Adaptive Network Reverse Engineering with L1-Magic

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Background

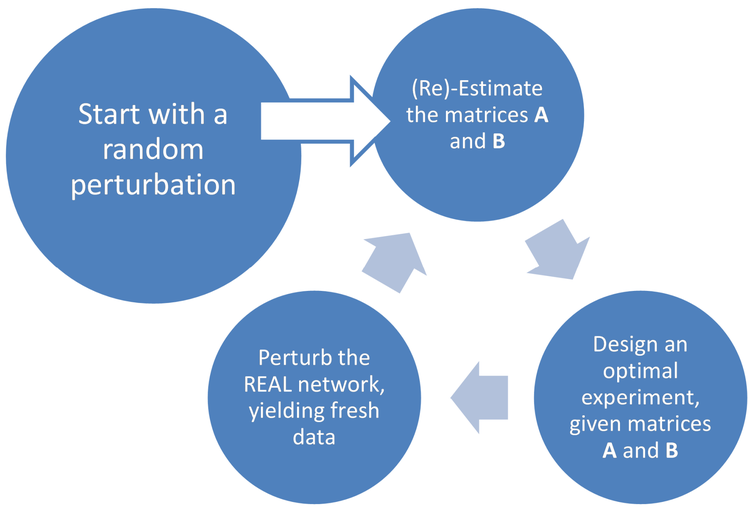
- Network Reverse Engineering addresses the question of finding the structure of a (unknown) network given input/output data (e.g. metabolic concentrations, transcription data, etc)
- We suggest
  - an innovative design of experiments based on *maximization of the information content* of the experimental data w.r.t. parameter estimation
  - Use of L_1 norm (Compressed Sensing Algorithm) for *sparse* network reconstruction

Method

1. Perform an arbitrary experiment and use the input-output data as a first guess for determination of the parameters in the Jacobi matrix[2]
2. Analyse the resulting linear system, where the primary goal is now to maximize information content w.r.t. the Jacobi matrix parameters, using input or state perturbations

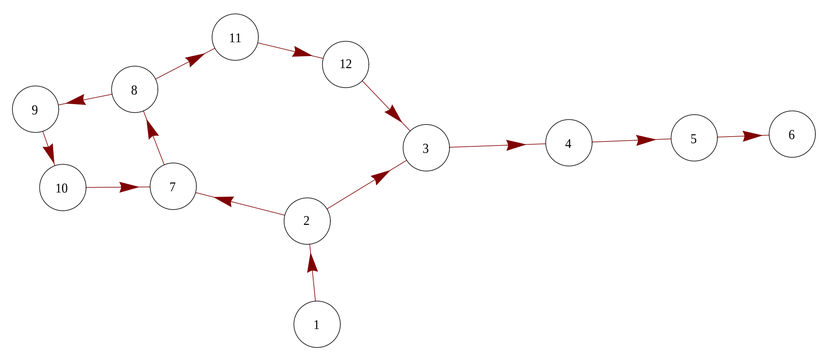
$$\frac{d(\delta x(t))}{dt} = A\delta x + B\delta u$$

3. The results of the second step yield an `optimal' perturbation that can now be used in an *improved* new experiment
4. If necessary, repeat step (2) with the new parameter estimates as to further improve the condition number of the Fisher Information Matrix

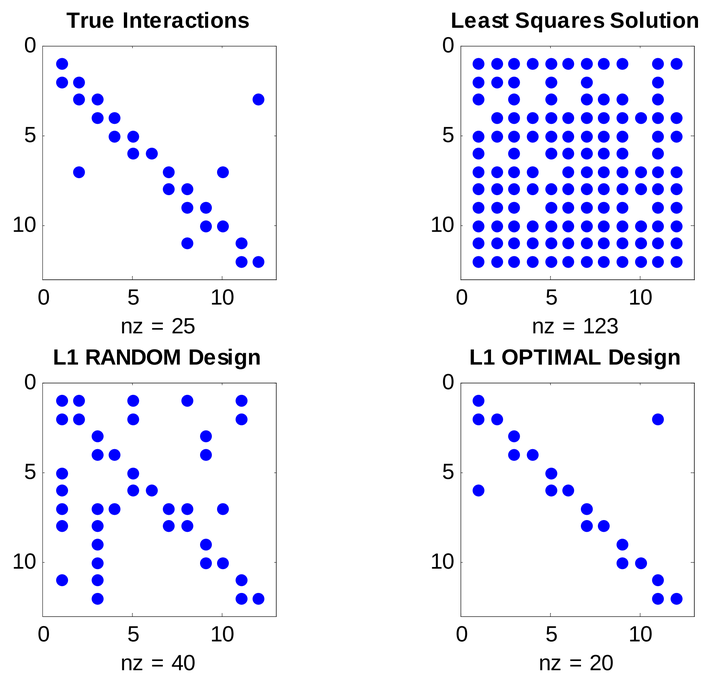


Test Case

DREAM6 Challenge – Model 1 (gene regulatory network)



Our method yields the interaction matrix (see figure below). The blue dots indicate a *direct* interaction between nodes.



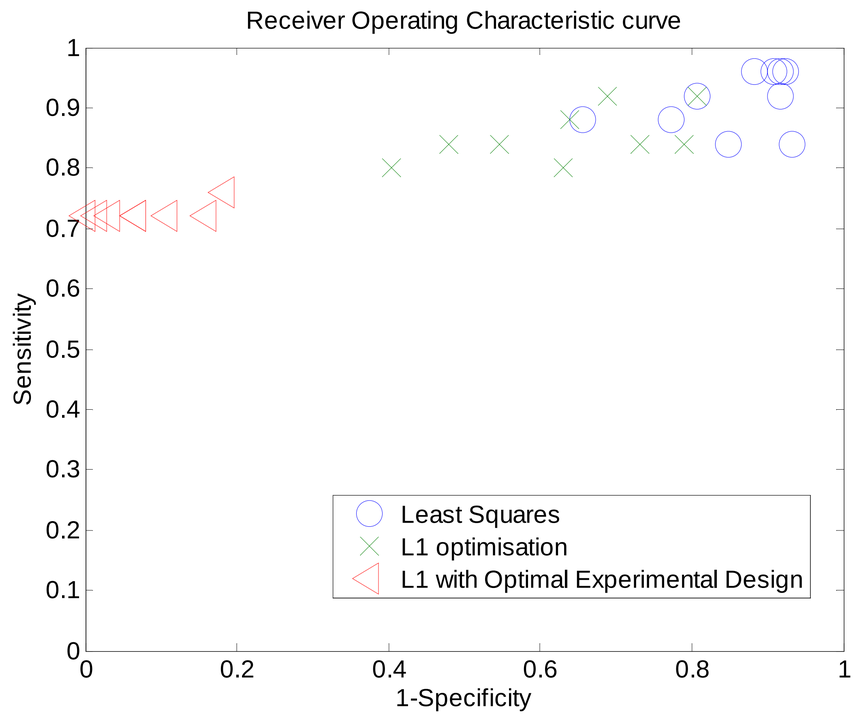
For different noise-levels in the (synthetic) data that were obtained after simulation of the DREAM6 model, we calculated *specificity, sensitivity,* and *accuracy* for our 3 network reconstruction methods: (i) Least-Squares, (ii) L1, and (iii) L1 with optimal experimental design. Below is the so-called ROC plot.

Conclusion: Optimal design with L1 norm on the parameter vector clearly has the best performance.

$$1 - Specificity = 1 - \frac{TN}{FP + TN}$$

$$Sensitivity = \frac{TP}{TP + FN}$$

TP = True Positive
FP = False Positive
TN = True Negative
FN = False Negative



References

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4. J.D. Stigter, D. Vries, and K.J. Keesman, *On adaptive optimal input design*, AIChE, Vol. 52, No. 9, p3290—3296, 2006.