Drug target identification by maximizing information flow

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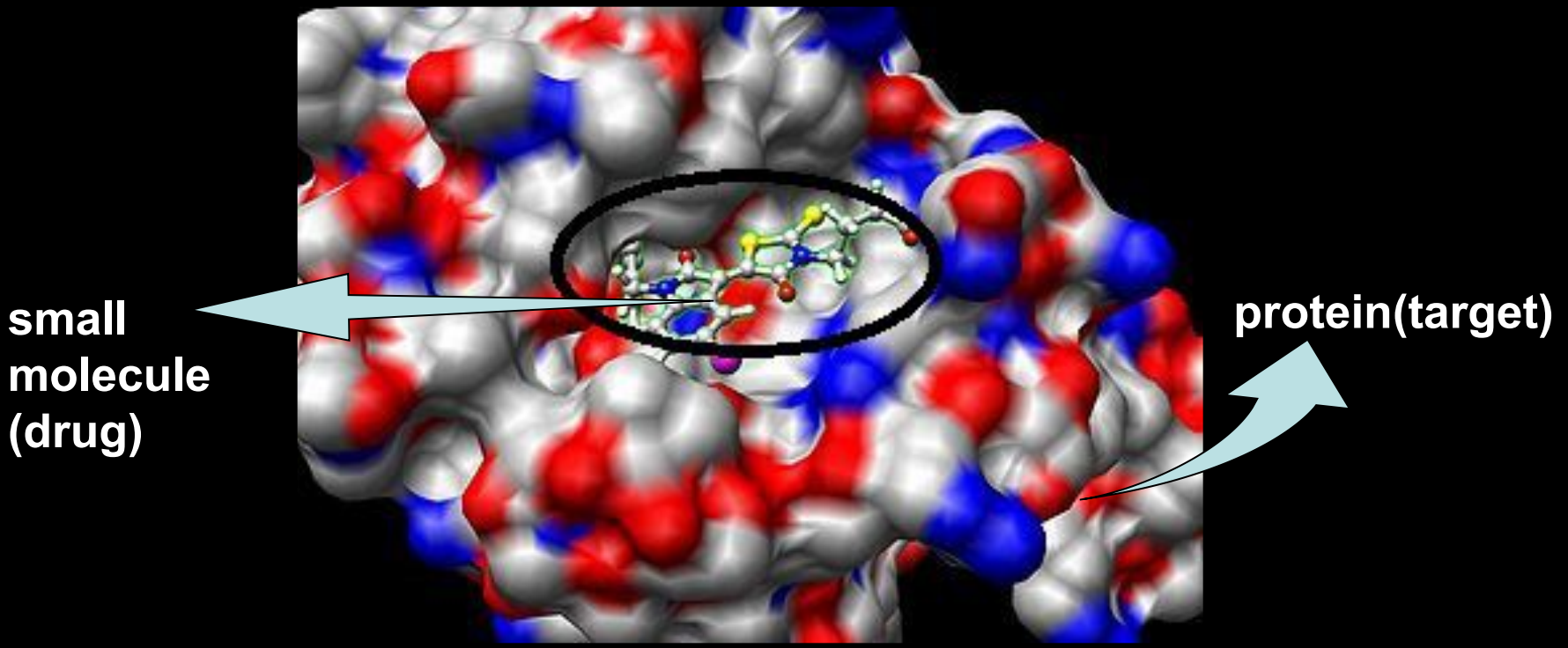
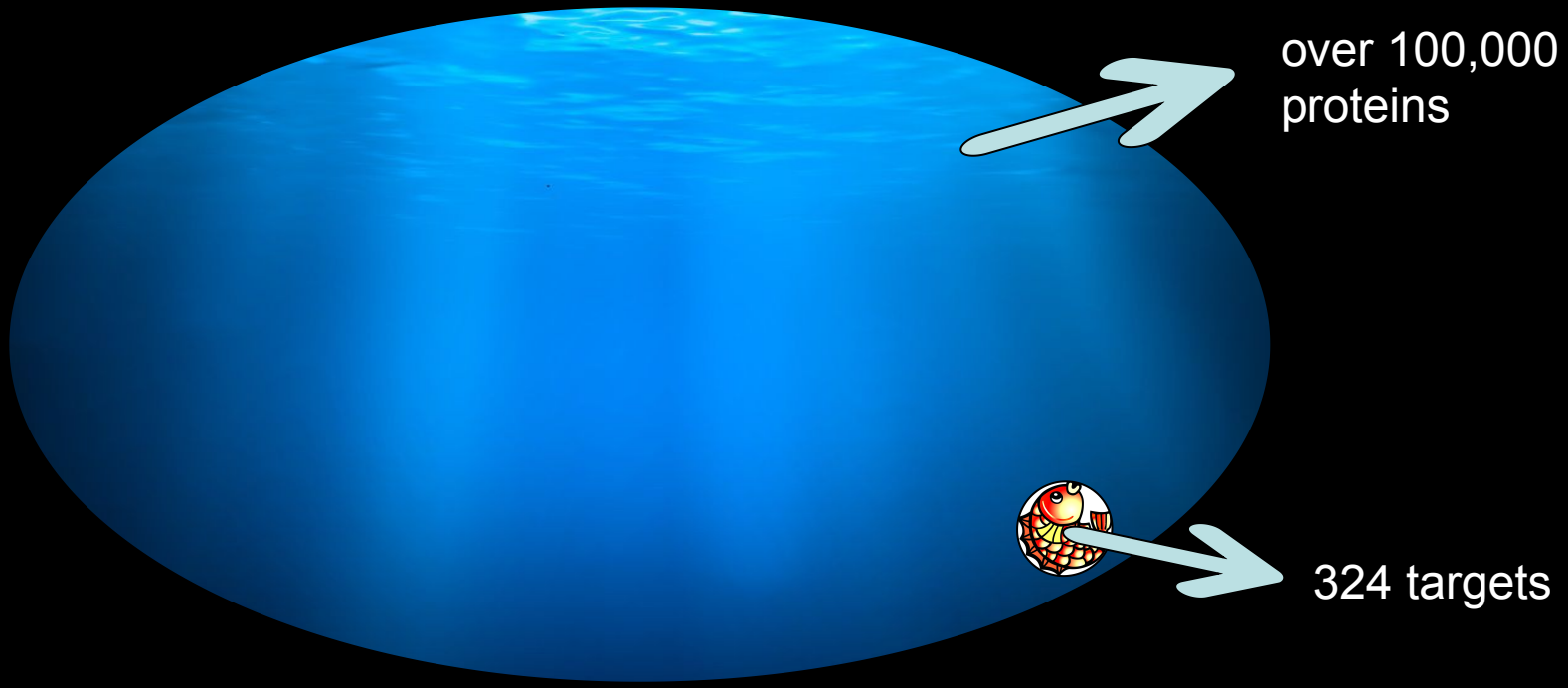
Drug target

Native **protein** in the body whose activity is modified by a drug resulting in a specific effect



Current situation

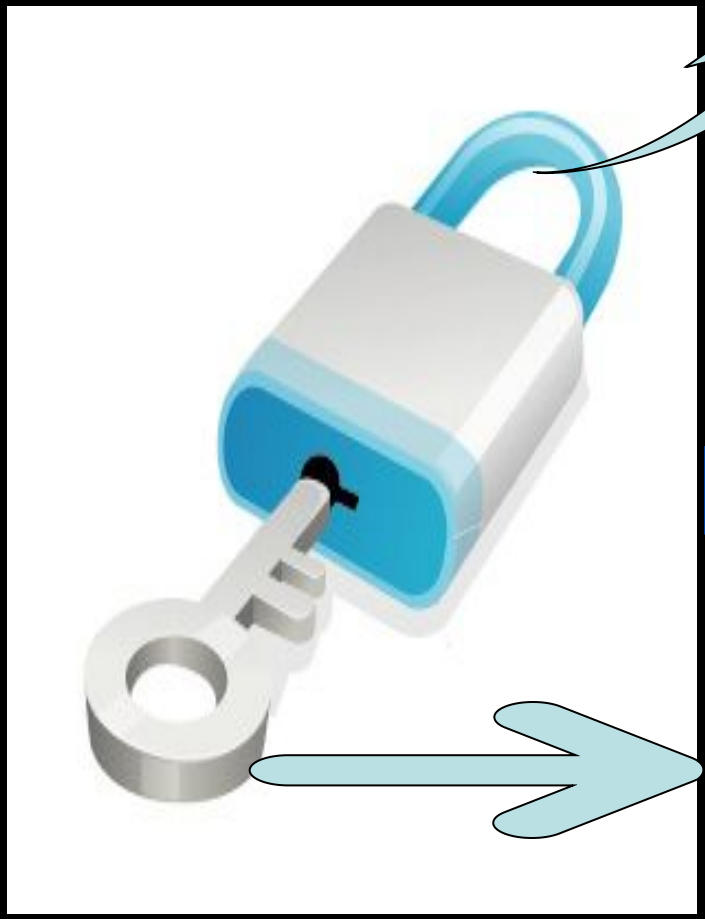
Up to now, only 324 targets have been known for clinical drugs.

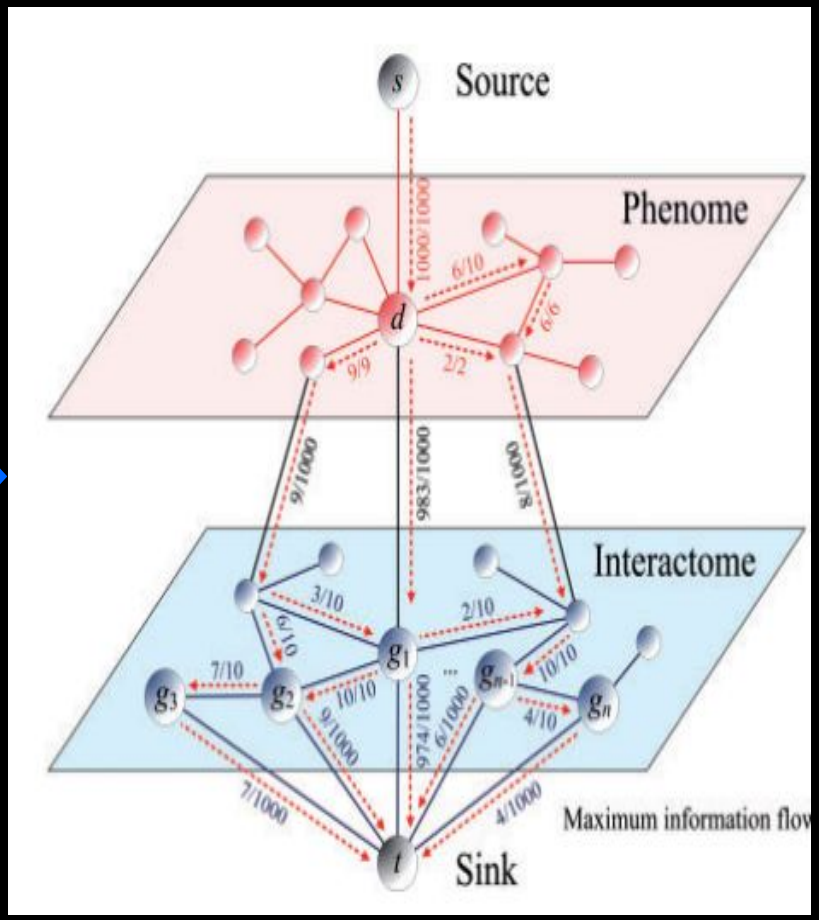


Application

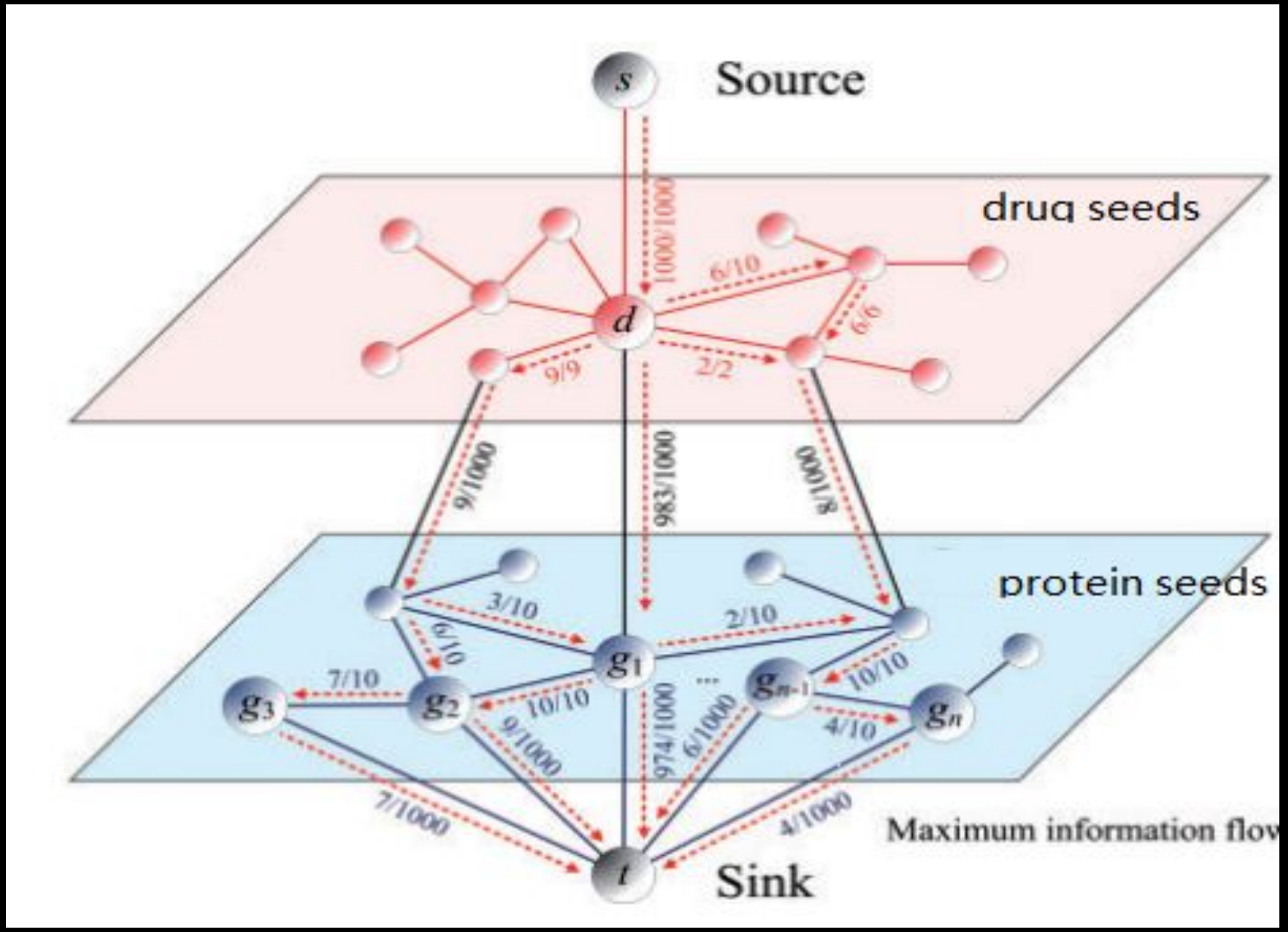
- Identify new drug targets efficiently
- New applications of existing drugs/create new drugs
- Understand side effects and toxicity
- Reduction of time and experiments costs in drug development

Network





Yong Chen et al.(2011)
Uncover disease genes by maximizing information flow in the phenome–interactome network ISMB,2011,i167–i176



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Collect Data

- Drug-drug similarity
- Protein-protein interaction
- Drug-protein interaction

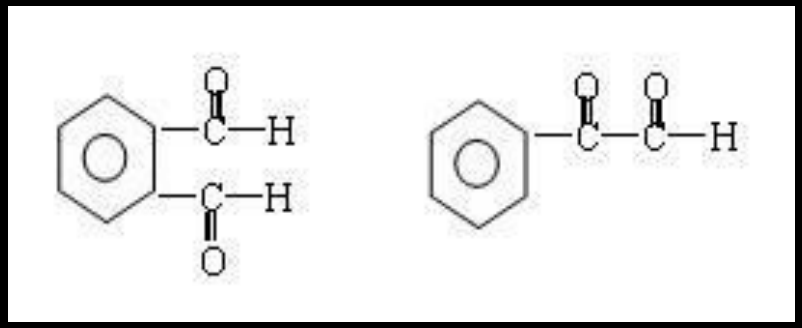
Data resources

Type of interaction	Drug-drug similarity	Drug-target interaction	Protein-protein interaction
Data source	www.drugbank.ca	www.string-db.org	www.drugbank.ca
Website version	Version 4.3	Version 10	Version 4.3

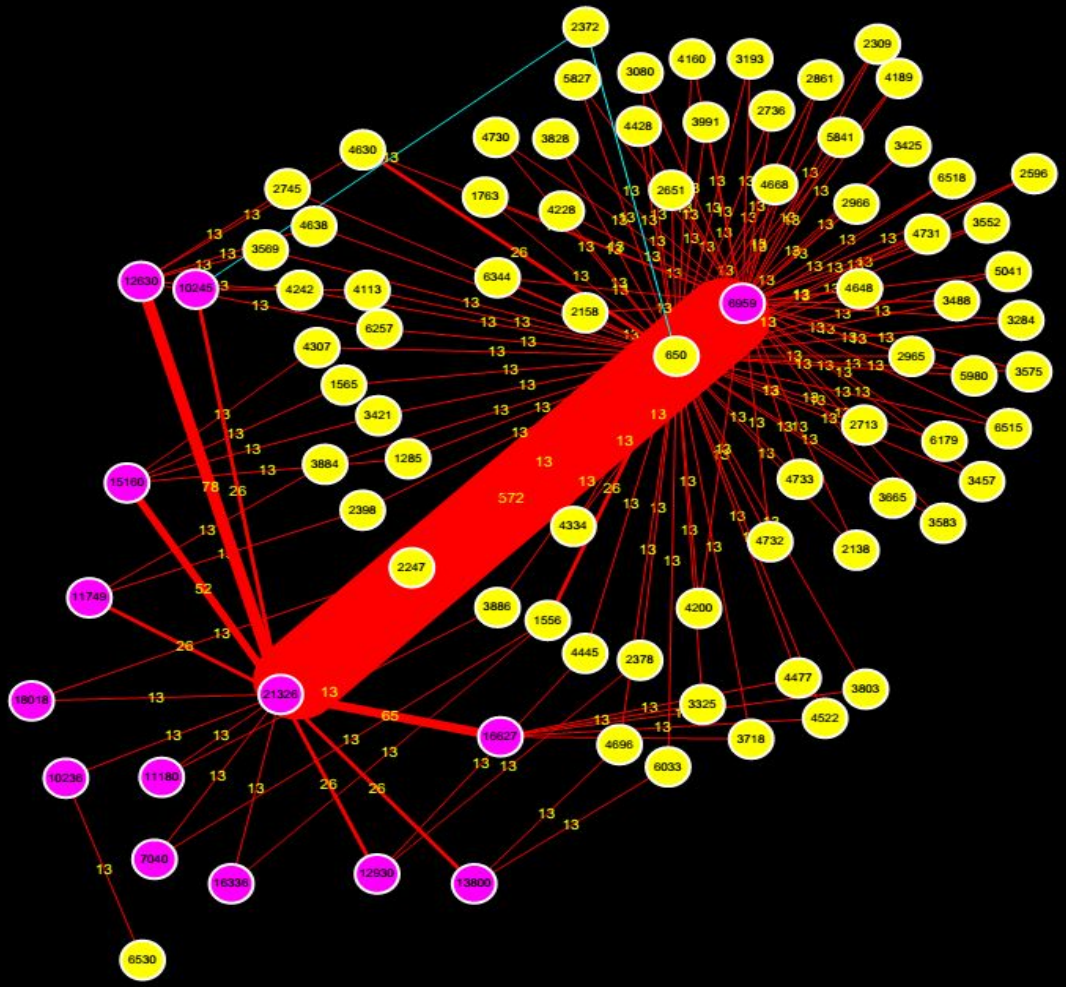
Drug-drug similarity

Assumption: drugs with more similar chemical structure have stronger associations

```
DB00150 N[C@@H](Cc1=CNC2=CC=CC=C12)C(O)=O
DB00151 N[C@@H](CS)C(O)=O
DB00152 CC1=C(CCO)SC=[N+]1CC1=CN=C(C)N=C1N
DB00153 CC(C)[C@@H](C)\C=C\[C@@H](C)[C@@]1([H])CC[C@@]2([H])\C(CCC[C@]12C)=C\C=C1\C
DB00154 CCCCC\C=C/C\C=C/C\C=C/CCCCCCC(O)=O
DB00155 N[C@@H](CCCNC(N)=O)C(O)=O
DB00156 C[C@@H](O)[C@H](N)C(O)=O
DB00158 NC1=NC(=O)C2=NC(CNC3=CC=C(C=C3)C(=O)N[C@@H](CCC(O)=O)C(O)=O)=CN=C2N1
DB00159 CC\C=C/C\C=C/C\C=C/C\C=C/C\C=C/CCCC(O)=O
DB00160 C[C@H](N)C(O)=O
DB00161 CC(C)[C@H](N)C(O)=O
DB00162 C\C(=C/CO)\C=C\C=C(/C)\C=C\C1=C(C)CCCC1(C)C
DB00163 CC(C)CCC[C@@H](C)CCC[C@@H](C)CCC[C@]1(C)CCC2=C(O1)C(C)=C(C)C(O)=C2C
DB00165 CC1=C(O)C(CO)=C(CO)C=N1
DB00166 OC(=O)CCCCC1CCSS1
```

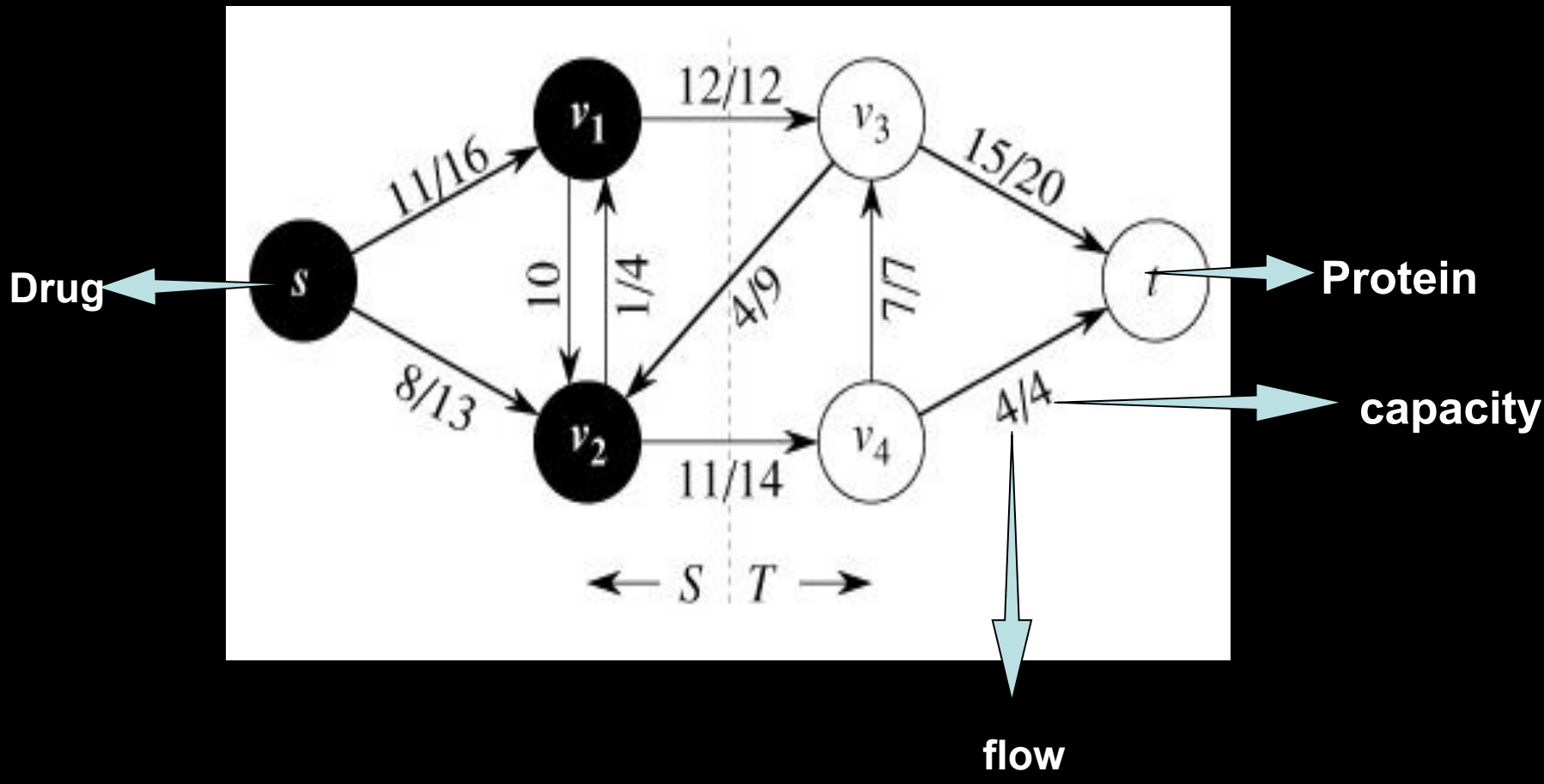


- 6810 drugs
- 14651 proteins
- 23177836 pairs of drug-drug similarities
- 650466 pairs of protein-protein interaction
- 5305 pairs of known drug-target links

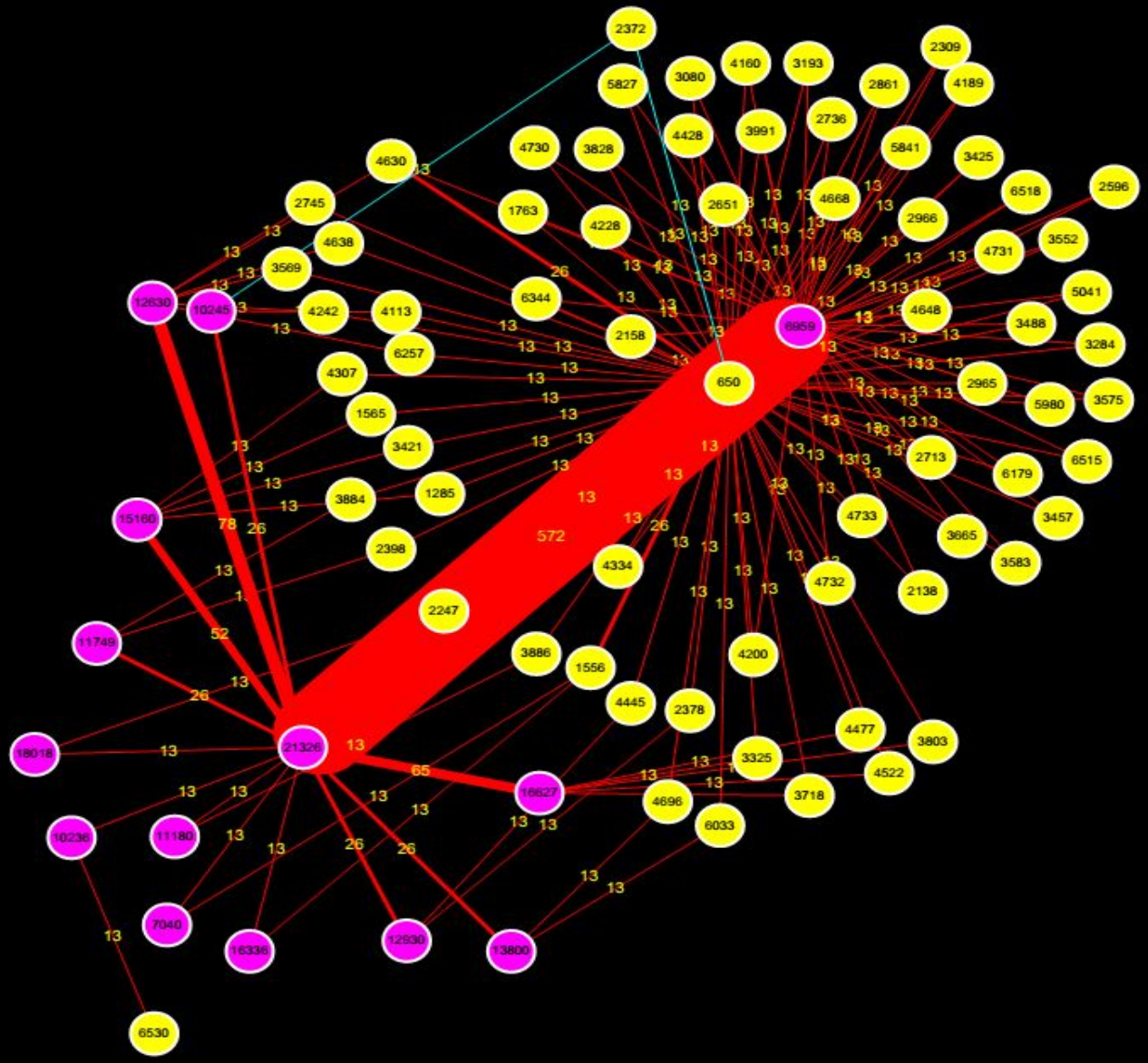


MAXIF

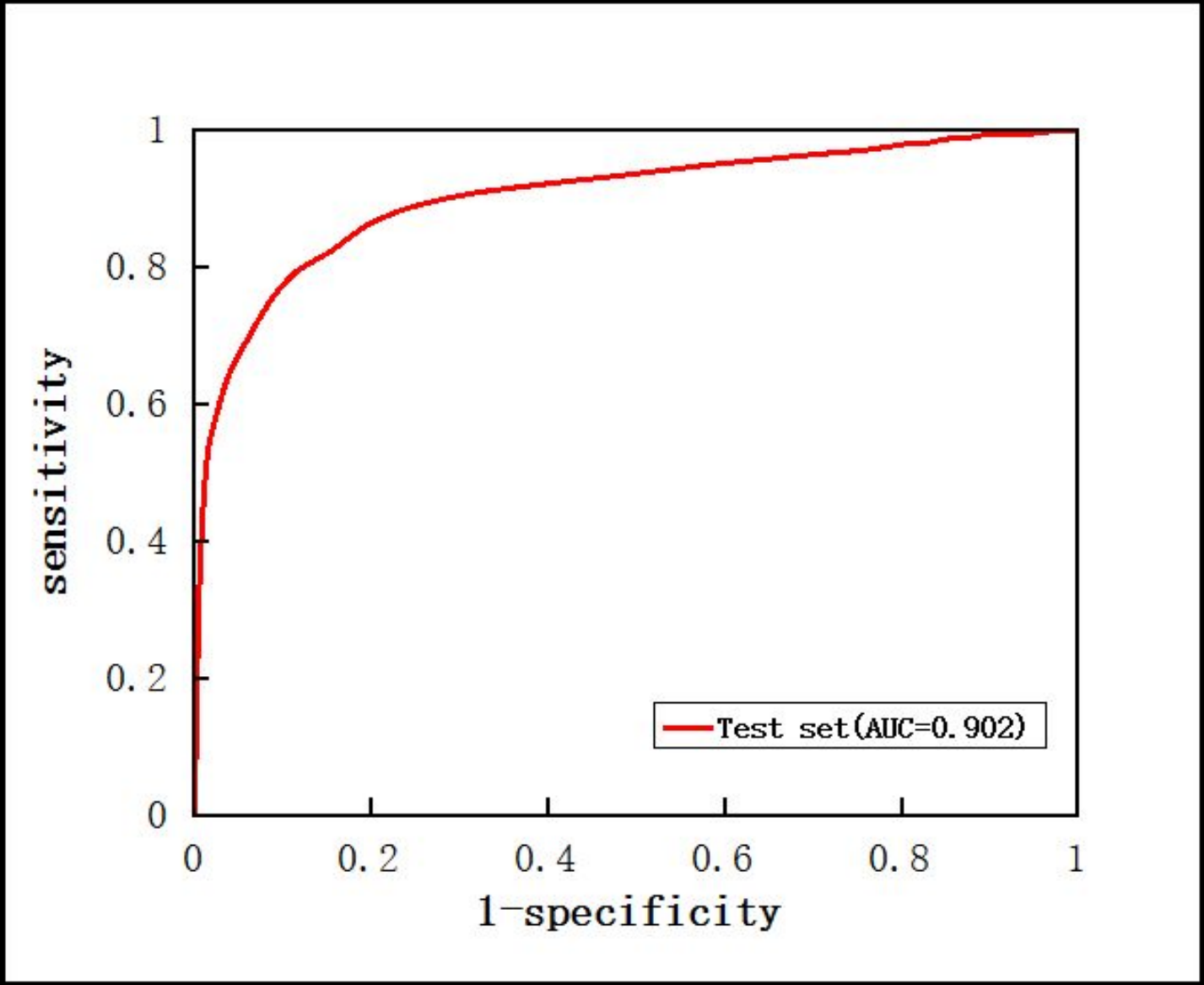
Maximizing information flow



Leave-one-out cross validation



Leave-one-out validation result



Conclusion

MAXIF has high level of sensitivity and specificity.Thus, the method could be applied to

- Predict drug targets efficiently
- Develope new applications of drugs
- Understand side effects
- Reduce time and cost of experiments

Discussion

- Other functional interaction between drugs
- Different levels of association between proteins
- Try different coefficients for different types of interaction

Acknowledgement

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- Ms.Ana and Mr.Chris
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- CEE
- Tsinghua university

Thank you for your attention