Timely *E. coli*
Engineering a standardised cellular oscillator

UQ-Australia
iGEM 2011 Regional Jamboree - Asia
Our Team

Inspiration

Circuitry

Modelling

The Future
Our Team

Asia Jamboree

University of Queensland

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Circadian rhythm regulates:

- Sleep-wake cycle
- Body temperature
- Feeding behaviour and appetite
- Hormone secretion and metabolism
- Glucose homeostasis
- Cell cycle progression
Effects of the circadian rhythm

Circadian Variation in the Expression of Cell-Cycle Proteins in Human Oral Epithelium
Georg A. Bjarnason, Richard C. K. Jordan, and Robert B. Sothern

Circadian clock coordinates cancer cell cycle progression, thymidylate synthase, and 5-fluorouracil therapeutic index

Effects of circadian disruption on cardiometabolic system
Melanie Rüger, PhD and Dr. Frank A.J.L. Scheer, PhD

Circadian Gating of the Cell Cycle Revealed in Single Cyanobacterial Cells
Qiong Yang, *, Bernardo F. Pando, †, Guogang Dong, ‡, Susan S. Golden, ‡, Alexander van Oudenaarden

Circadian and age-related modulation of thermoreception and temperature regulation:
mechanisms and functional implications
Eus J.W. Van Someren, *, Roy J.E.M. Raymann, a, Erik J.A. Scherder, b, Hein A.M. Daanen, c, Dick F. Swaab, a

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Other effects

24 Hour GH Secretion

Hypertension. 2005; 45: 874-879

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Human circadian circuit

Key features:

- Time delay
- Negative feedback loop

Gallego et al. Molecular Cell Biology. 2007; 8: 139-148
Mammalian Model

Prokaryotic Models

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Prokaryotic Models

- Simpler circuit
- Dual response promoter

Our system

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glnG

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araC

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Mathematical Model
Model Analysis

- Modelling of a novel synthetic system
- Kinetics sourced from pre-existing work
  - Limited by differences in experimental conditions
Gene dosage effects


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Chromosome integration

1. Landing pad
   - Use a pre-determined landing site to target our constructs

2. Homologous recombination
   - Via identity with the landing pad site

3. Integration!
   - Now we have no need to worry about fluctuations in gene dosage

Applications

- Standardised platform for modeling oscillating systems
- Periodic medicine: potential drug or hormone delivery system
- Biological Battery Cell: Generating current through periodic stimulation of ion channels
...And along with the science
...And along with the science

- Share your human practices and outreach activities
- Catch up (and collaborate!) with iGEM’ers

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• Oscillatory circuits are important in nature

• We are standardizing the biological ‘clock’

• Outreach is an important part of science too!
Kuhlman & Cox (2010) Chromosome Integration

1. pTKRED
   - IPTG
   - Chromosome
   - Landing Pad

2. L-arabinose
   - pTKIP
   - Chromosome
   - IPTG

3. Chromosome