TXTL Workshop 2013.

TXTL modeling toolbox
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Agenda

- Motivations

- 'the magic 10 lines of code'

- Gene expression demo

- Under the hood

  - Components

  - Extract specific

  - List of reactions, species (cmd, Simbio view)

- Hands on demo

  - Installation

  - Run examples (negauto,induction,IFFL)

Motivations

- Measurement of hidden states
  - Real time protein and mRNA measurement
  - What about the other species?
- Rapid testing of **many** variants
  - Simulation of ranges of initial concentrations and kinetic parameters
  - Exploring the quantitative behavior of the circuit in the parameter space
- Automated generation of ODE model (18-100 reactions)
  - Keep track of the concentration of all species

10 lines of code

- Create a tube containing TX-TL extract, 'E6'. The extract contains RNAP, ribosomes, sigma factors exonucleases and RNA-ase.

  tube1 = txtl_extract('E6');

  – content: RNAP, Ribo, RNAse (measured or literature)

- Create a tube containing TX-TL buffer, 'E6'. This contains amino acids and nucleotide pairs.

  tube2 = txtl_buffer('E6');

  - content: NTP, AA (part of the txtl protocol)

10 lines of code

- Create a new tube that will contain the DNA to be expressed, and name it 'circuit'.

  tube3 = txtl_newtube('circuit');

- Use txtl_add_dna to add custom deGFP DNA to tube3, under control of a constitutive p70 promoter:

  dna_deGFP = txtl_add_dna(tube3, 'p70(50)', 'rbs(20)', 'deGFP(1000)', 4.0, 'plasmid');

- The numbers in brackets are the lengths of the respective regions in number of base pairs (BP). These are used to calculate reaction rates for transcription, translation and degradation. The number 4.0 specifies that the initial concentration of the DNA (in nM) in the experiment once all the tubes have been combined. The last input argument species that the DNA is placed on a plasmid, and thus is not susceptible to exonuclease action.

10 lines of code

- Combine the tubes containing the extract, buffer and circuit into a final tube (referred to as Mobj) in a fixed ratio defined in the experimental protocol.

  Mobj = txtl_combine([tube1, tube2, tube3]);

- Define simulation time:

  simulationTime = 15*60*60;

- Simulate the model:

  [t_ode,x_ode] = txtl_runsim(Mobj,simulationTime);

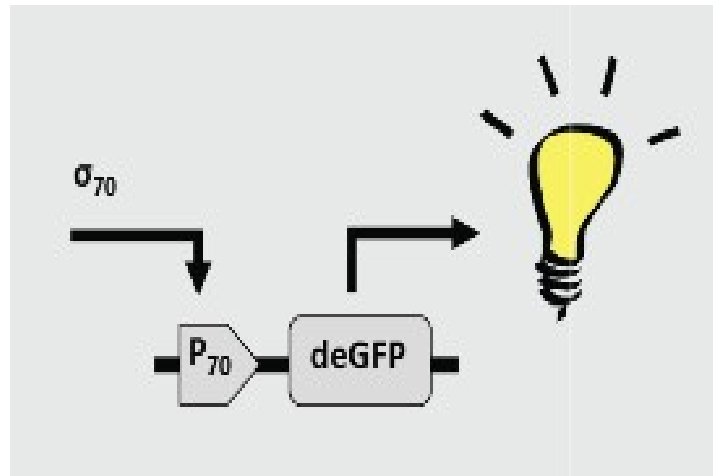- This simulates the model object using the associated configuration set, and returns the time evolution of the concentration of the species in the model.

- Produce a standard plot:

  txtl_plot(t_ode,x_ode,Mobj);

Gene expression demo

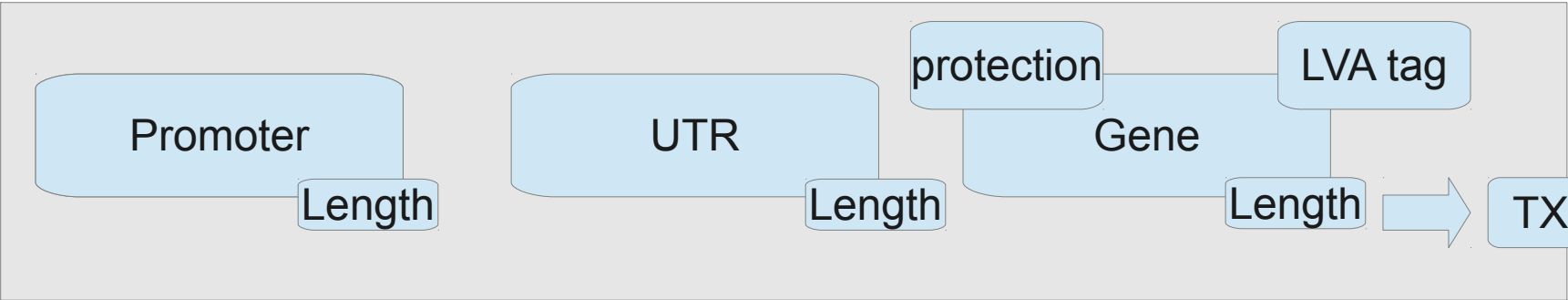- constitutive promoter
- deGFP (TXTL optimized, 5min maturation time)

- Access Simbiology object
  - Species
  - Reactions (geneexpr vs combinatorial promoter)
  - Open in Simbiology
    - Diagram view

Hands on demo

- Installation of the toolbox
  - Sourceforge.com → search: txtl
  - Unzip tar.gz
  - Open documentation from the doc folder (pdf)