Logical cooperativity of TFs with time delays

DW&TG

2015-3-4

Application of Loregic to worm embryonic expression

-- Expression profiles of **~20K** protein-coding genes across 25 time points (30 min each)

-- **520** (TF1, TF2, Target) triplets

-- For each triplet consider all combinations of
TF1_delay = 0 .. max_delay and TF2_delay = 0 .. max_delay,
such as (for max_delay = 3):

TF1_delay = 0, TF2_delay = 2

	X0	X0.5	X1	X1.5	X2	X2.5	X3	X3.5	X4	X4.5	X5	X5.5	X6	X6.5	X7	X7.5	X8	X8.5	X9	X9.5	X10	X10.5	X11	X11.5	X12
TF1	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0
TF2	0	0	0	0	0	0	0	0	0	0	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0
Target	0	0	0	0	0	0	0	0	0	0	1	1	0	0	1	1	1	1	1	1	1	1	1	1	0

TF1_delay = 3, TF2_delay = 2

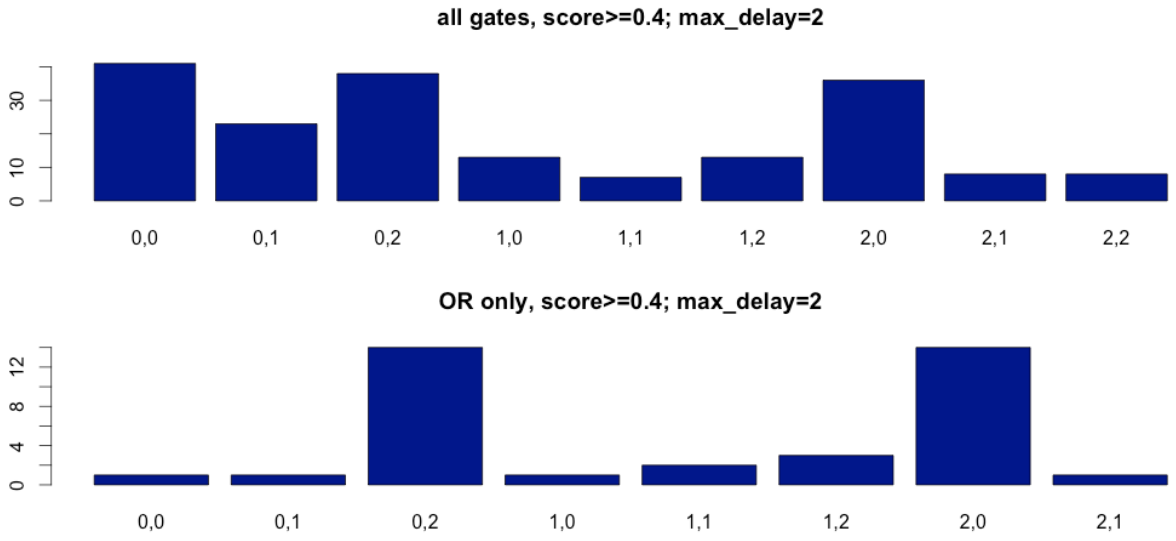
	X0	X0.5	X1	X1.5	X2	X2.5	X3	X3.5	X4	X4.5	X5	X5.5	X6	X6.5	X7	X7.5	X8	X8.5	X9	X9.5	X10	X10.5	X11	X11.5	X12
TF1	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0
TF2	0	0	0	0	0	0	0	0	0	0	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0
Target	0	0	0	0	0	0	0	0	0	0	1	1	0	0	1	1	1	1	1	1	1	1	1	1	0

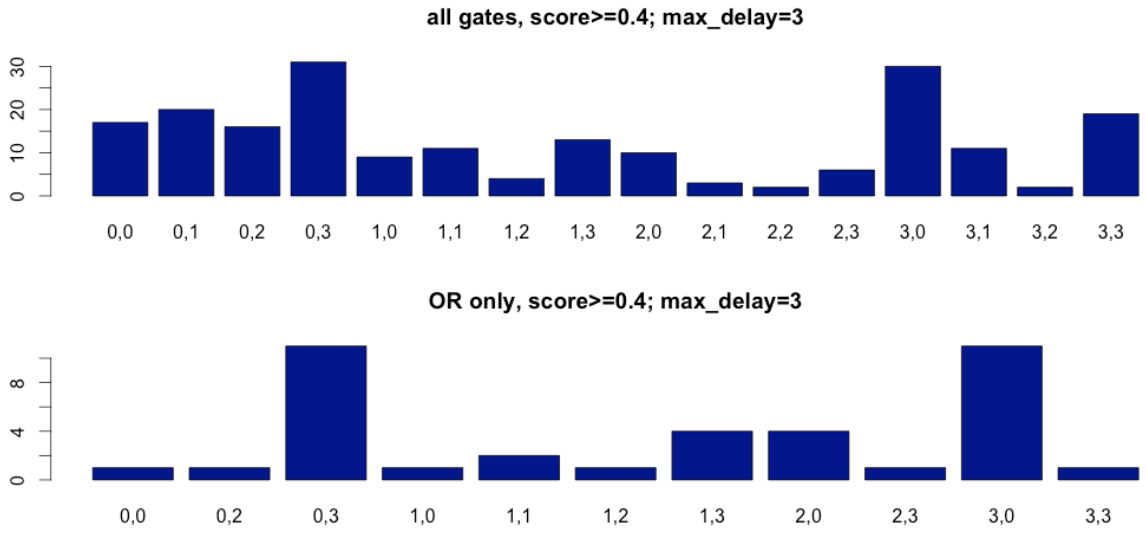
TF1_delay = 0, TF2_delay = 0

	X0	X0.5	X1	X1.5	X2	X2.5	X3	X3.5	X4	X4.5	X5	X5.5	X6	X6.5	X7	X7.5	X8	X8.5	X9	X9.5	X10	X10.5	X11	X11.5	X12
TF1	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0
TF2	0	0	0	0	0	0	0	0	0	0	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0
Target	0	0	0	0	0	0	0	0	0	0	1	1	0	0	1	1	1	1	1	1	1	1	1	1	0

25 – max_delay

-- Find maximum Loregic-scores for each triplet across all logic-gates and all (TF1_delay, TF2_delay) combinations





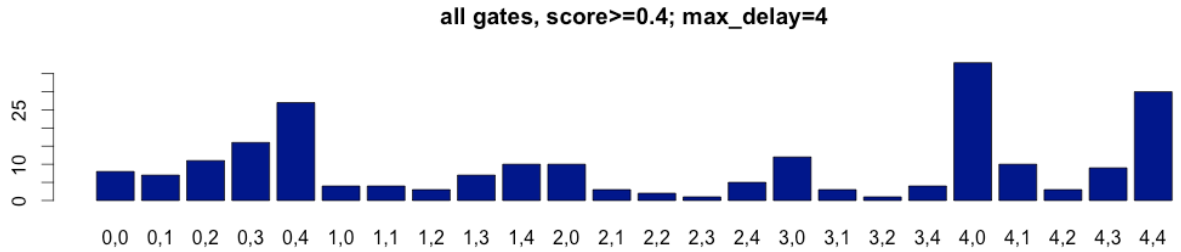
most of the high-scored triplets have either

(TF1_delay=0,TF2_delay=max_delay)

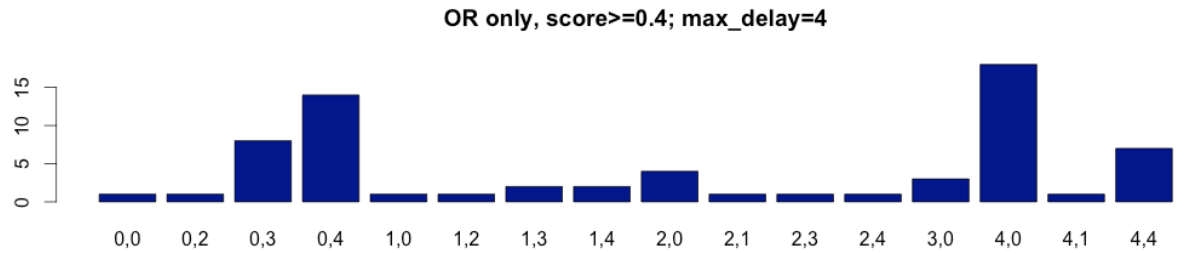
or

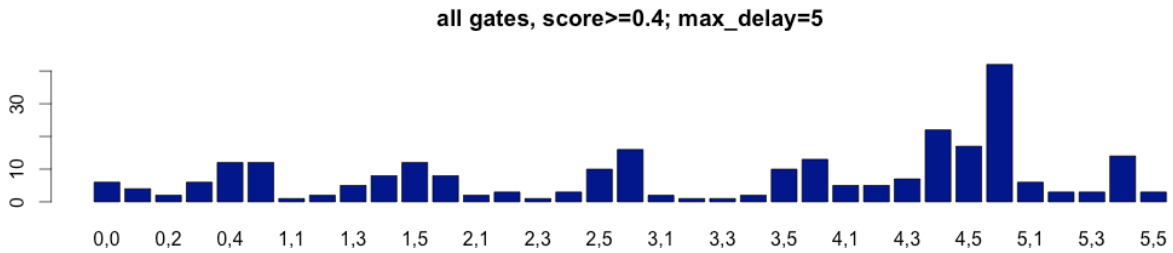
(TF1_delay=max_delay,TF2_delay=0)

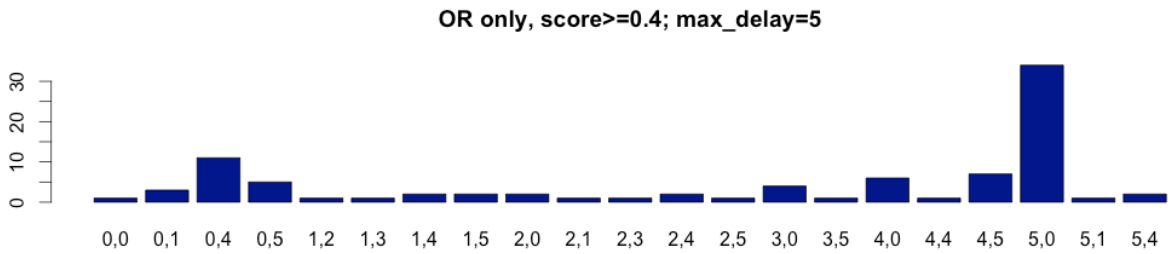
??



2h delay ??

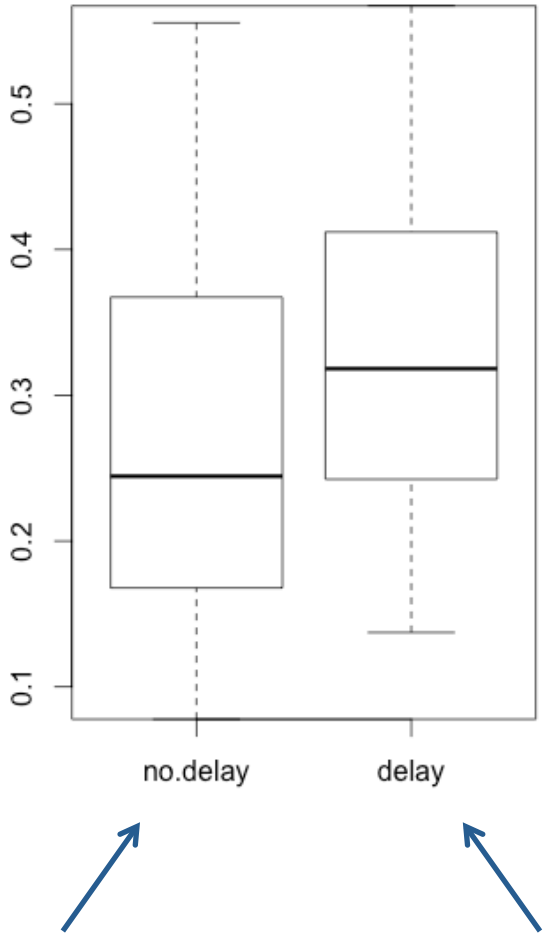






2.5 h delay ??

-- Delay *vs* no delay



What is the proper significance test for increase in scores with delays in TF activity?

Simulate many randomly shuffled (within rows) expression matrices and compare *P* values from t-test?

Highest (across all logic gates) scores for each triplet with (TF1_delay=0,TF2_delay=0)

Highest (across all logic gates *and* all TF1_delay>0,TF2_delay>0) scores for each triplet

Trying other methods

- Information theory

BMC Bioinformatics

METHODOLOGY ARTICLE Open Access

TimeDelay-ARACNE: Reverse engineering of gene networks from time-course data by an information theoretic approach

Pietro Zoppoli[1,2], Sandro Morganella[1,2] and Michele Ceccarelli*[1,2]

- Cross-correlation, LASSO

Inferring Time-Delayed Gene Regulatory Networks Using Cross-Correlation and Sparse Regression

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