Establishing Baseline Performance Scores for the CAGEN Robust Gene Response Challenge

Shaunak Sen

Caltech CDS

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CAGEN - Critical Assessment of Genetically Engineered Networks

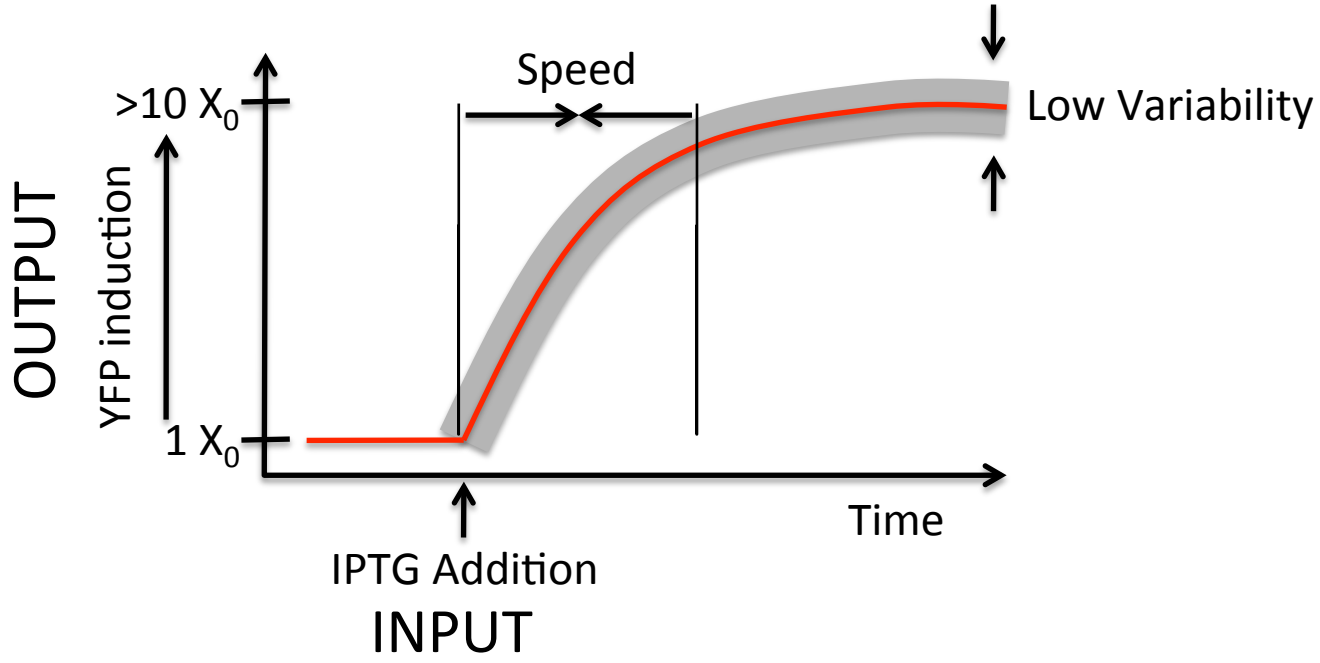
- Systematize the design of genetic networks
(address issues of robustness, connectability)

- Facilitate applications, for ex. in agriculture, medicine

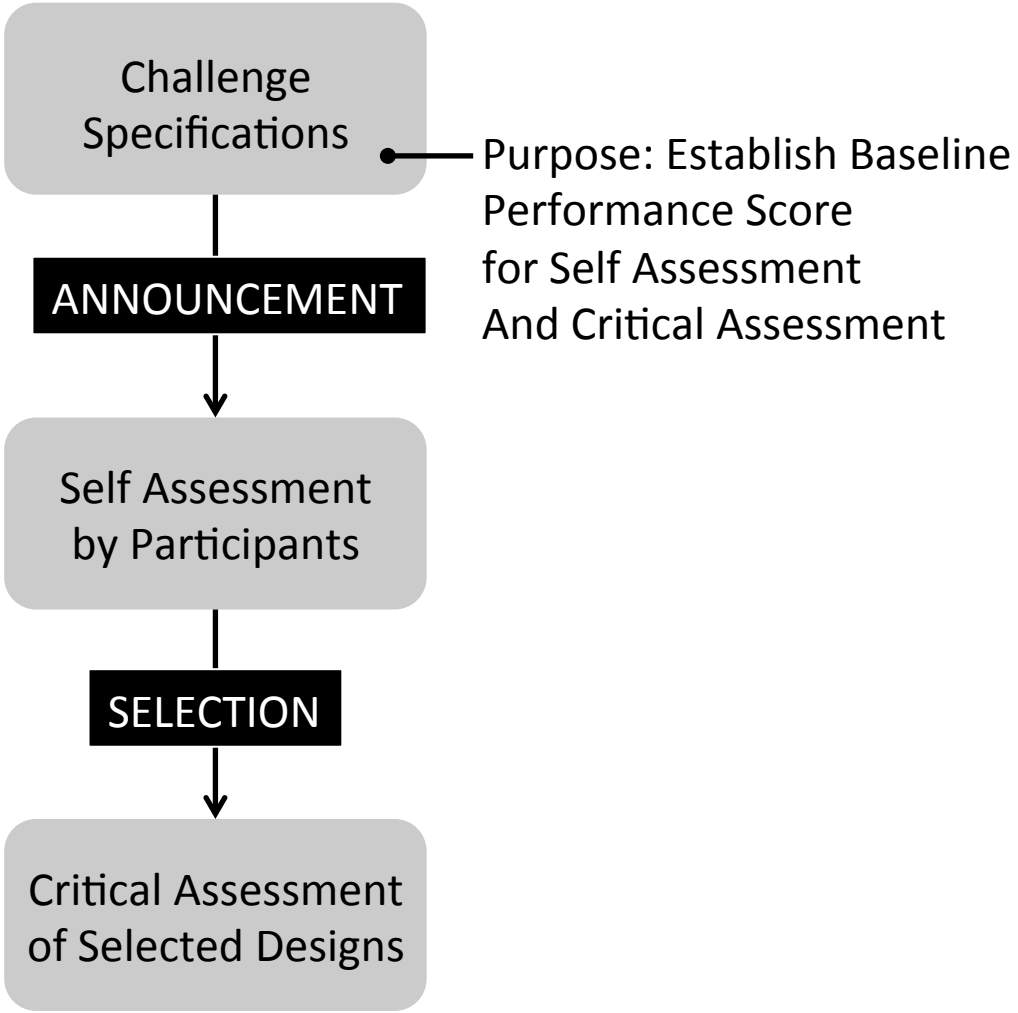
CAGEN Challenge #1 : Robust Gene Response

Induce OUTPUT (YFP) in response to INPUT (IPTG), so that,

1) Detectable: >10 fold induction
2) Robust: Low variability across cells & temperatures
3) Fast: Quick response



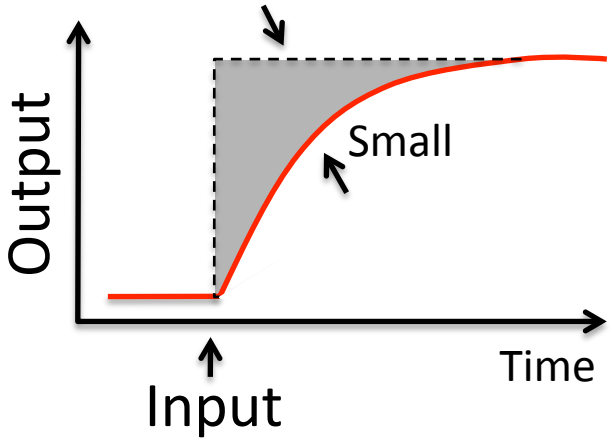
Purpose
Establish Baseline Performance



Performance metric to score robustness and speed of designs

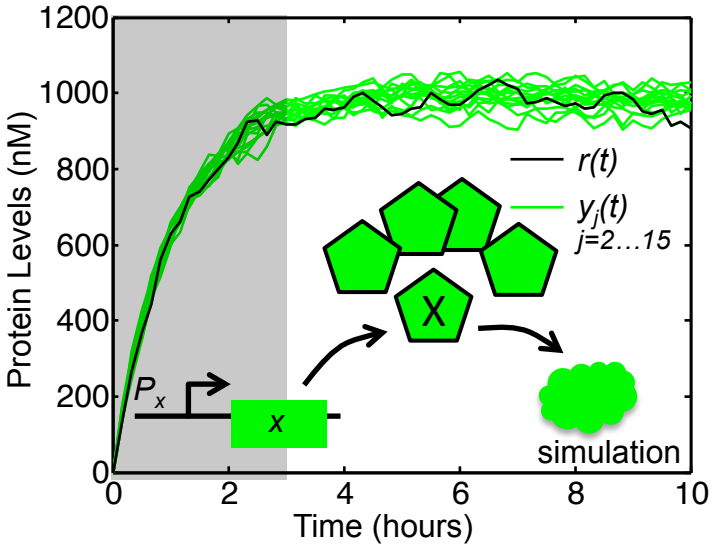
$$S = \frac{\text{Worst Case}\ \overline{\max_j \int_{T_1}^{T_2} |y_j(t) - M|^2 dt}\ \text{Time integral of square error}}{M^2}$$

Normalizing factor
(equilibrium amplitude of reference trace)

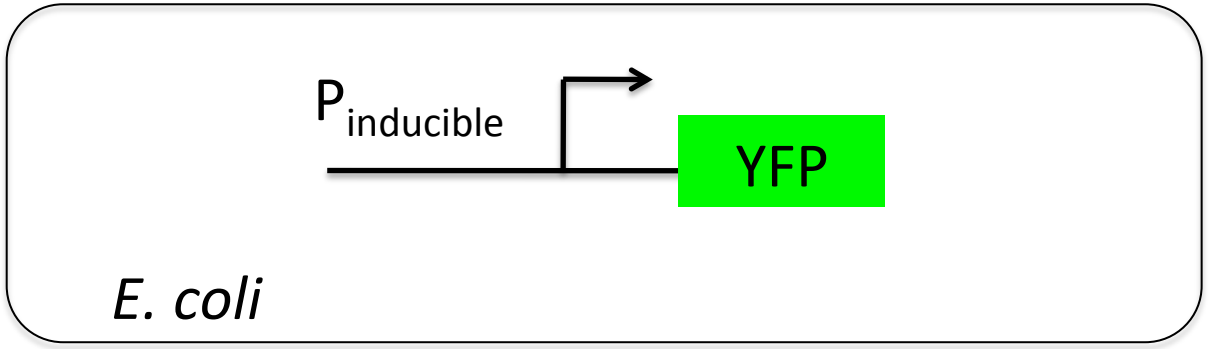


j = 1, 2, 3, … 15
(at least 5 traces for 3 temperatures)

r(t) is a trace chosen as reference,
M is equilibrium amplitude of *r(t),*
T_1 is time when *r(t)* is *10%* of *M*, and
T_2 is time after which *r(t)* stays within *10%* of *M*.

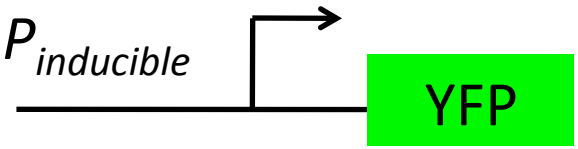


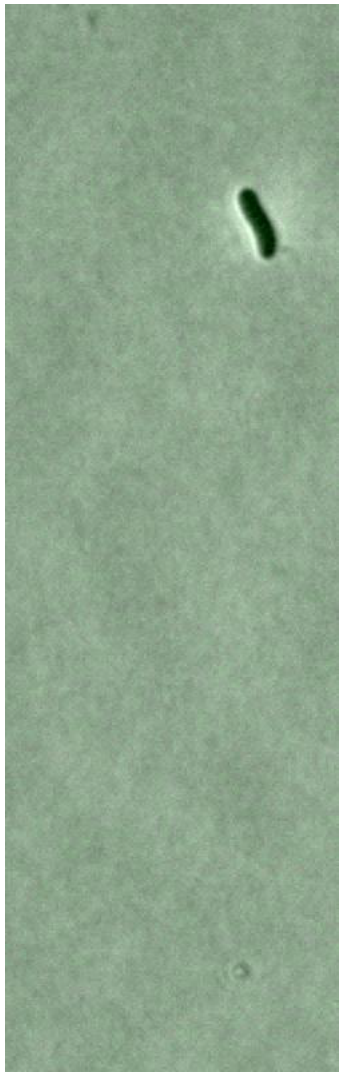
Single cell dynamics are measured for a simple reference design, for different temperatures

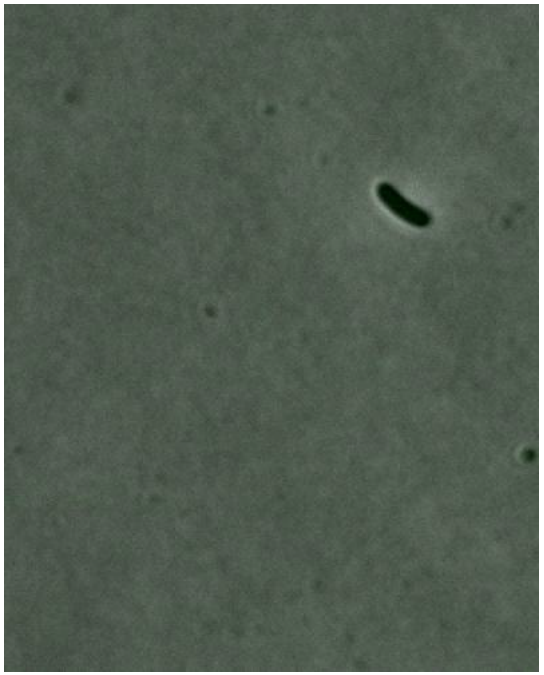


		30 °C	32 °C	34 °C
#1	#1 P_{lac} *yfp* IPTG	?	?	?
#2	#2 P_{lac} *cI-yfp* IPTG	?	?	?

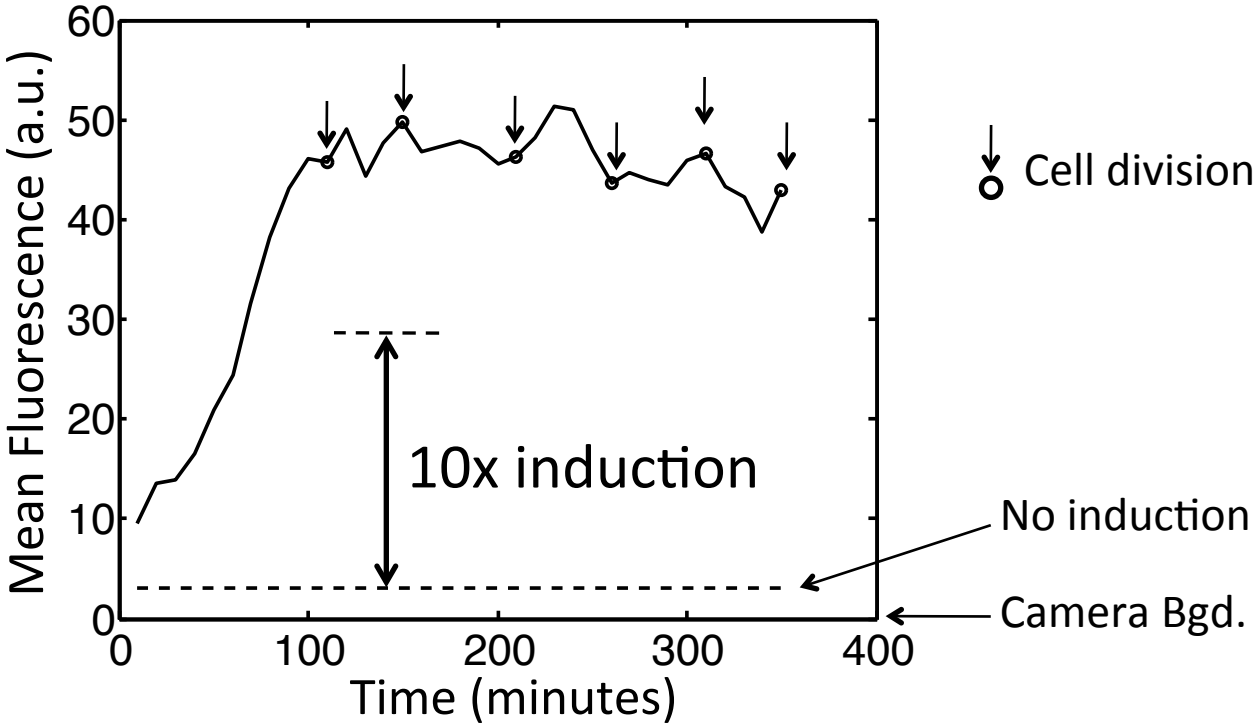
Movies





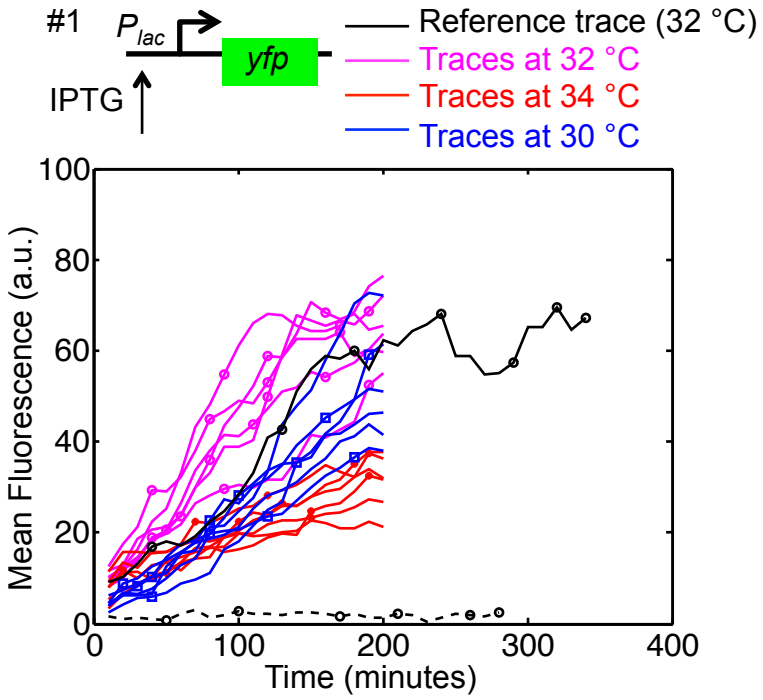


Reference trace exhibits > 10x induction

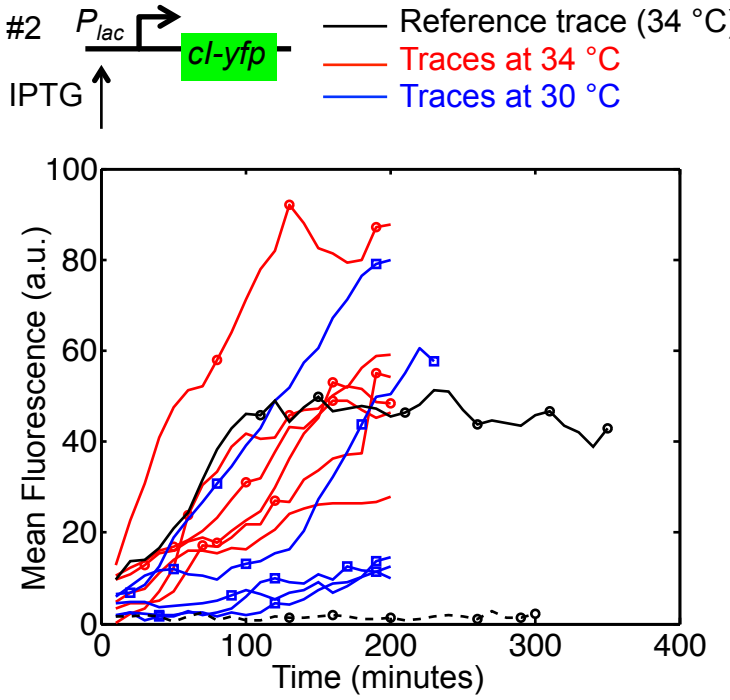


Performance scores for inducible protein expression circuits

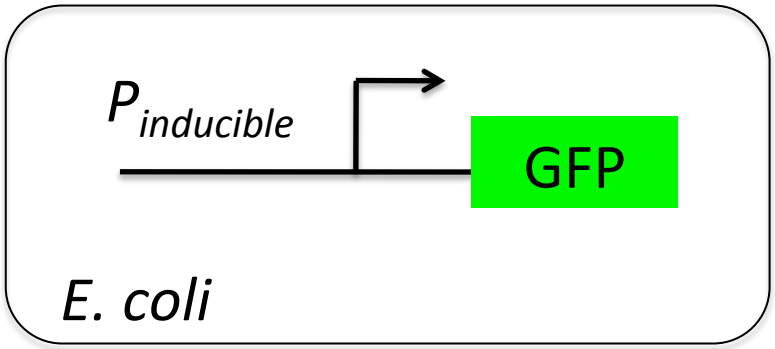
S = 1.45



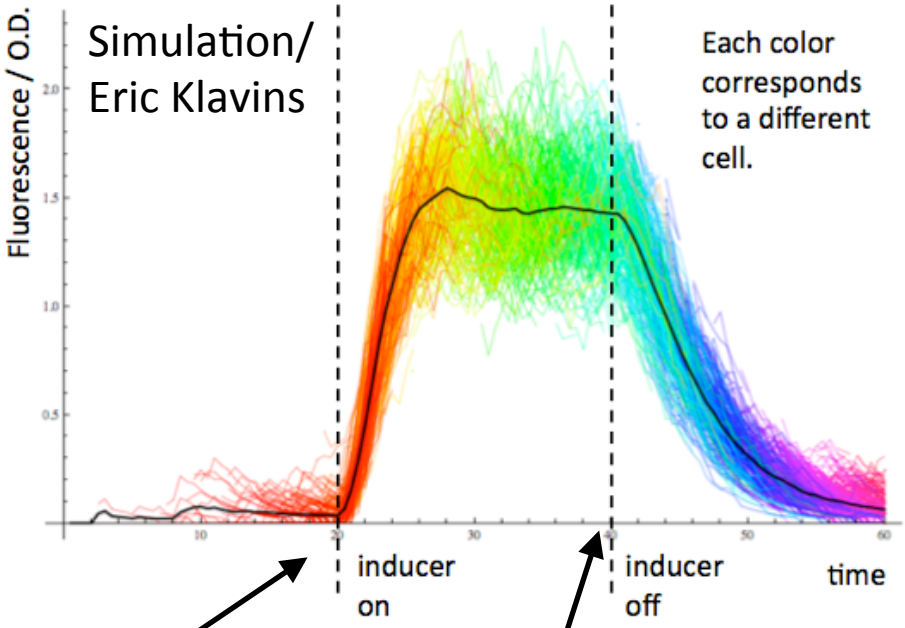
S = 1.22



Critical assessment will be on a μfluidic platform allowing for controlled induction time



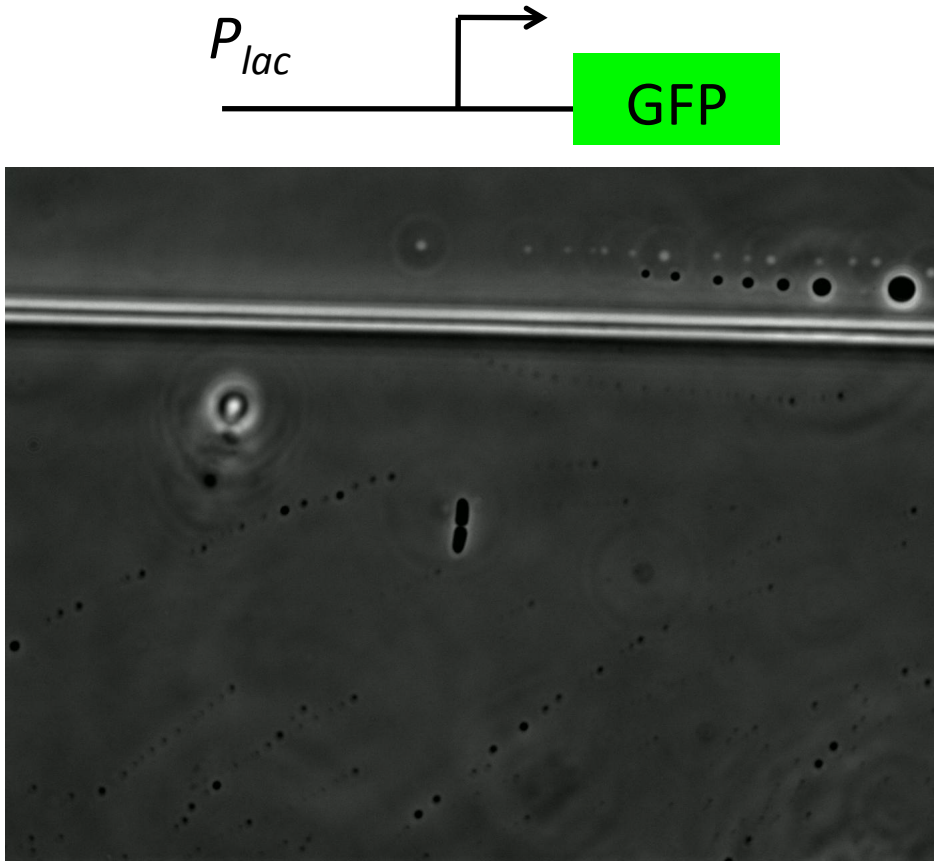
	30 °C	32 °C	34 °C
P_{lac} *gfp* IPTG	?	?	?



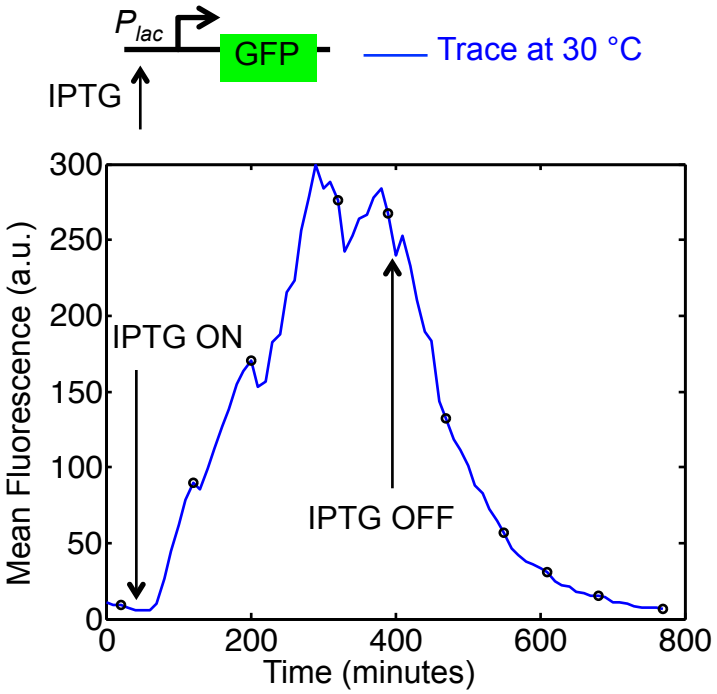
Benefit #1.
Exact induction time measurement.

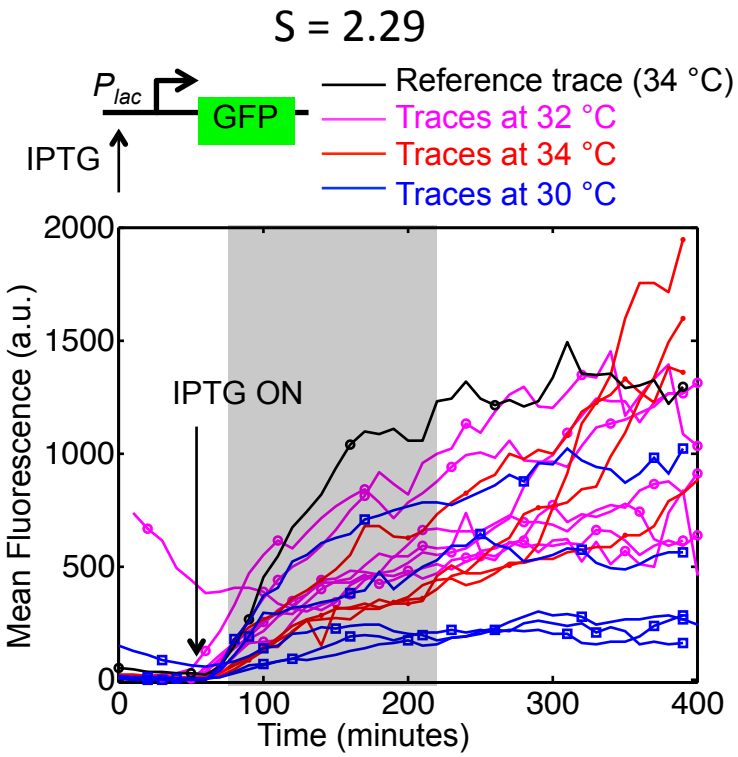
Benefit #2:
Similar decay time measurement.

Movie



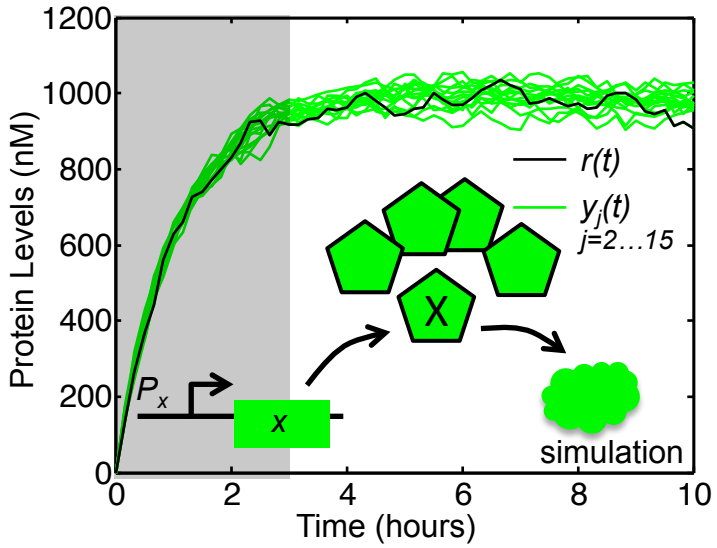
Single-Cell Dynamics with Controlled Induction Time



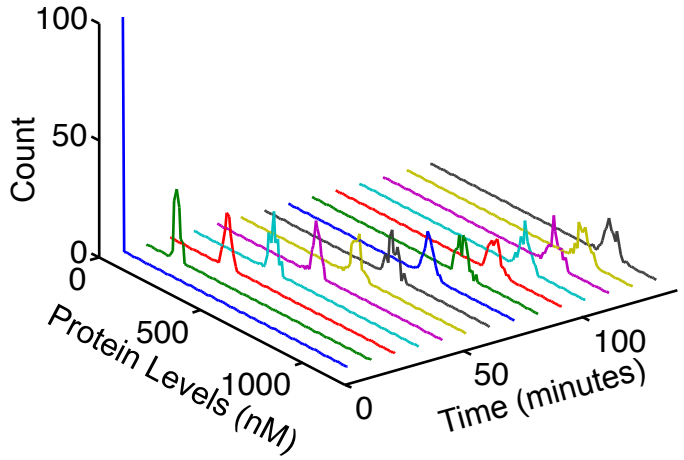


Population level metric to estimate performance score

Single-Cell Dynamics/ Microscopy



Population Dynamics/
Flow Cytometry



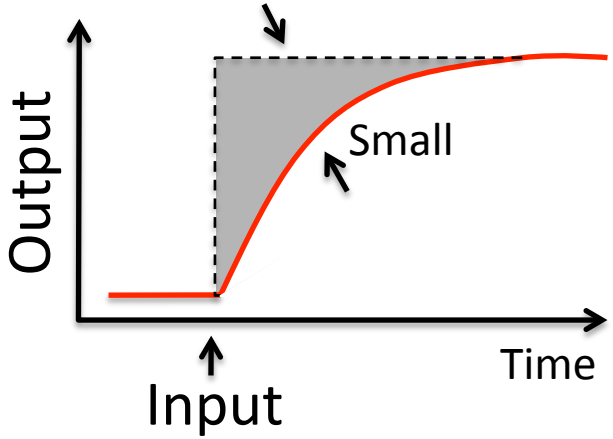
$$S = \frac{\max_j \int_{T_1}^{T_2} |y_j(t) - r(t)|^2 dt}{M^2}$$

$$S = \frac{\int_{T_1}^{T_2} |\mu(t) - M|^2 dt}{M^2}$$

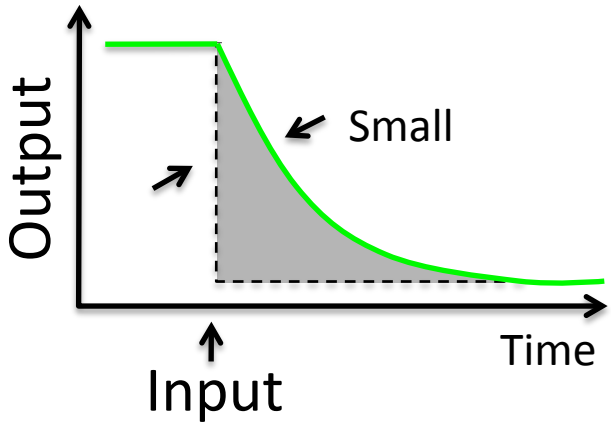
Future Work

Fast Linear Amplifier in 3 Steps

1. Fast Increase
(this CAGEN Challenge)



2. Fast Decay



3. Linear Response