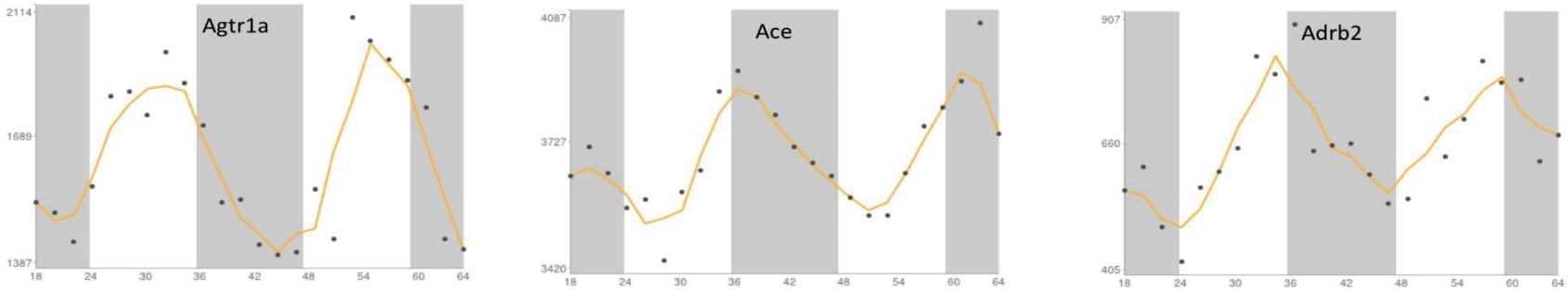
BioChronicity (BioC): Chronotherapeutics

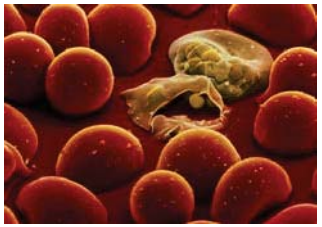
Targets of 56/100 WHO essential medicines & best-selling drugs are clock-regulated (half-life often < 6 hours)

Example: anti-hypertensive drugs



Zhang and Lahens, PNAS, 2014

Plasmodium clocks
Cell cycle
Developmental
Metabolic



Coupled?

Synchronous erythrocyte bursting every 48 hr

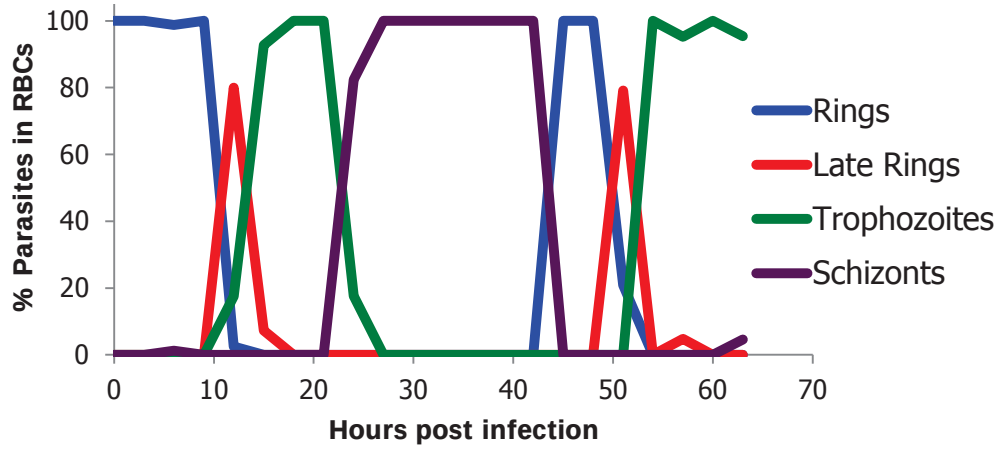
Host clocks
Innate response
(e.g., TNF-α, IL-6)
Circadian systems

Clock-based therapy: Asynchronizing the clocks between host and parasite will reduce parasite fitness

Identifying Clock-Controlled Genes in Parasites

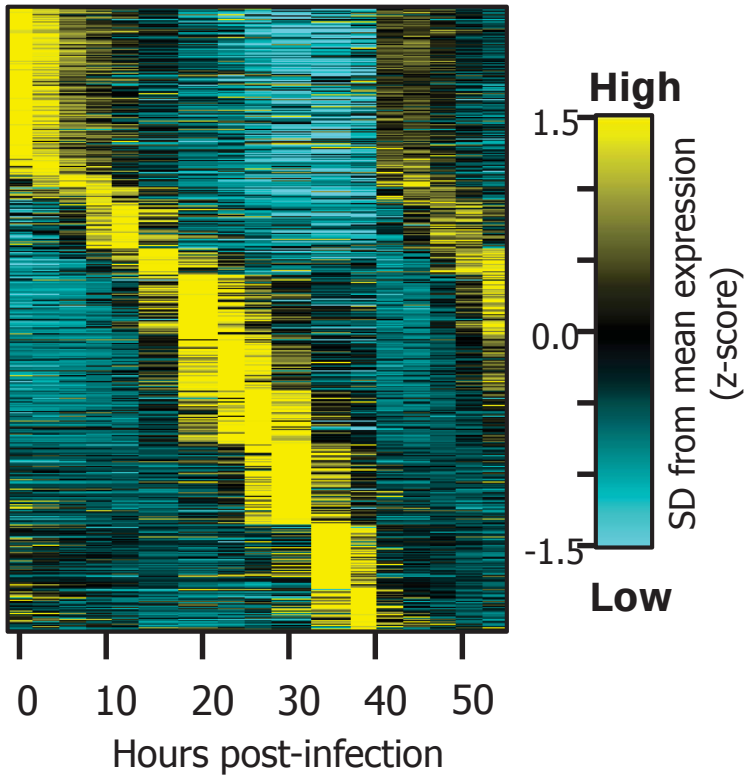
In vitro erythrocyte infection system

- Thriving malaria parasites
- High-density time series RNA-Seq
- Data collected every 3 hr for 48+ hr



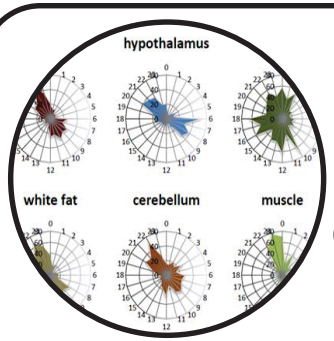
Unpublished data
Steve Haase (U Penn; BioC performer) in collaboration with
LTC Norman Waters, PhD (Director, Malaria Vaccine Branch, MMRP)

P. falciparum
All genes (5425)



BioChronicity Quantitative Tools
Network inference from time-series data

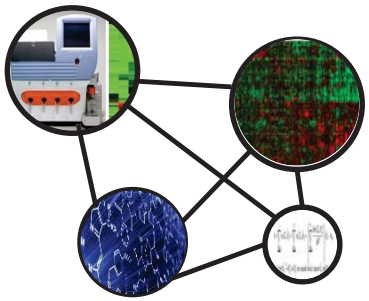
BioC Grand Challenge



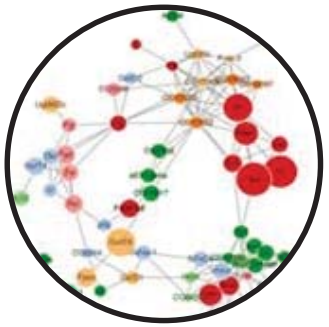
Chrono-therapy

Enhanced diagnostics

Raise awareness of timing and molecular cycling in biological systems and impact on health & disease



Spark collaboration among multiple disciplines to develop and test integrated models



Validate using big data analysis of circadian and/or temporal signatures

Generate new directions in prediction, treatment, & prognosis

Approach:

Longitudinal clinical datasets:
- Chronic disease
- Acute infection

→

Challenge participants:
Predict illness and recovery

→

Model evaluation:
Objective metrics, expert panel of judges, modest cash prizes