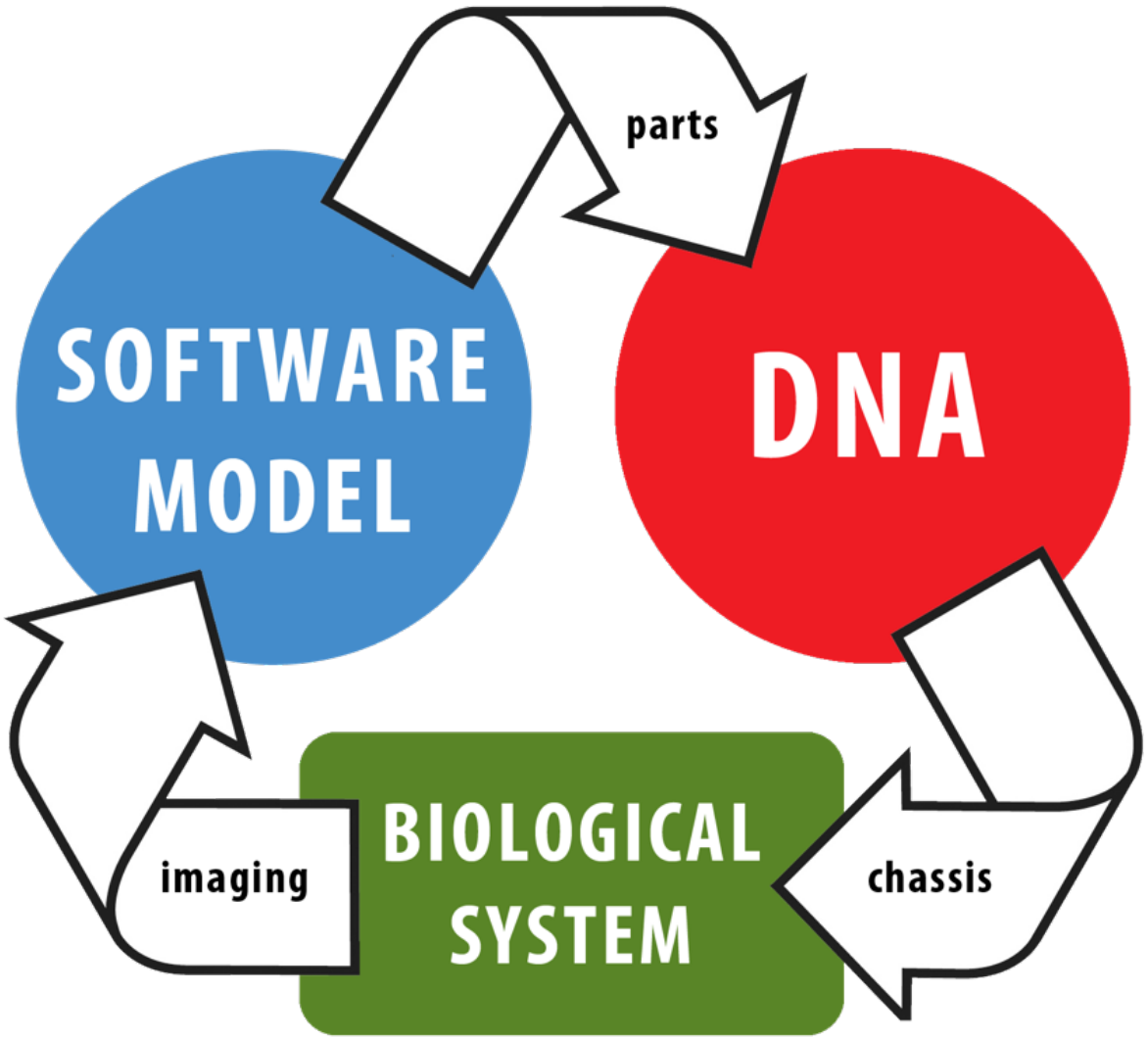


Design cycle for Synthetic Biology systems

1. Specification and design of the system using computer models of the biological system

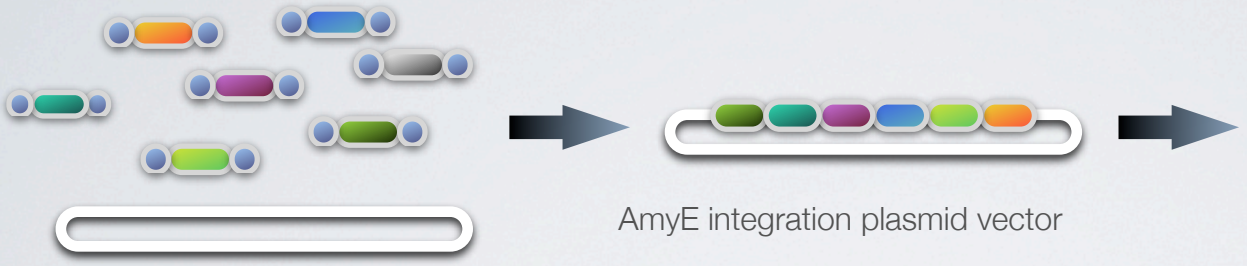
2. Construction of genetic circuits using standard DNA parts and high throughput assembly techniques

3. Transformation of chassis and visualisation of gene expression, cell states and phenotype



High throughput chromosome engineering

Bacterial chromosome integration

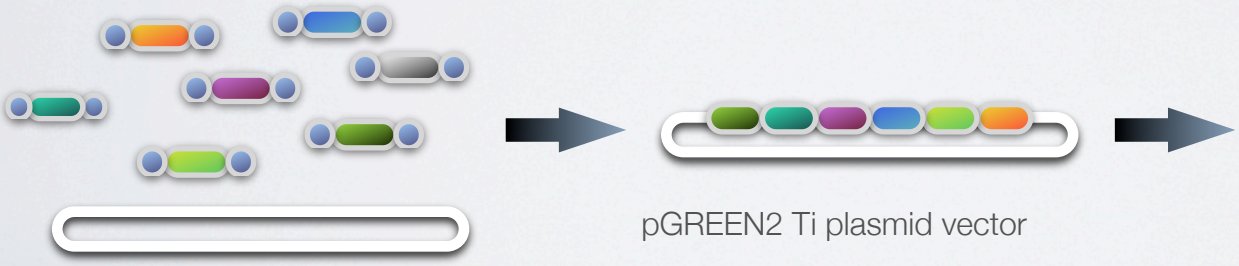


Gibson assembly

AmyE integration plasmid vector

homologous recombination in Bacillus subtilis

Plant chromosome integration



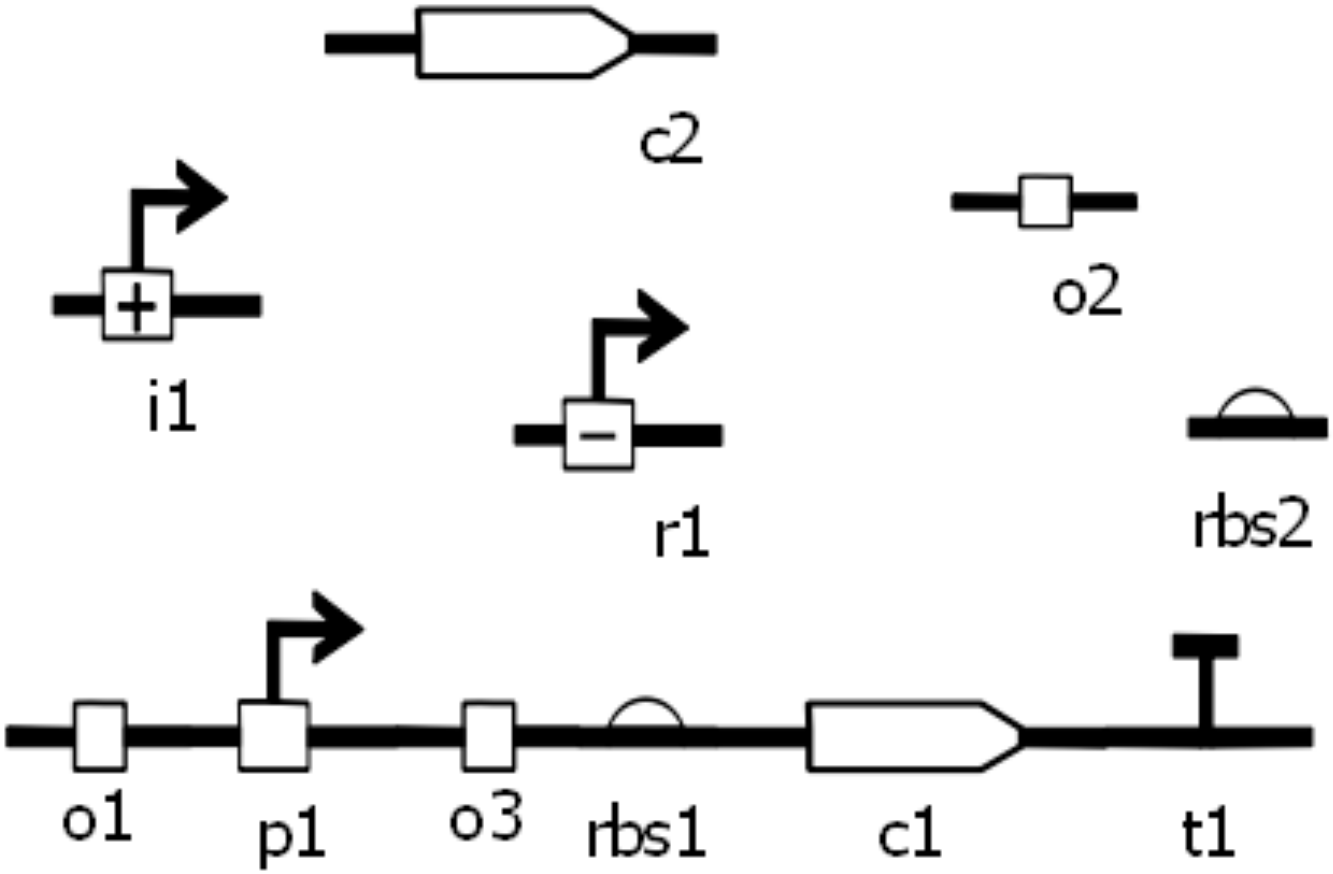
Gibson assembly

pGREEN2 Ti plasmid vector

Agrobacterium mediated plant transformation

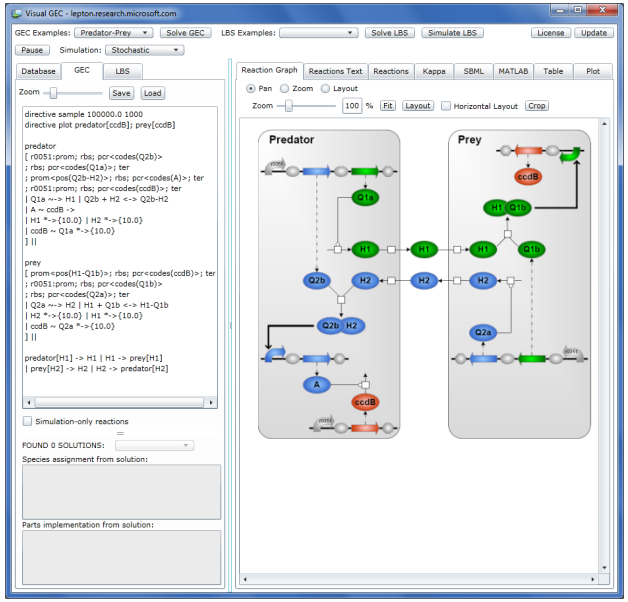
SBOL: symbolic description of DNA parts

Synthetic Biology Open Language: is a software standard for the electronic exchange of specifications and descriptions of genetic parts, genetic devices, genetic modules, genetic systems, and engineered genomes.

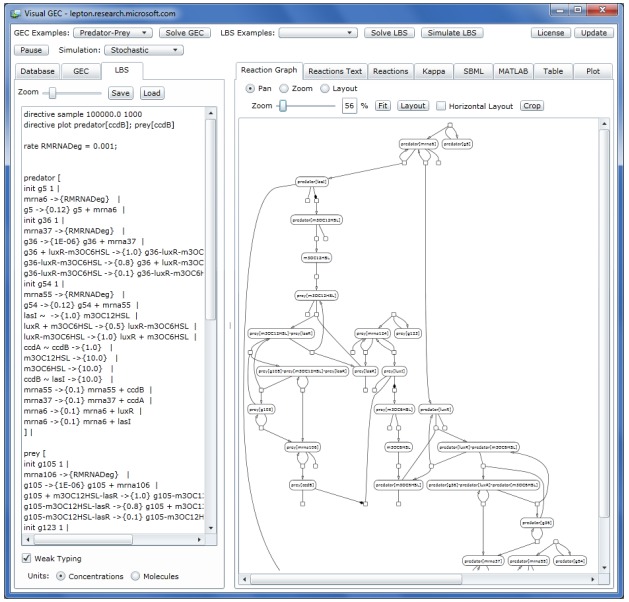


Software for compilation of DNA circuits

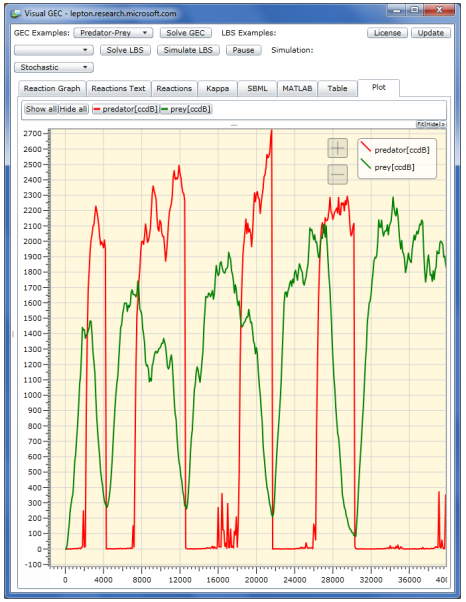
Step 1: Program device design



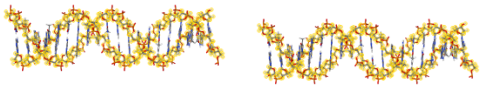
Step 2: Compile device behaviour



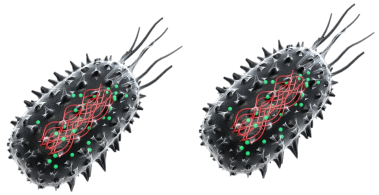
Step 3: Simulate device



Step 4: Compile device to DNA



Step 5: Insert DNA into cells



Genetic Engineering of Cells (GEC): a tool for programming cells

Microsoft Research Cambridge

Pedersen & Phillips. Royal Society Interface, 2009

CELLMODELLER

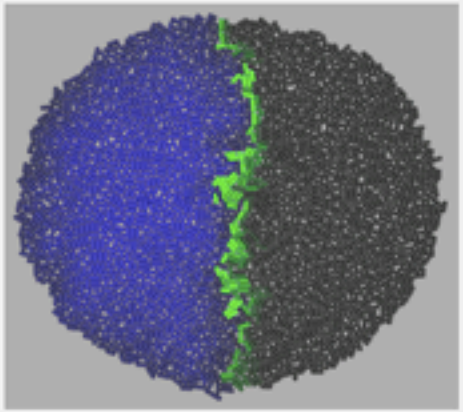
Software framework for modelling cell interactions

CellModeller version 4

CellModeller is a framework for modelling multicellular systems, including biophysics, regulatory dynamics, intercellular signalling, and rule-based behaviours. It is implemented using OpenCL, a parallel computation standard, allowing very large numbers of cells to be simulated

Morphogenesis is the process of creating and maintaining form through coordinated cell-division and growth. We have developed a software environment for modelling plant morphogenesis – an interactive virtual laboratory with a front-end called CellModeller4.

We have implemented cellular models of rod-shaped bacteria (3D) and plant tissues (2D). The bacterial model is a novel growing rigid-body method, described here. The plant model is a finite element method based on the work of Lionel Dupuy in the lab, and implemented using a matrix-free approach. The plant model is in the final testing stage, and will be released soon. The bacterial model is a constraint solver, and so can incorporate growth conditions like a flat substrate or microfluidic chamber by including additional constraints.



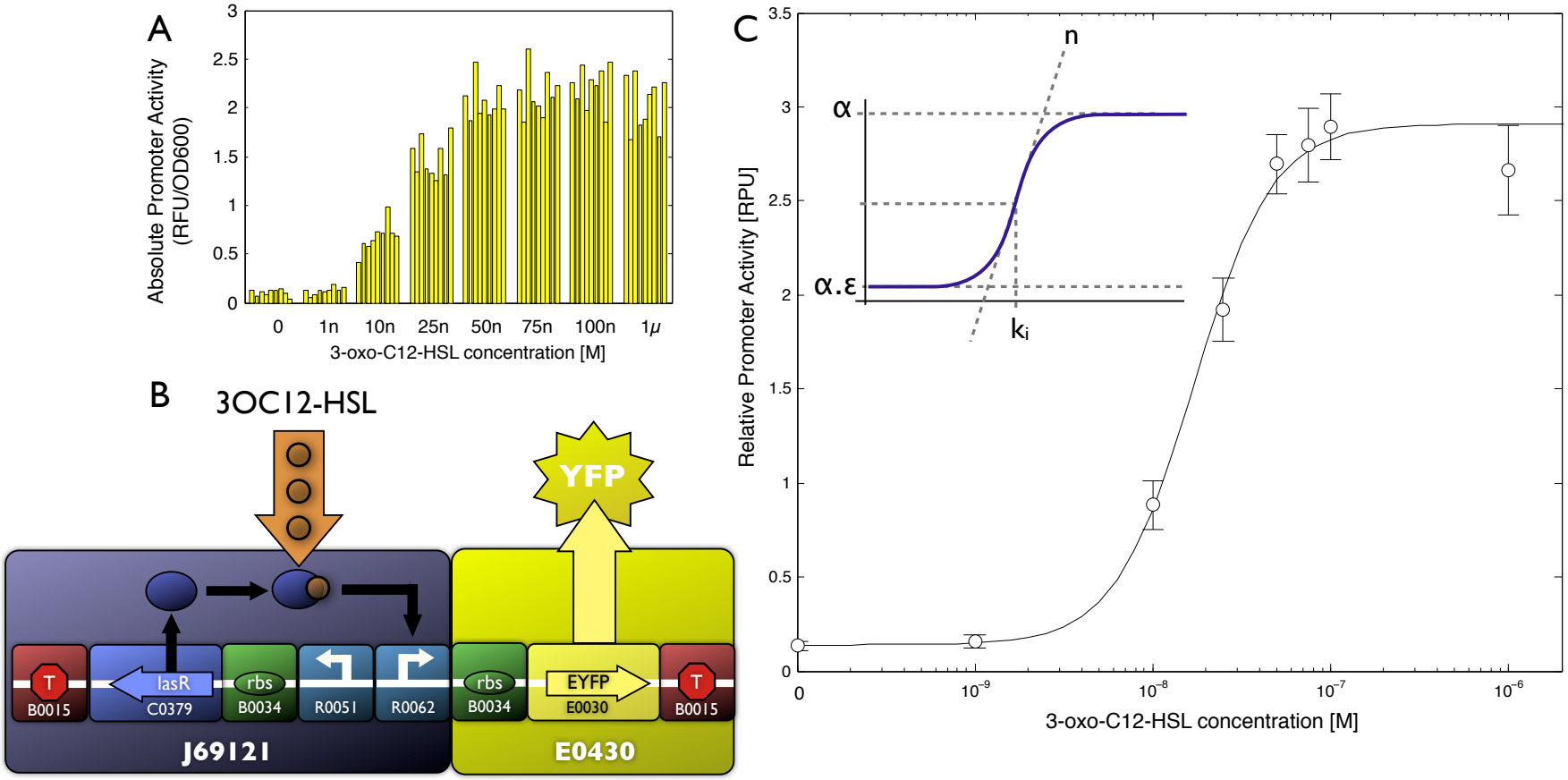
This is based on a spatial/mechanical model of cells coupled to an arbitrary user-defined set of reaction-diffusion systems and a genetic script. Essentially the system allows us to grow plant-like synthetic tissue which generates patterns of morphogens. The morphogens influence the behaviour, growth and division of the cells via the genetic script, forming a feedback loop between patterning and growth.

The 2D model is a matrix of linear walls controlled by the adjacent cells. Using the model we can design patterns, shapes and structures by constructing genetic scripts, effectively a kind of genetic sculpture. This is of great value in testing hypotheses about how genes and signalling molecules direct the growth and development of

CellModeller
Design
Plant biophysics
Cellular automata
Genetic system
Download software
Cambridge-Microsoft
Archiroot site

Measurement of circuit behaviour *in vivo*

122:pSB3K3C1 Las Receiver

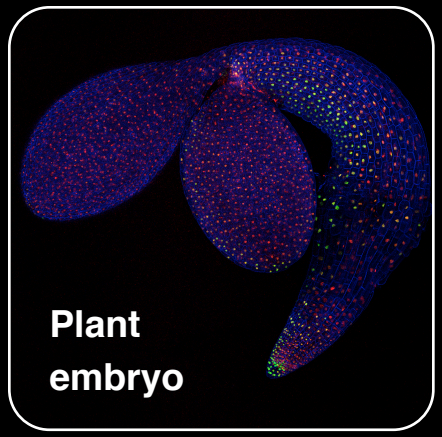


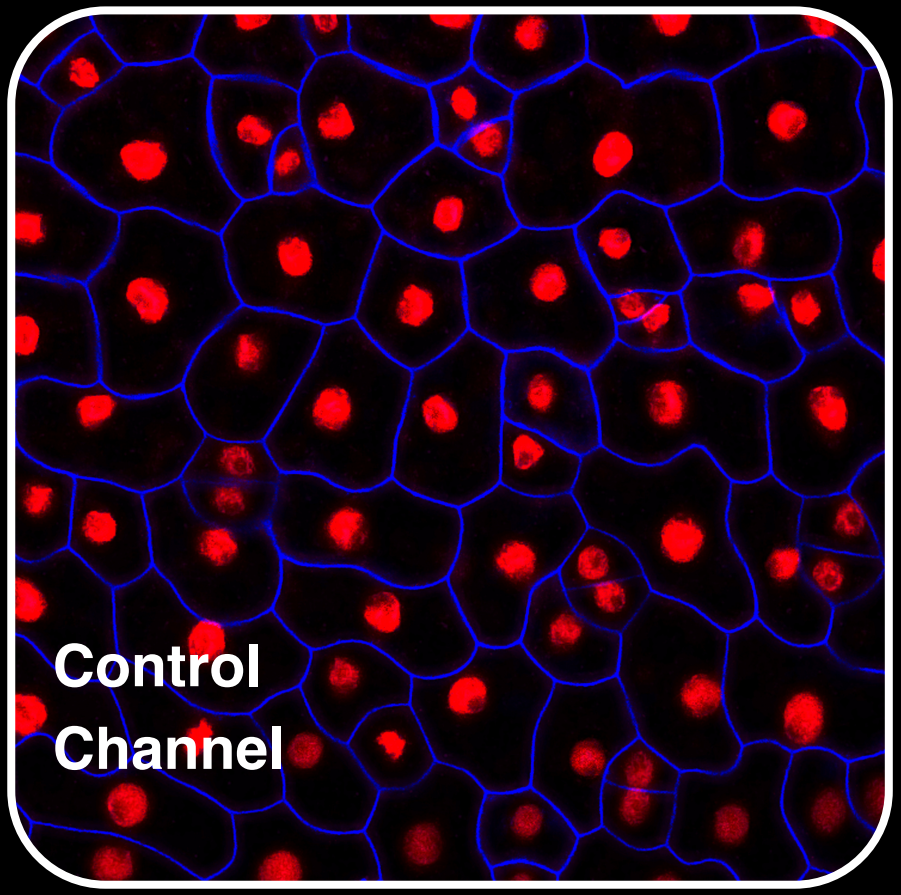
James Brown

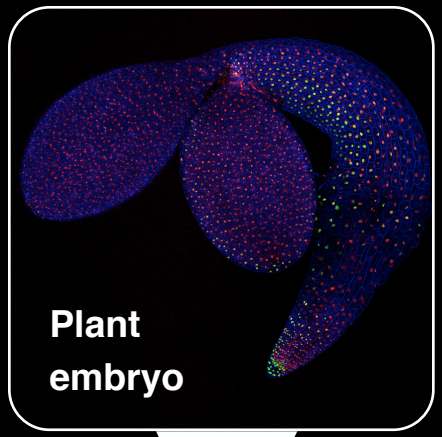
Characterisation of DNA parts for plants

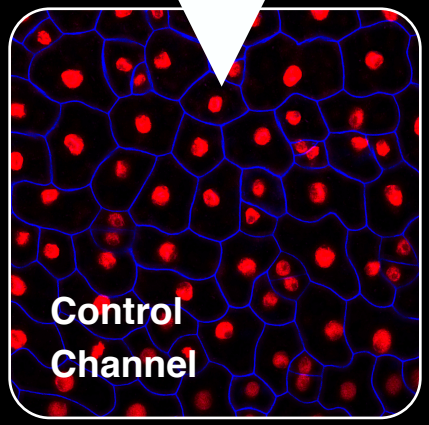
In planta cytometry

*Federici F., *Dupuy L.,et al. **Nature Methods (2012) 9: 483-485.**


Plant
embryo


Control
Channel


Plant
embryo


Control
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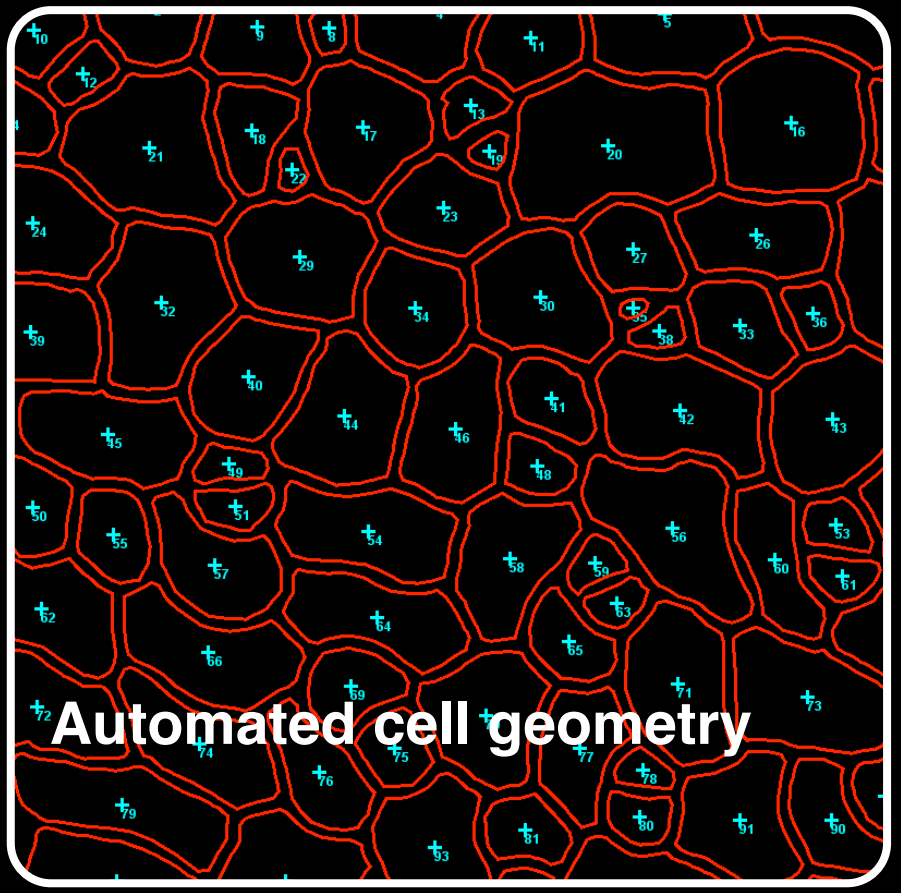
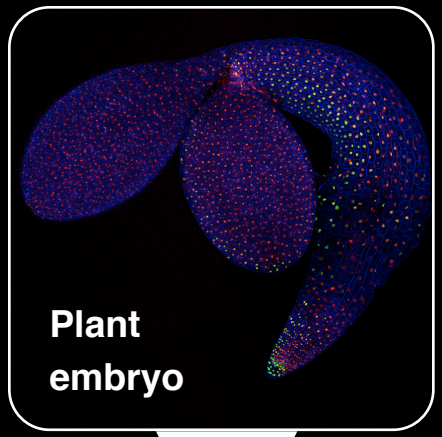
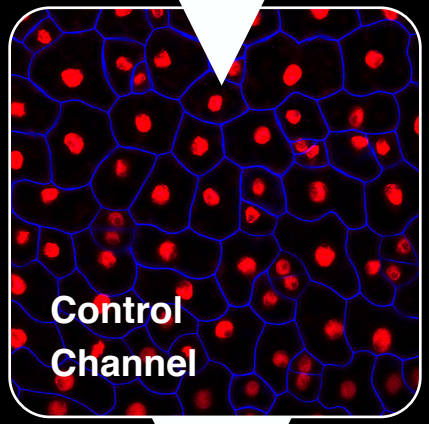

Automated cell geometry


Plant
embryo


Control
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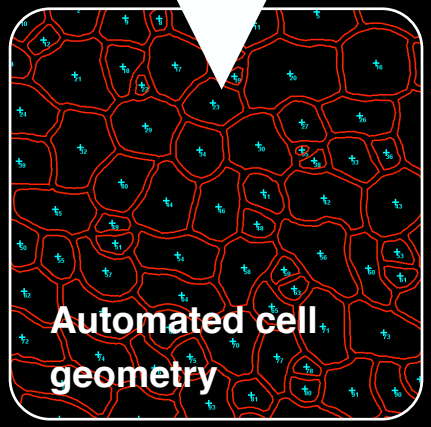
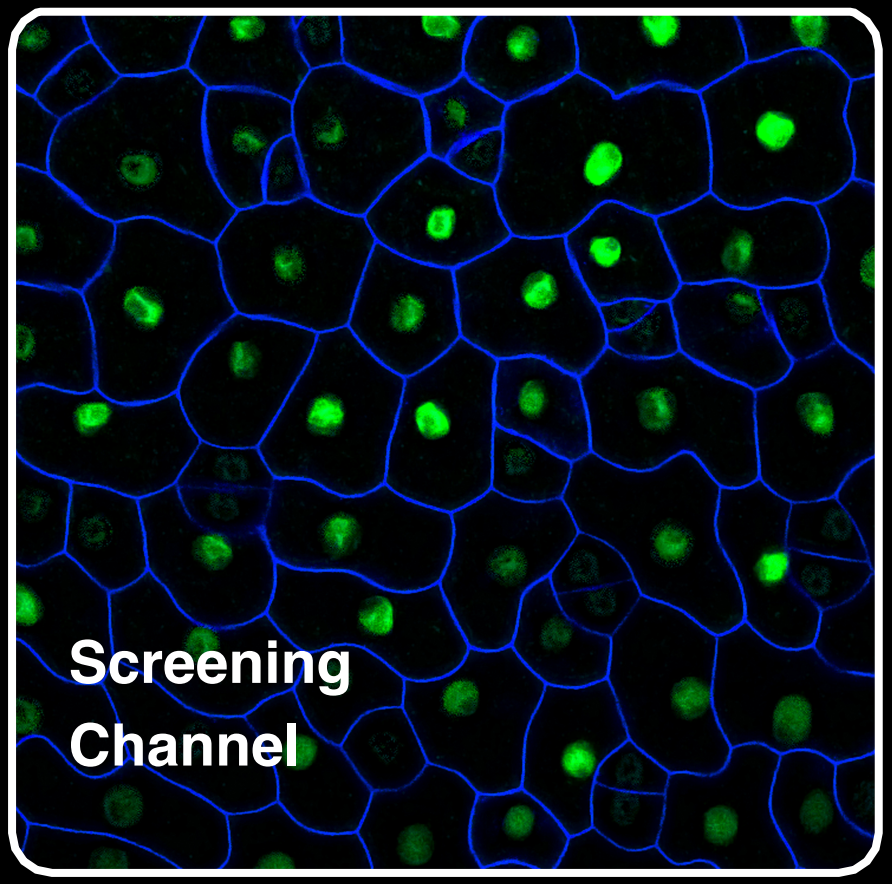
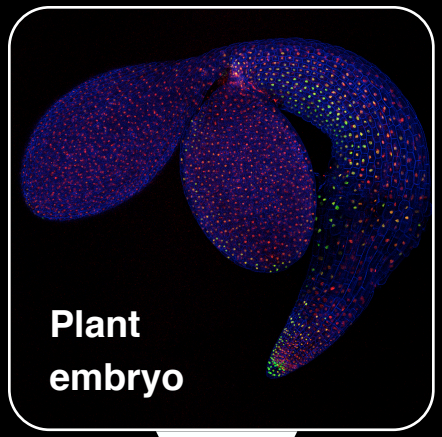
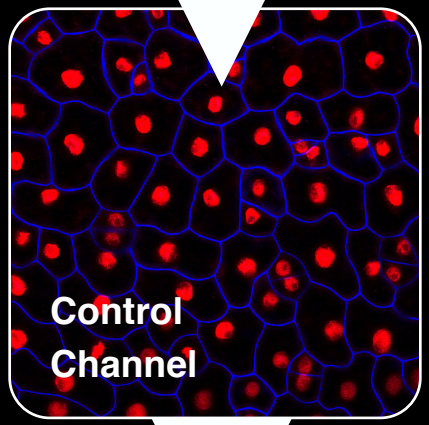

Automated cell
geometry


Screening
Channel


Plant
embryo


Control
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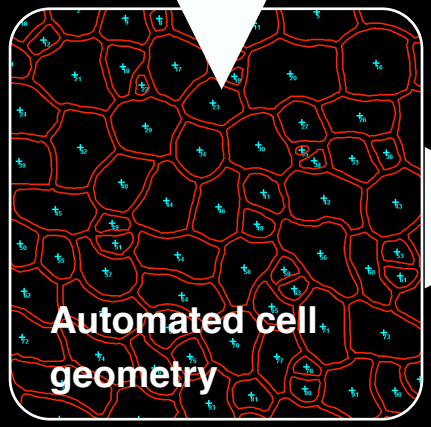
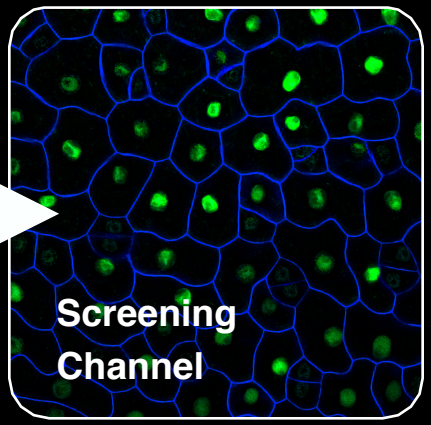
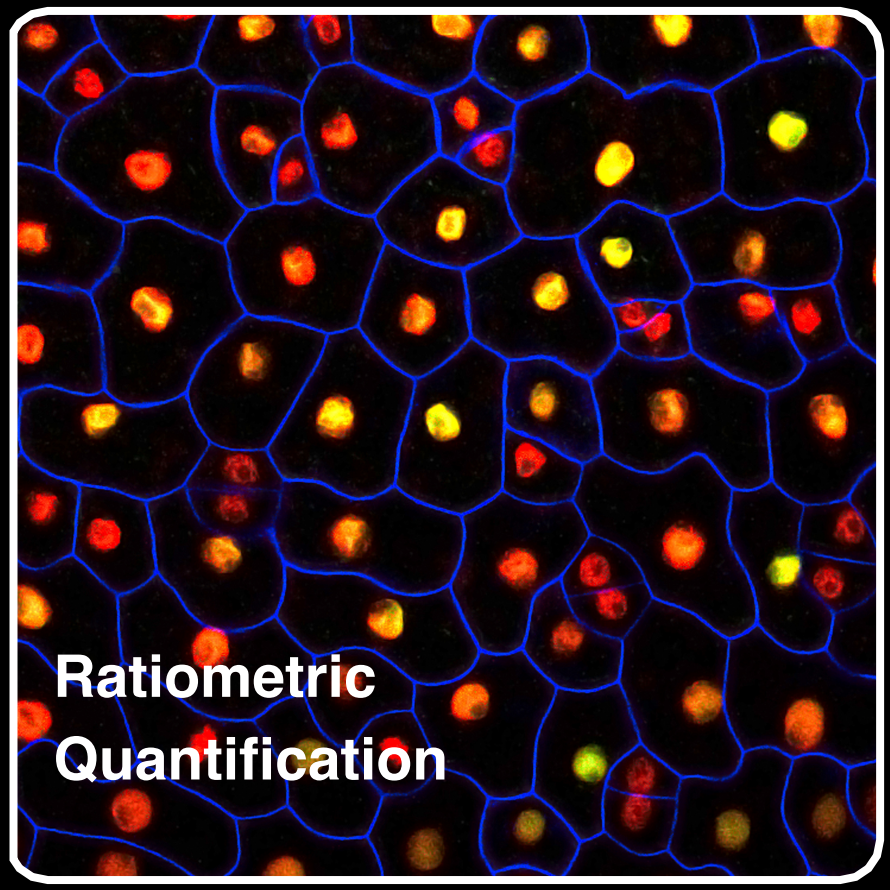
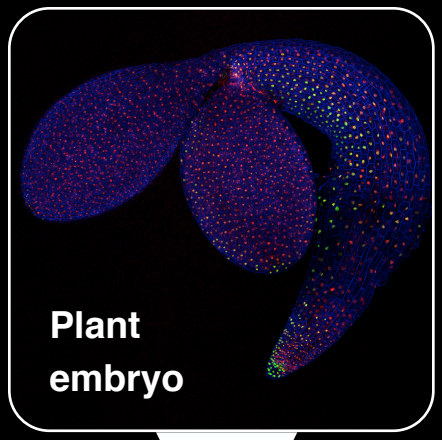
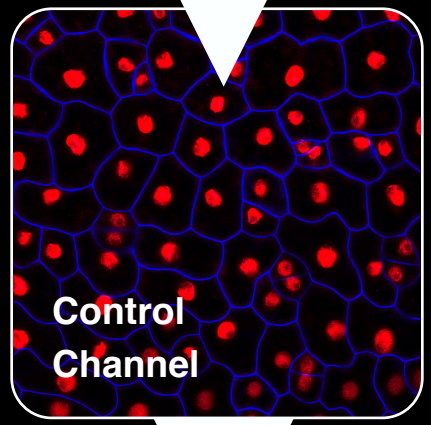

Automated cell
geometry


Screening
Channel


Ratiometric
Quantification


Plant
embryo


Control
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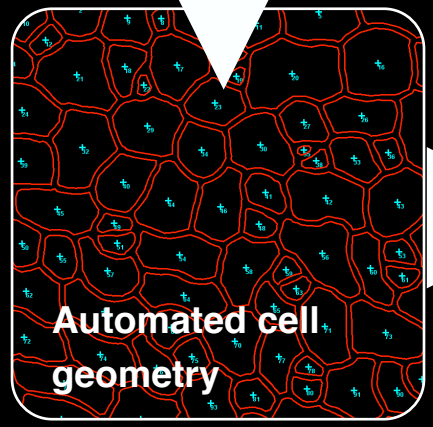
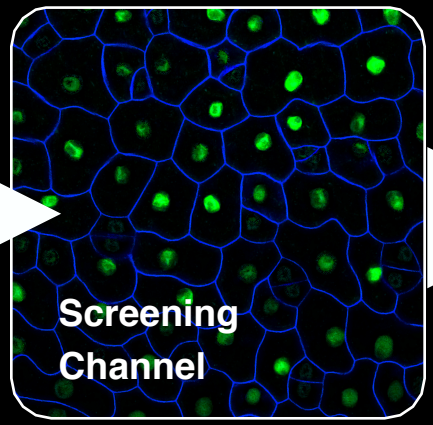

Automated cell
geometry


Screening
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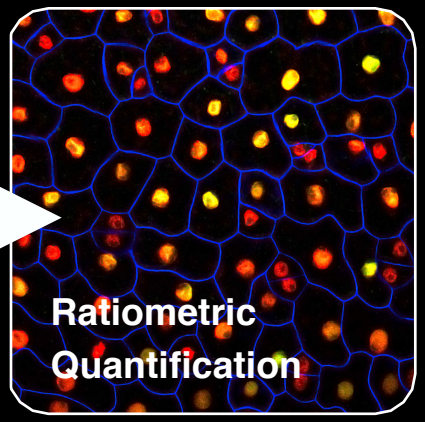
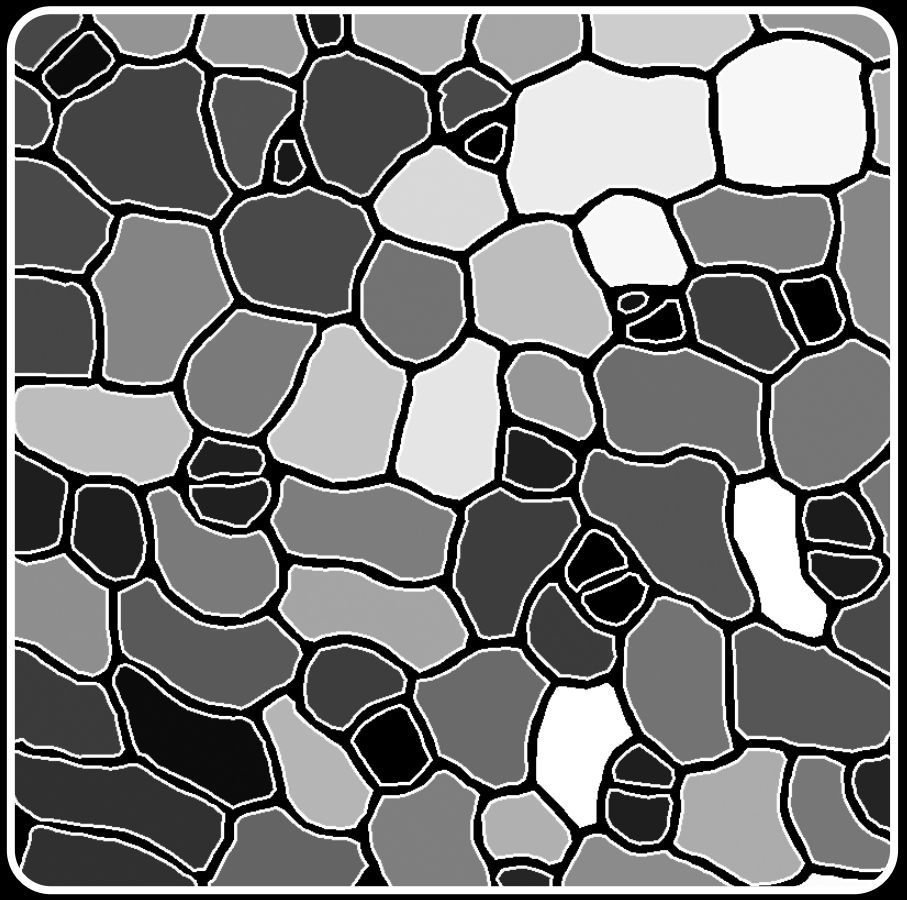
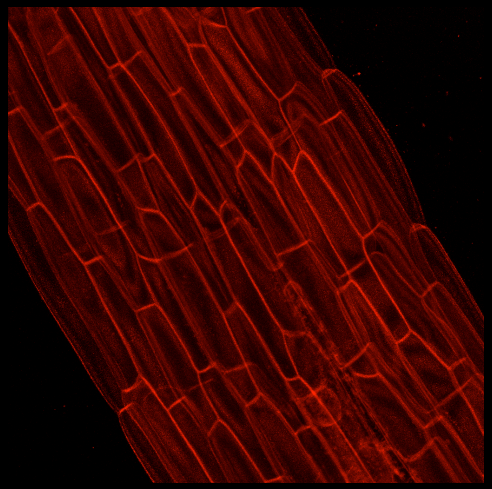

Ratiometric
Quantification




Max
Min

In planta cytometry II

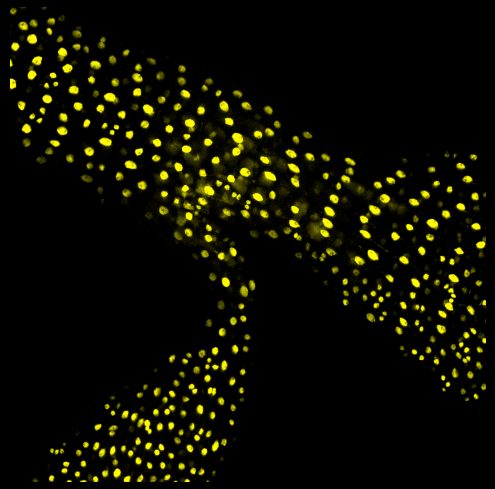
Sharing numbers



mKate2-LTI6b

TagRFP-T-LTI6b

sfGFP-LTI6b



H2B-mKate2

H2B-mTurquoise2

H2B-sfGFP

H2B-Venus

Reference Standard Promoters for Plants

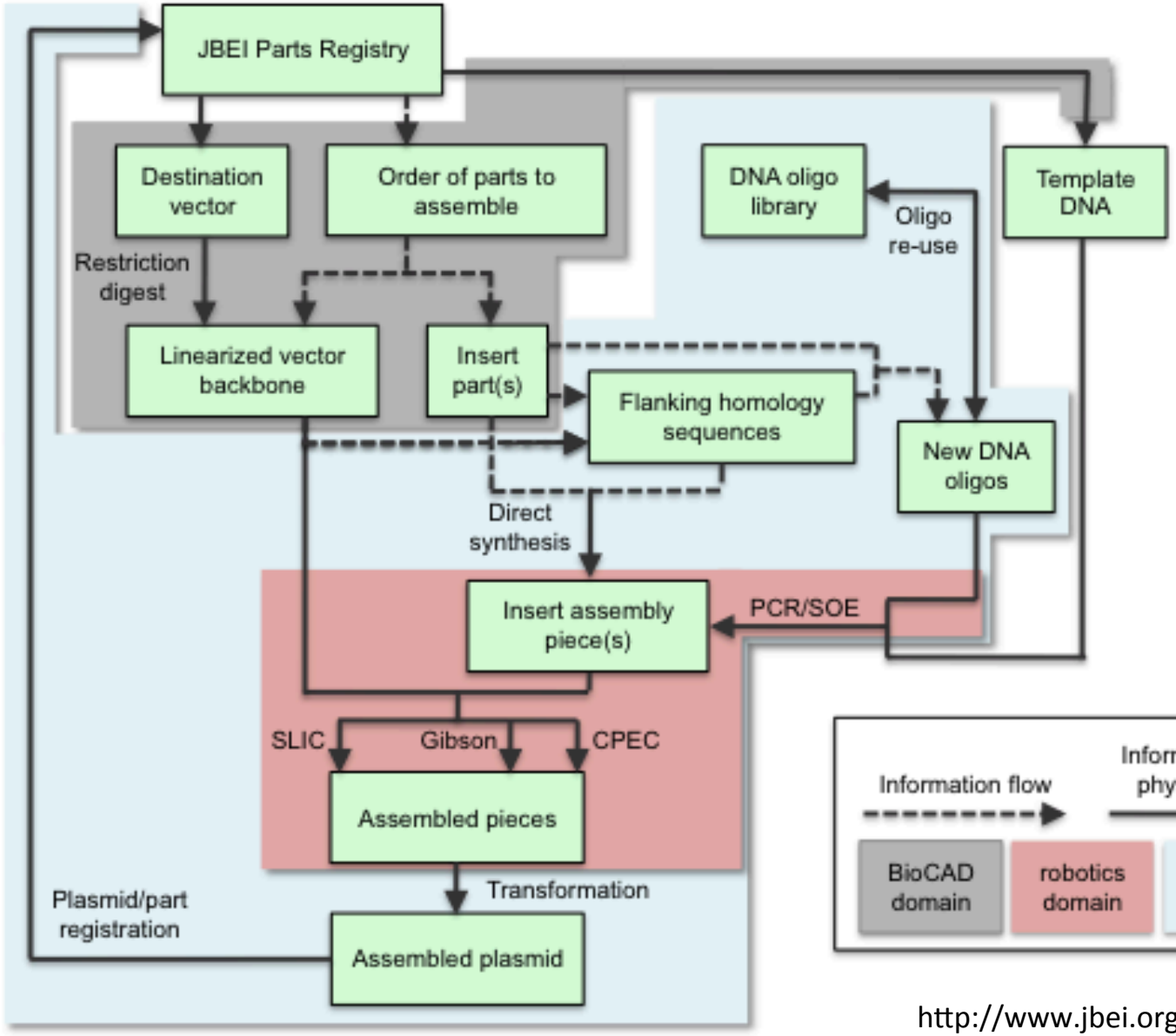
UBQ10

Calculation of transcription rate

$$P^{ss} = \frac{\gamma_M (a + \gamma_I + \mu)(\gamma_F + \mu)[F]^{ss}_{cell}}{\rho a n}$$

Federici Rudge Robertson & Haseloff (work in progress)

Smart Registry for DNA parts

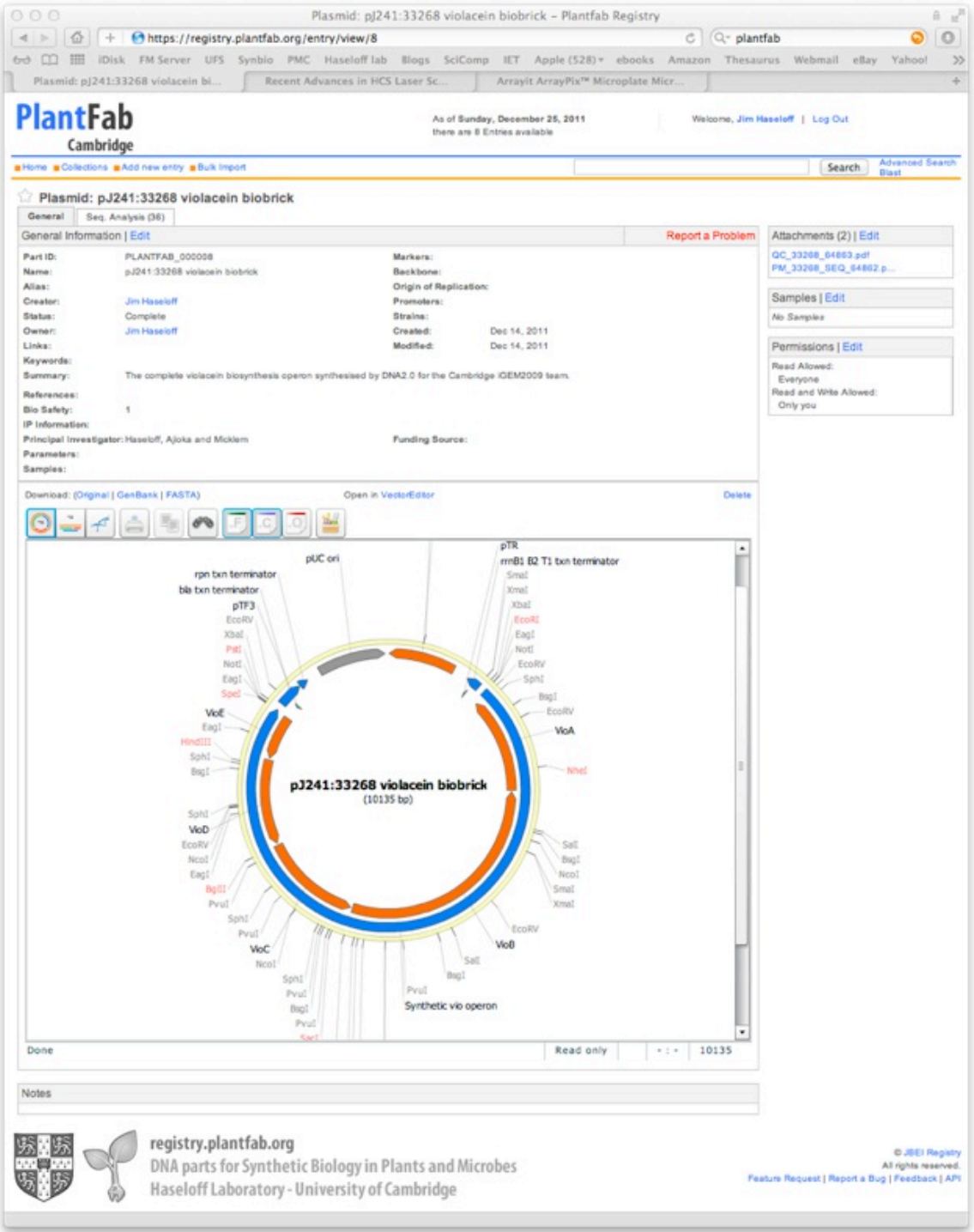


JBEI Inventory for Composable Elements (ICE)

Open source registry software for DNA parts

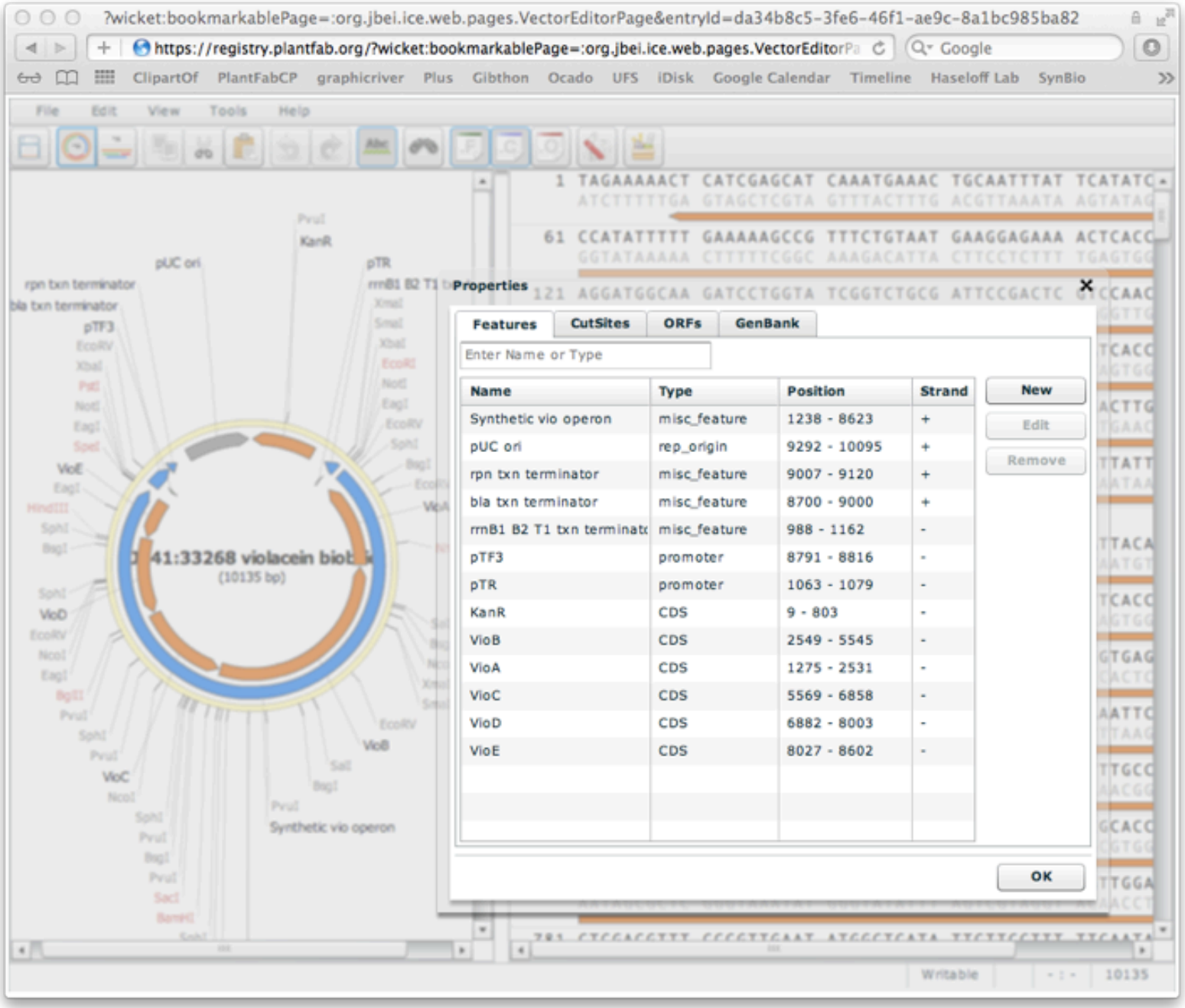
Nathan Hillson
Tim Hamm

http://www.jbei.org/fuels-synthesis/synth.shtml

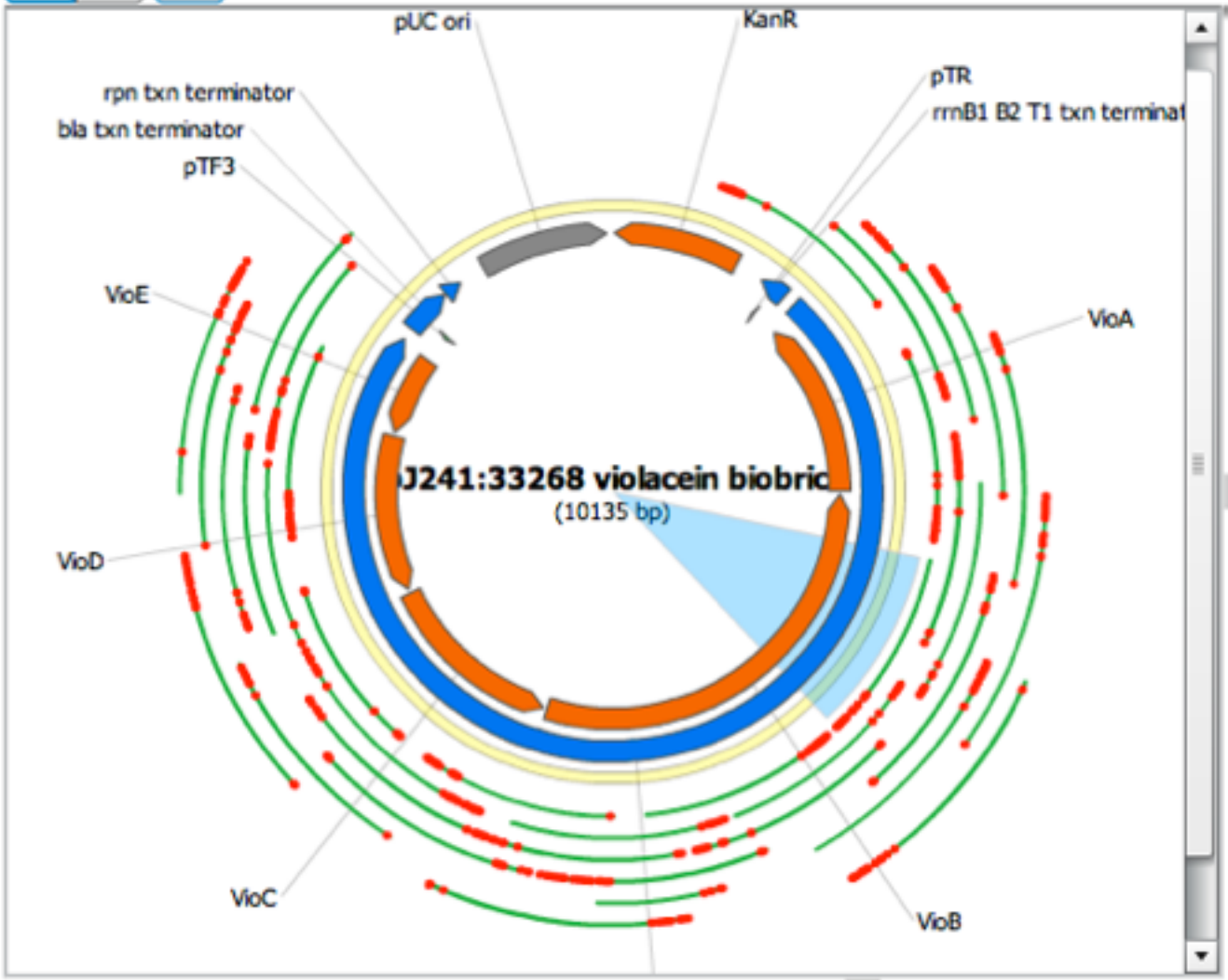


Display page for a plasmid entry in the PlantFab Registry.

Import/export compatibility with Genbank sequence annotations.



Storage and automatic display of sequence trace files.



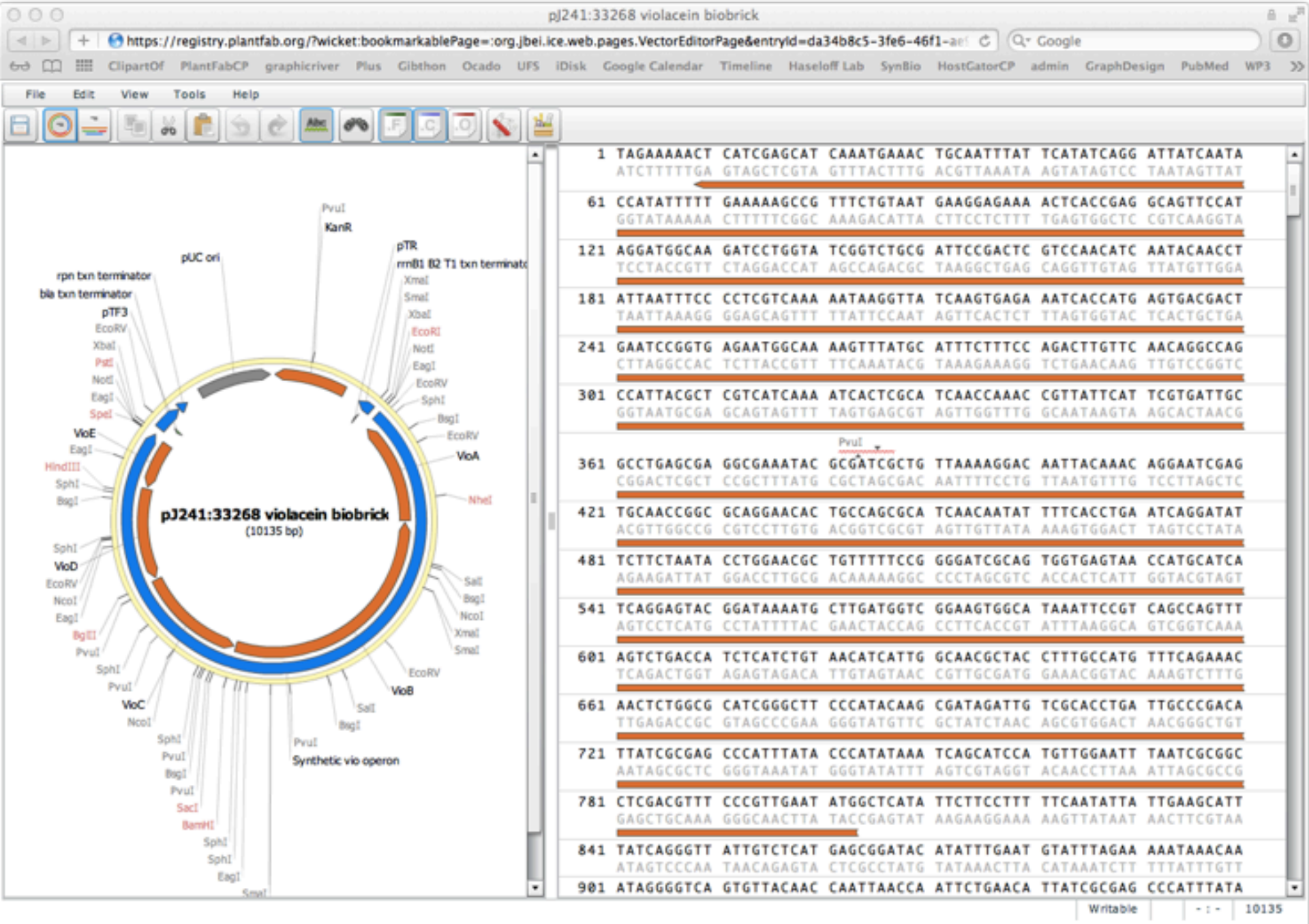
Name	Score	
1657501.ab1	1866	☑
1669855.ab1	1938	☑
1669858.ab1	1922	☑
1674875.ab1	1760	☑
1657494.ab1	1866	☑
1657504.ab1	1802	☑
1669837.ab1	1880	☑
1669848.ab1	1886	☑
1669849.ab1	1990	☑
1657482.ab1	1892	☑
1657490.ab1	1734	☑
1669846.ab1	1984	☑
1669850.ab1	1956	☑
1669856.ab1	1944	☑
1674872.ab1	1774	☑
1657500.ab1	1810	☑
1669838.ab1	1972	☑
1669847.ab1	966	☑
1669852.ab1	1910	☑

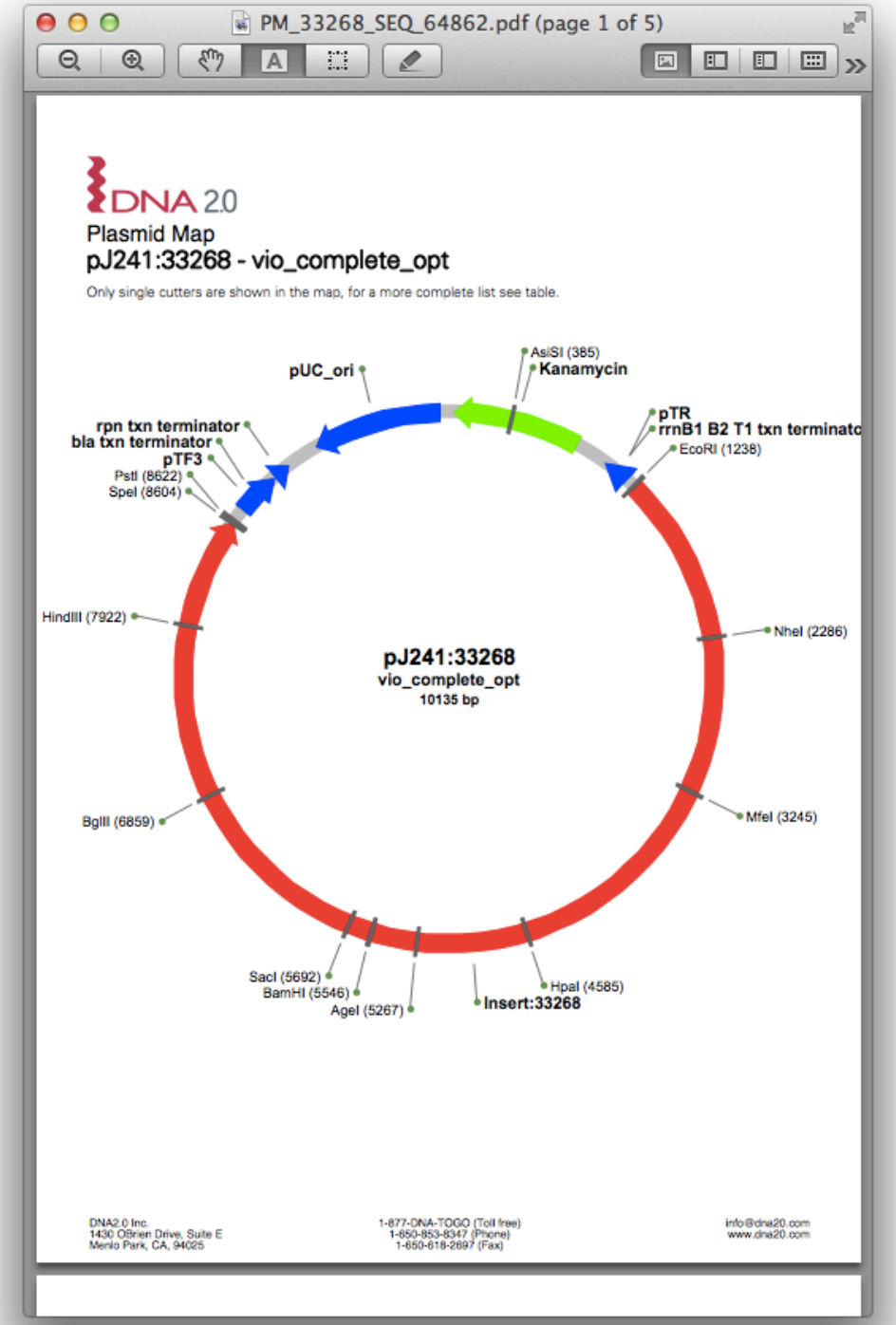
```
Expected  2876: GGTGACGGTCTGGTCGGTGCTCGTTTGGCACTGTGGGGTCACTACAATGATTATCTGCGT
Trace       28: GGTGNNGGTCTGGTCGGTGCTCGTTTGGCACTGTGGGGTCACTACAATGATTATCTGCGT

                ACCACCTTCAATCGTGCTCGTTGGGTCGACAGCGACCCGACGCGCCGTGACGCTGCACAA
                ACCACCTTCAATCGTGCTCGTTGGGTCGACAGCGACCCGACGCGCCGTGACGCTGCACAA
```

1657501.ab1 | 2876 : 3846 (971) | 10135

Built-in vector editing functions.





Documents can be attached to sequence entries.

www.plantfab.org

Registry of DNA parts for Plants

DNA parts for the fabrication of new genetic systems in plants and related microbes.

(construction in progress, Dec 2011)

Registry of DNA parts

A new resource for sharing details of DNA parts for use in Synthetic Biology experiments in plants.

The recent development of genome-scale DNA assembly techniques allows fast, efficient multiplex fabrication of large-scale DNA assemblies - with no need for restriction enzymes or low-efficiency ligation reactions. This places new demands on the availability of reliable and well characterised DNA parts for assembly.

This site contains a registry of DNA parts dedicated to use in plant and related microbial systems. The formation of the registry was driven by by the lab's need to keep our own DNA parts in an orderly manner - many of the parts will be "work-in-progress", and not accessible without password. Details of published DNA constructs will be available.

The PlantFab Registry is based on the Inventory for Composable Elements (ICE), developed as an open source registry for biological parts by the Joint Bio Energy Institute (JBEI), UC Berkeley (with many thanks to Tim Ham

biofab

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about the biofab

The BIOFAB: International Open Facility Advancing Biotechnology (BIOFAB) was founded in December 2009 as the world's first biological design-build facility. This professionally staffed public-benefit facility was initiated by a grant from the National Science Foundation (NSF) and is led by bioengineers from UC Berkeley and Stanford University. The BIOFAB is operated in partnership with Lawrence Berkeley National Laboratory (LBNL), the BioBricks Foundation (BBF), and the Synthetic Biology Engineering Research Center (SynBERC).

BioFab projects will be designed to produce broadly useful collections of standard biological parts that can be made freely available to both academic and commercial users, while also enabling the rapid design and prototyping of genetic constructs needed to support specific needs of partner efforts such as SynBERC Testbeds. The BioFab will thus also represent the first significant focused investment in the development of open technology platforms underlying and supporting the next generation of biotechnology. Once fully operational the BioFab facility will be capable of producing tens of thousands of professionally engineered, high quality standard biological parts each year.

Read the full announcement here:
http://www.berkeley.edu/news/media/releases/2010/01/20_biofab_synthetic_biology.shtml

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The BioBricks Foundation

- Develop and implement legal strategies to ensure that BioBrick™ standard biological parts remain freely available to the public.
- Support the development of open technical standards that define BioBrick™ standard biological parts.
- Develop and provide educational and scientific materials to allow the public to use and improve existing BioBrick™ standard biological parts, and contribute new BioBrick™ standard biological parts.

BioBricks FOUNDATION

Biotechnology in the public interest

biobricks.org

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@biobricks

The BioBricks Foundation SB6 Conference registration is now open! Space is limited. http://t.co/LLLQCaVL
25 Jan 2013 · reply · retweet · favorite

Thanks, @GerdMoeBehrens for a really important paper:http://t.co/FFdN5oTH
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Tom Knight, BBF Founding Director, Emeritus, profiled in "New Scientist" on @biobricks, @igem & craziest synbio: http://t.co/F8yWXplF
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BIOFAB success to continue in partnership with the BBF. Learn more »

Synthetic Biology 6.0 Conference

BioBrick™ Public Agreement

Stanford BIOFAB

The BBF's mission is to ensure that the engineering of biology is conducted in an open and ethical manner to benefit all people and the planet.

We believe fundamental scientific knowledge belongs to all of us and must be freely available for ethical, open innovation. This is a new paradigm.

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The Synthetic Biology Network

Applications

- open source and free-to-operate tools
- open standards to promote innovation
- international scientific exchange

Cambridge website for Synthetic Biology resources

Compiled by Jim Haseloff at the University of Cambridge.
This site contains details of recent papers and activity in Synthetic Biology, with particular emphasis on: (i) development of standards in biology and DNA parts, (ii) microbial and (iii) plant systems, (iv) research and teaching in the field at the University of Cambridge, (v) hardware for scientific computing and instrumentation, (vi) tools for scientific productivity and collected miscellany.

Similar to the Cambridge-based Raspberry Pi and OpenLabTools initiatives, we promote the use of low cost and open source tools - in our case for use in biological engineering.

SYNBIO **CALENDAR**

11 MAY — **First International Mammalian Synthetic Biology Workshop**
12:00 AM to 12:00 AM
Recognizing the fast emergence and potential significance of this field, the aim of this workshop is to bring together practitioners of mammalian synthetic biology together with experts from other relevant

20 MAY — **Introduction to opportunities in plant synthetic biology**
07:00 PM to 07:00 PM
This meeting will introduce and showcase the many and varied applications of synthetic biology at the molecular, cell, and whole plant level to introduce synthetic biology to a broad UK plant science base.

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RESEARCH **STUDIES**

PhD Studentships in Cambridge

The Board of Graduate Studies manages admission of the University's graduate students. Prospective students should start here - for an introduction to the University of Cambridge, the courses we offer, how to

Scientific instrumentation and computing hardware

Latest news in scientific computing and development of low-cost hardware for laboratory instrumentation. The pages in this section contain links to web sites with DIY instructions for building hardware, specialised components and open-source or low-cost software, with a focus on Arduino and Raspberry Pi.

Water Cooled Raspberry Pi Case

Hacker Phame has taken a low powered Raspberry Pi mini PC, which is available to purchase for around $35, and added a pimped up cooling system creating a water cooled Raspberry Pi mini computer. To re-cap the Raspberry Pi mini computer which is manufactured in Wales, UK, is equipped with a a 700 MHz ARM11 processor, which can safely be overclock it to 1 GHz if desired. (...) Original Story...

| 14 hits | **Read more**

Pick the Right Electronics Board for Your DIY Projects

The Arduino, Raspberry Pi, and BeagleBone are all low-cost controllers that are great for your DIY projects, but it's a little confusing when you're trying to figure out which one is best suited for you. Make has a breakdown of all three and what types of projects they're best for. Read more... Pick the Right Electronics Board for Your DIY Projects (Via Lifehacker.)

| 20 hits | **Read more**

Eyes-on with Ninja Blocks 'home automation for hackers' (video)

Yet another Kickstarter success story is here on the Hardware Alley Floor

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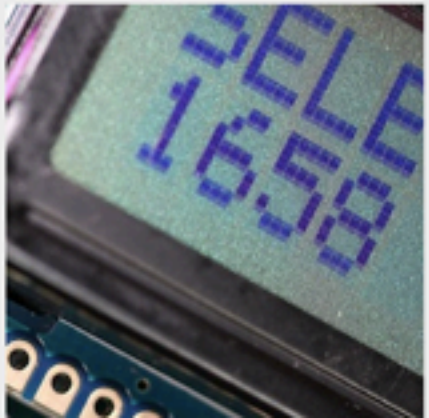
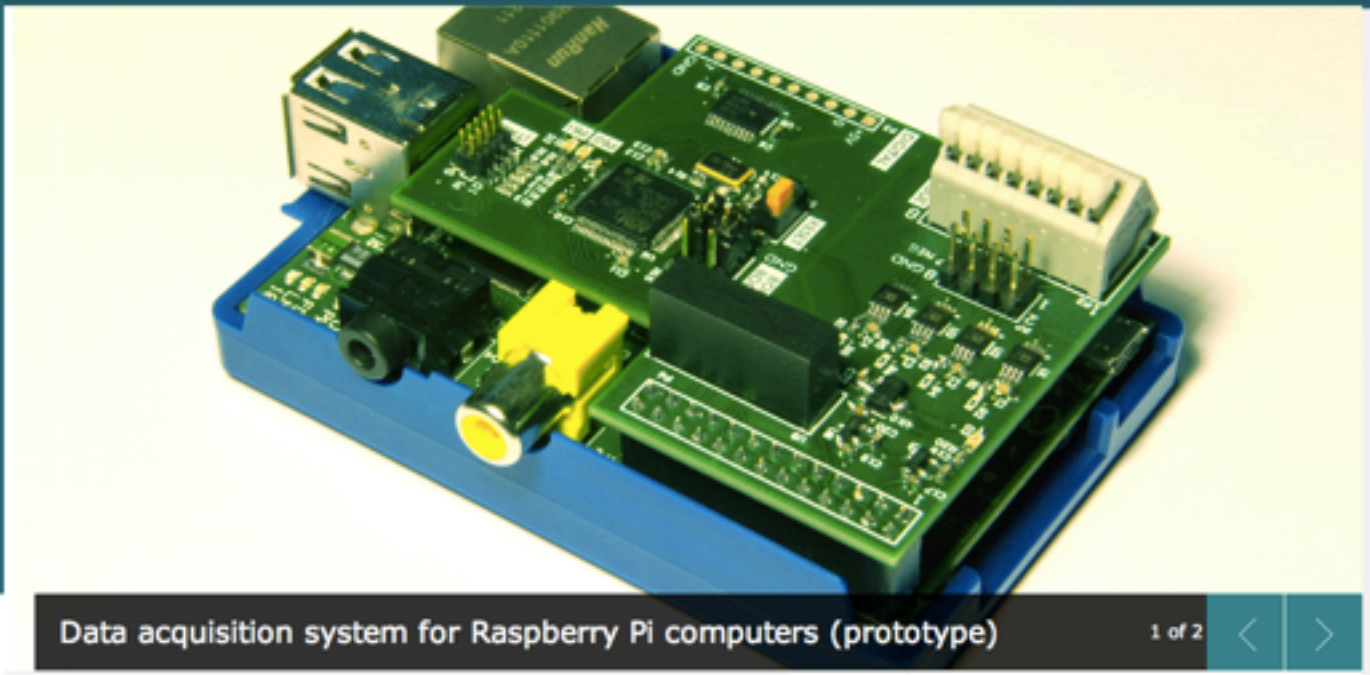
OPENLABTOOLS **IN CAMBRIDGE**



OpenLabTools



Data acquisition system for Raspberry Pi computers (prototype) 1 of 2

The OpenLabTools project

The OpenLabTools initiative aims to provide a forum and knowledge centre for the development of low cost and open access scientific tools, with an emphasis on undergraduate and graduate teaching and research. The programme will officially start in October 2013. In order to bootstrap this initiative, a number of MEng projects (4-5 per year) will be offered to establish the core components required for such tools; these include data acquisition, sensing, actuating, processing and 3D manufacturing. Protocols, designs and tutorials will be published on this website. These components will be subsequently combined to establish a documented collection of instruments, to be developed and maintained by a community of undergraduate and graduate students of the University.

We anticipate that the core tools will be rolled out in undergraduate laboratories from 2014 onwards. We would like to invite anybody interested in this programme to get in

Academic team

Anurag Agarwal
(Fluids - Acoustics)

Oliver Hadeler
(CamBridgeSens)

Jim Haseloff
(Synthetic Biology)

Simone Hochgreb
(Fluids - Reacting flows)

Alexandre Kabla

Related initiatives

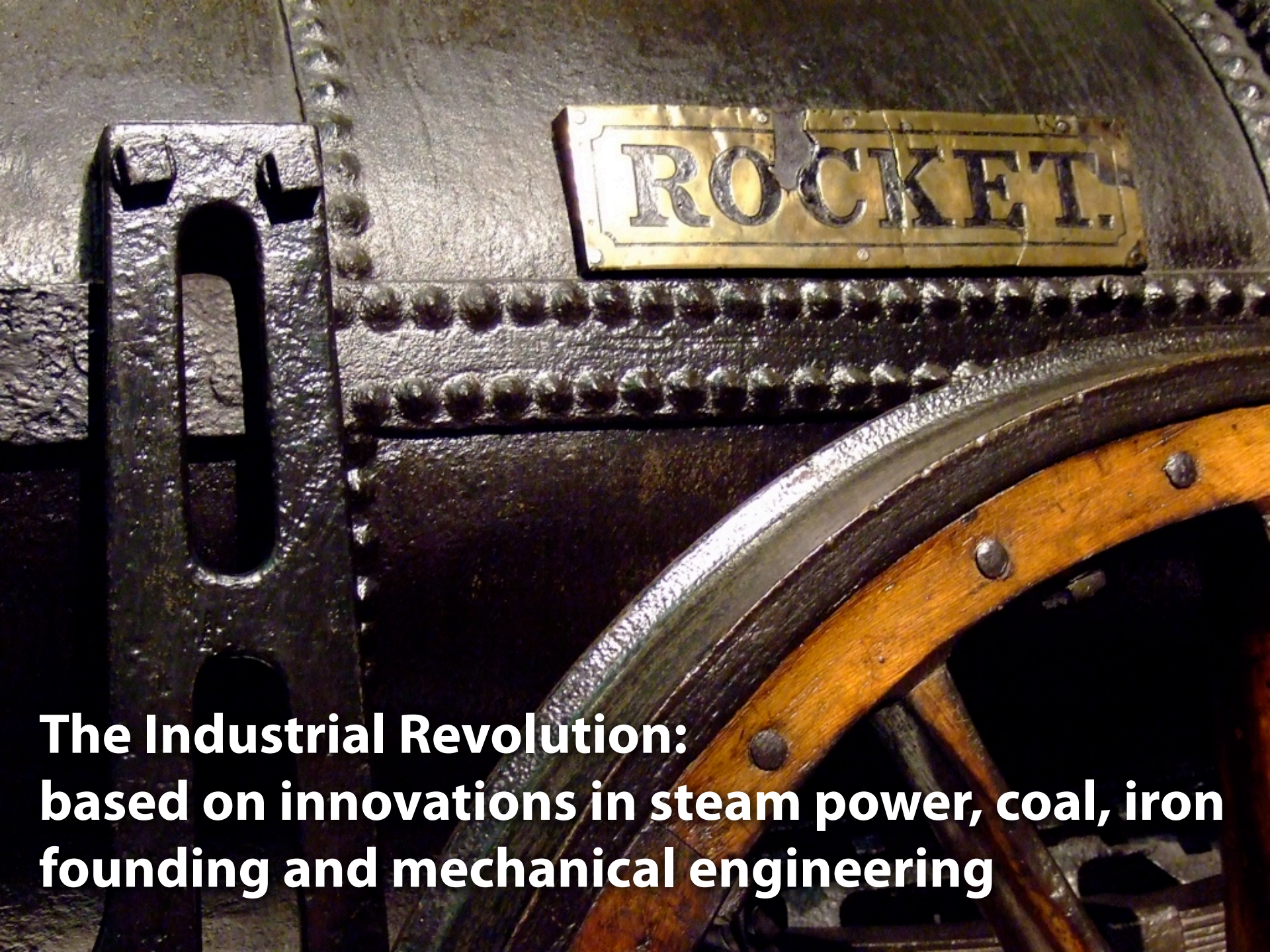
The Raspberry Pi fundation

Arduino

Synbio.ork.uk

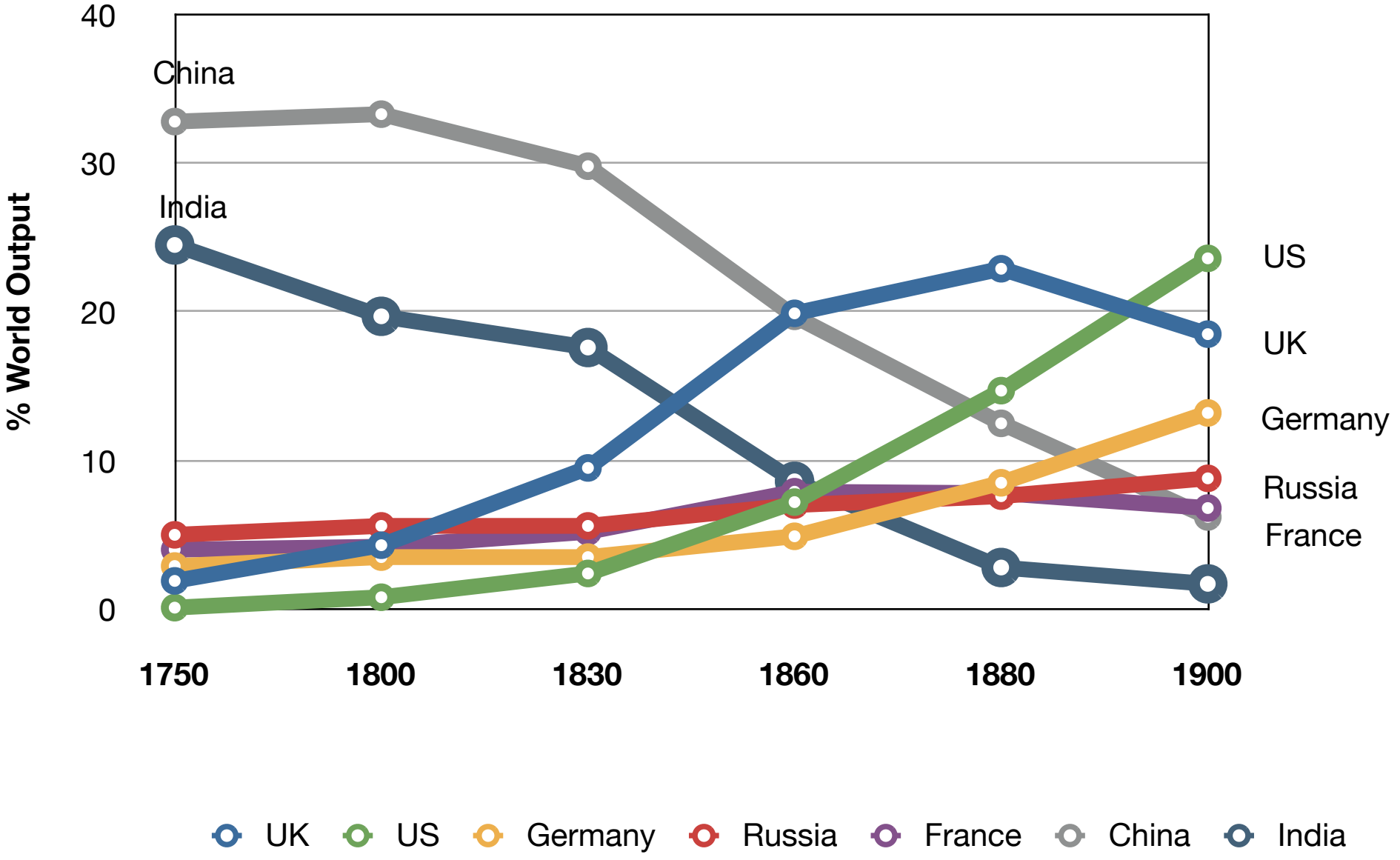
Makespace (Cambridge, UK)

CamBridgeSens

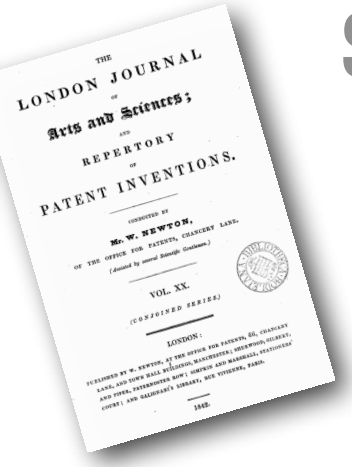


The Industrial Revolution:
based on innovations in steam power, coal, iron founding and mechanical engineering

Relative shares of world manufacturing output 1750-1900



Standardisation of parts for construction


THE
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OF
Arts and Sciences;
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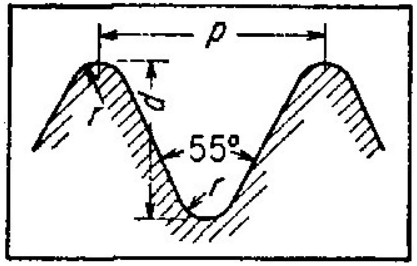
OF
PATENT INVENTIONS.
CONDUCTED BY
Mr. W. NEWTON,
OF THE OFFICE FOR PATENTS, CHANCERY LANE.
VOL. XX.
(CONTINUED SERIES)
LONDON:
1842.

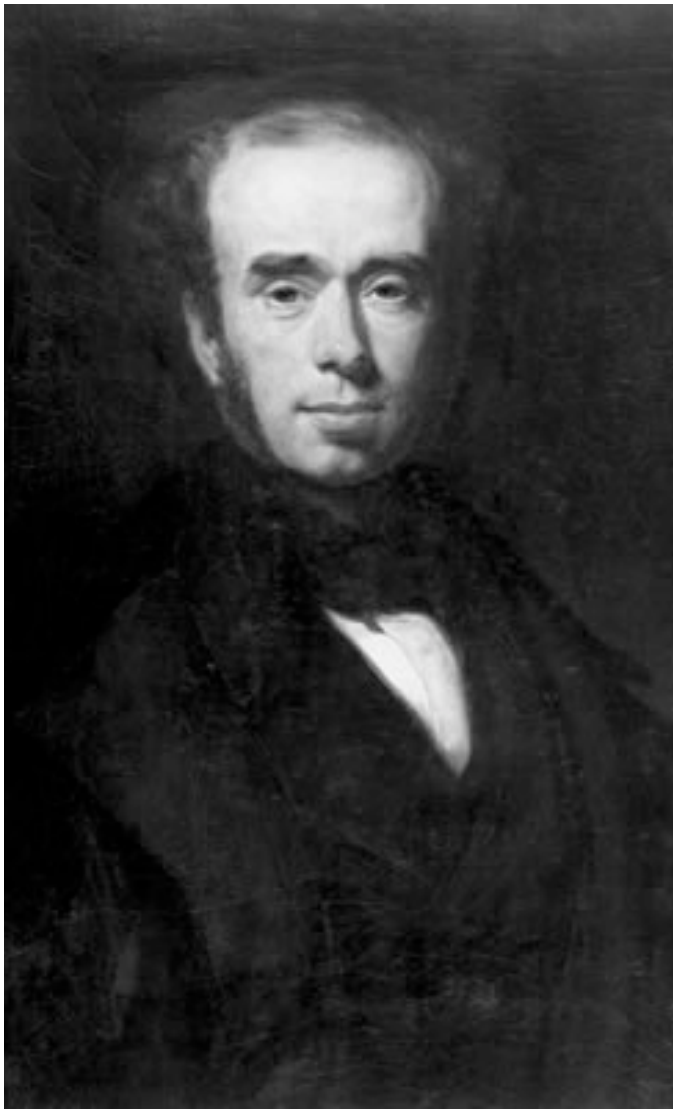


"On an uniform system of Screw Threads."

By Joseph Whitworth, Assoc. Inst. C. E.

The subject considered in this paper, is the importance of having a constant thread for a given diameter in all screws used in fitting up steam engines and other machinery. It is argued, that uniformity of thread would be productive of economy, both in the use of screwing apparatus, and in the consumption of bolts and nuts. The refitting shop of a railway or steam packet company, affords a striking instance of the advantage to be derived from the application of this principle. If the same system of screw threads were common to the different engines, a single set of screwing tackle would suffice for any repairs.

No attempt appears to have been hitherto made to attain this important object. Engineers have adopted their threads without reference to a common standard. Any such standard must be in a great measure arbitrary, and hence its absence may be accounted for.



Joseph Whitworth 1842

Interchangeable parts led to continuous production methods