Motivation
- Functions of proteins can be modulated by drugs
- Growing knowledge about chemical space of drugs and genomic space of proteins
- Limited knowledge about relationship between these two spaces
- A small number of experimentally validated interactions in existing databases
- Computational methods for identifying interactions between drugs and proteins

Traditional Methods
- Docking simulations ⇒ requires structural information of target protein
- Ligand-based approaches ⇒ requires a large number of known ligands for target protein
- Literature text mining ⇒ can not predict unknown interactions and suffers from nonstandard naming practices

Machine Learning Methods
- Machine learning methods operate on
  1. chemical properties of drug compounds
  2. genomic properties of target proteins
  3. known interaction network

Materials
- Four drug–target interaction networks

Exploratory Data Analysis
- By displaying low-dimensional projections on NR dataset

Out-of-Sample Prediction
- Average AUC (area under ROC curve) values over 25 replications
  Dataset Yamanishi et al. (2010) KBMF2K
  \[
  \begin{array}{ccc}
  \text{Dataset} & \text{Yamanishi et al. (2010)} & \text{KBMF2K} \\
  E & 0.821 & 0.832 \\
  IC & 0.692 & 0.799 \\
  GPCR & 0.811 & 0.857 \\
  RR & 0.814 & 0.824 \\
  \end{array}
  \]
- Average AUC values with changing subspace dimensionality

Completing Given Interaction Network
- E dataset has 2,926 interacting and 292,554 noninteracting (i.e., not known to interact) drug–target pairs

Table: Drug–Target Interactions

<table>
<thead>
<tr>
<th>Rank</th>
<th>Pair</th>
<th>Annotation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>D00437</td>
<td>Nifedipine (JP16/USP/INN)</td>
</tr>
<tr>
<td>2</td>
<td>D00542</td>
<td>Halothane (JP16/USP/INN)</td>
</tr>
<tr>
<td>3</td>
<td>D00997</td>
<td>Salicylic acid (JP16/USP)</td>
</tr>
<tr>
<td>4</td>
<td>D6561</td>
<td>Pentoxifylline (INN/JP16/USP)</td>
</tr>
<tr>
<td>5</td>
<td>D00139</td>
<td>Methoxsalen (JP16/USP)</td>
</tr>
</tbody>
</table>

Conclusions
- First fully probabilistic method for drug–target interaction inference
- Empirical evidence on four drug-target interaction networks
- Matlab code is at http://users.ics.aalto.fi/gonen/kbmf2k