Modeling - Overview

- HEARTBEAT
- HEARTBEAT GUI
- Modeling

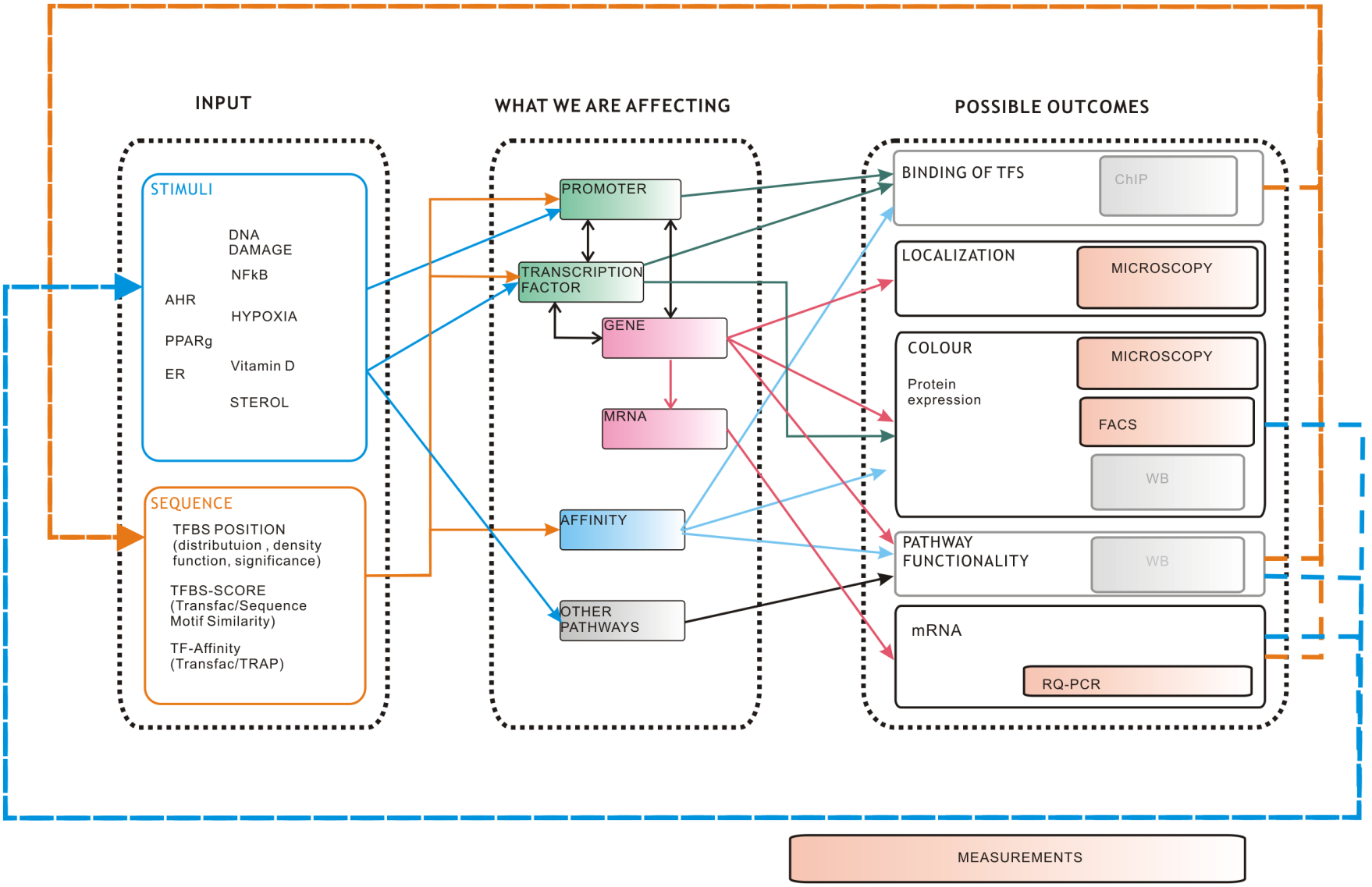
HEARTBEAT (Tim)

- statistics: characterization / scoring of our data
  - TRAP
  - 20bp-AUC + amplitude? peak width?
  - absolute density function?
- Documentation
  - until 17./18.October

HEARTBEAT – GUI (Tim)

- Screenshot: GUI

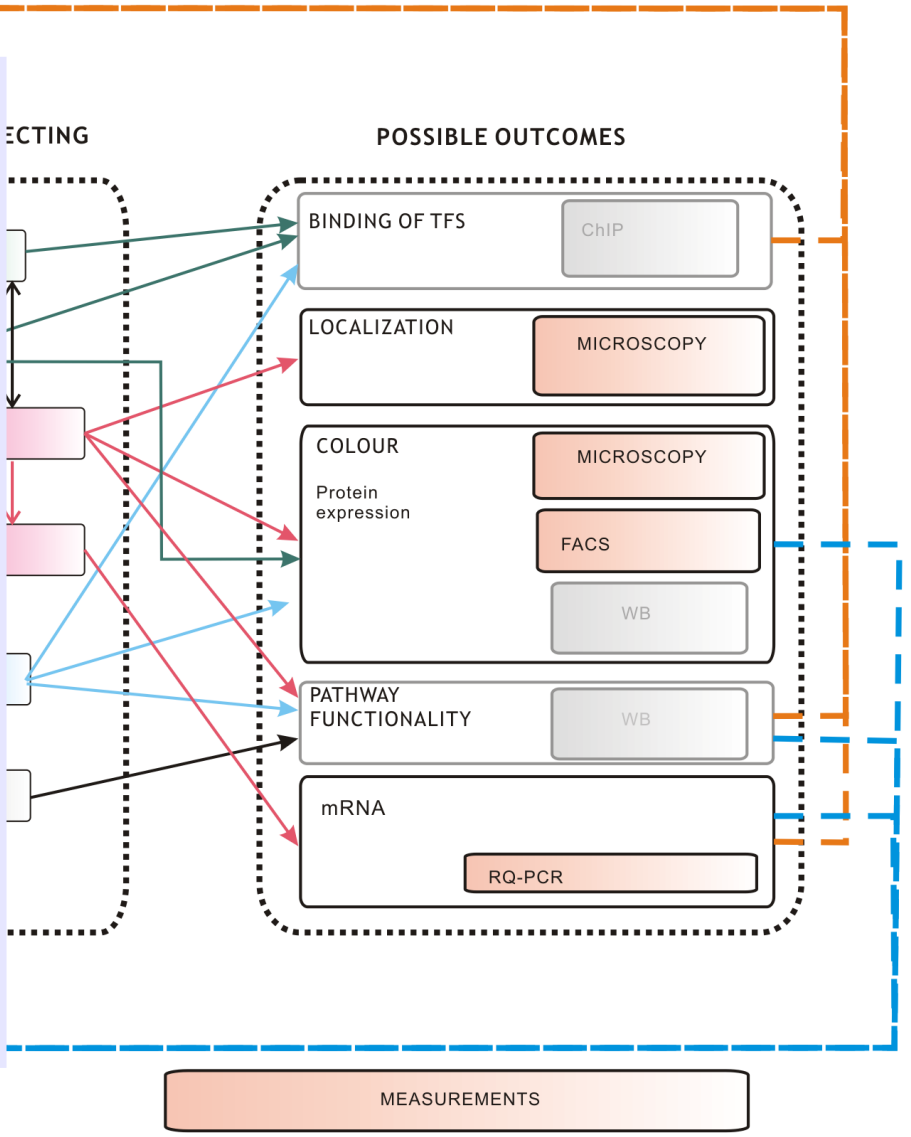
Modeling Our Network



Modeling Our Network

– during this part of the presentation –

- Please take a look at our basic network and collect ideas and available informations
  - experimental setup
  - available data/output
  - general ideas
  - hypothesis
- I will collect the handouts after the presentation & brainstorming :)

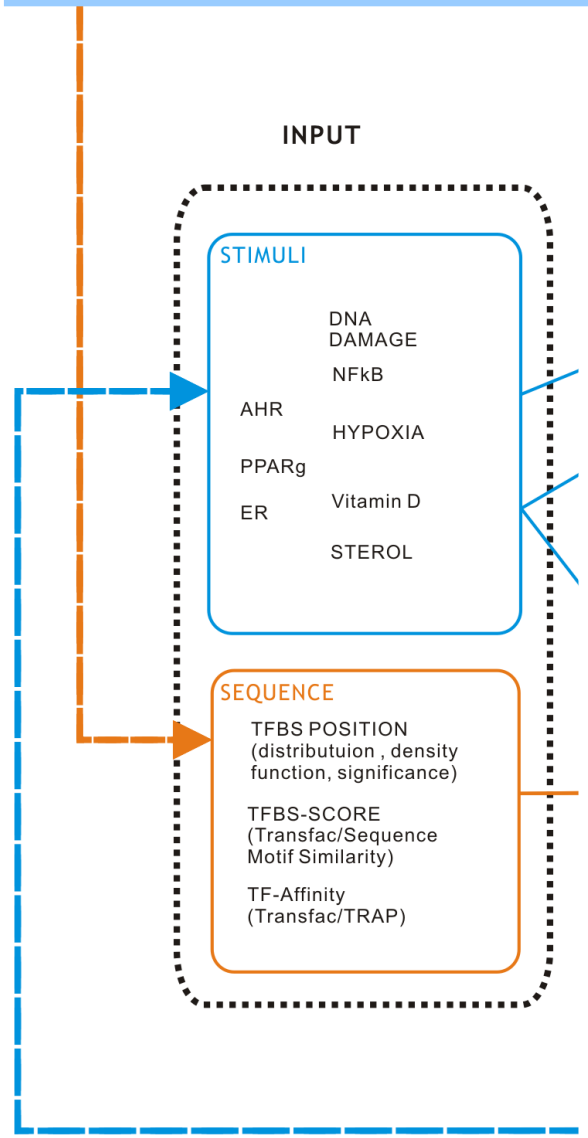


What modeling is good for...

so far we came up with the ideas...

- error checking / proof of concept
  - expectation vs experimental outcome
- *in silico* simulation
  - „assuming we have a promoter X with TFBS Y and Z... how would the outcome look like, depending on factor A, input B and stimulus C?”
- exclusive pathway activation
  - assume several synthetic promoters
  - combine single activation scenarios

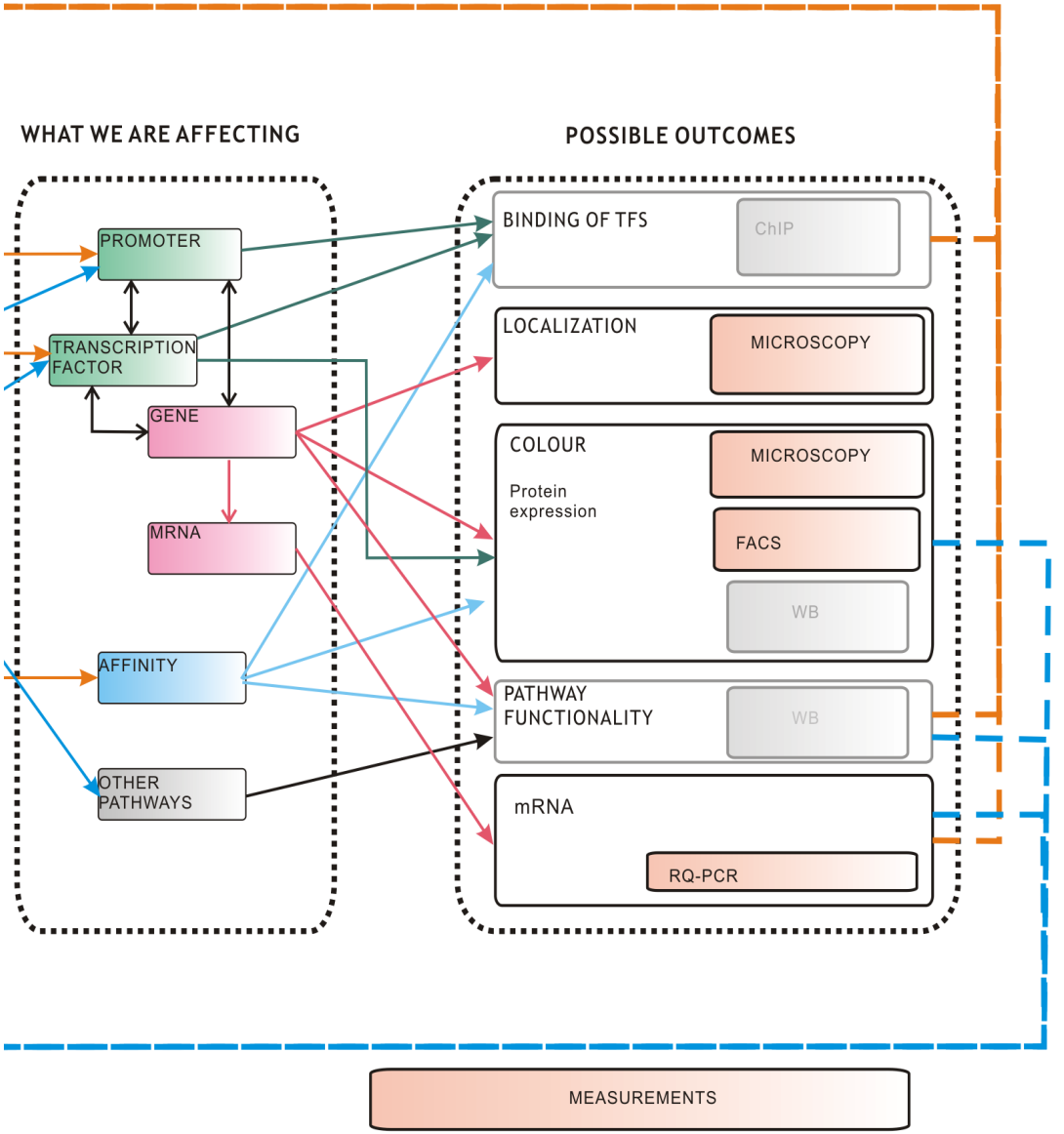
model: basic concept



- build up model from available “reference data” (CMV/JeT) and also literature
- possible INPUTS:
  - STIMULI
    - stimulant type (drug?) / concentration
    - experimental setup
    - cell type
  - SEQUENCE
    - TFBS position
    - TFBS sequence
    - TF affinity

model: basic concept

- "What we are affecting"
  - promoter
  - transcription
  - TF
  - mRNA level
  - other pathways
- OUTPUT
  - WHAT: colour, localization, promoter strength, mRNA concentration, dynamics (?)
  - HOW: microscopy, flow cytometry, RQ-PCR, (also POPS measurements(?))



modeling: first outcomes – and then?

- model training / model improvement
- expectation/simulation vs. experimental result
  - error checking:
    - what's wrong with our sequence?
    - will the right pathway be activated?
  - pathway induction
    - are there any cross-activation of pathways?
  - exclusiveness
    - are our promoters really exclusive?
- simulate several *in silico* / exp. relevant scenarios

Modeling: Tool

- Basic concept:

  build up network topology – simulation – visualization

- we will use MATLAB Fuzzy Logic Toolbox

  Basic Concepts

  - list up what is available (data, pathway information)
  - select data to use for building up the model
  - define fuzzy rules
  - select network subset (if whole network will be too complex)
  - we will/can introduce you to fuzzy logic in an additional meeting

Modeling – what we need from you

- Promoter
  - which core / proximal promoter
  - sequence
  - natural vs. random synthetic vs. synthetic
- Data
  - values: FACS // Microscopy // qRT-PCR // PoPS (?)
  - experimental setup: stimulant, pathway... "**SCENARIOS**"
  - **! REFERENCE measurements !**
- General
  - target pathways
  - literature

Modeling – what we need from you

- Promoter
  - which core / proximal promoter
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  - what experimental setup: stimulant, pathway
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- General
  - target pathways
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basically we need everything
and every small piece of
information will help us!
(but well documented, please ;-)

Computer Team – Time Schedule

- HEARTBEAT
- HEARTBEAT GUI

MODELING

- activate MATLAB licence
- build up model:

collect sequences

COLLECT DATA!

simulate,
simulate,
simulate...