




# Collaborative filtering for drug discovery

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# Credits

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- Pierre-Jean L'Heureux
- Yoshua Bengio
- Olivier Delalleau
- Shi-Yi Yue & AstraZeneca

# Motivation

- amazon.com
  - Customer ratings, tags
  - Customers also bought<sup>TM</sup>
  - What do customers ultimately buy?
  - Items to go with / items instead of
- last.fm, radiolibre.ca
  - Ratings
  - Recommended artists, songs
- \$\$\$

# Motivation II

- Preferences of a user == 1 task
- Preferences of many users == many tasks
- Previous work:
  - Multi-task NNets (Caruana)
  - Bayesian approaches (Baxter)
  - Theory (Baxter)
  - “Modern” (==kernel) ways (Evgeniou)
- *Learn a new task by using intelligently information from other tasks*

# Drug Discovery



- Complicated, expensive process
- High-Throughput Screening (\$\$\$)
- Interested in QSAR (Quantitative structure-activity relationship)
- Bunch of molecules (“items”), a target (“user”)
- Virtual Screening (saves \$\$\$)



# Drug Discovery II

- Assume:
  - lots of molecules
  - a family of “related” targets
  - a new target
- Dense “user-item” ratings table
- Few rows
- *Predict new (very long!) row*

# Formally speaking

- Data:
  - $N$  molecules  $x_i, i = 1 \dots N$
  - $M$  targets  $t_j, j = 1 \dots M$
  - Set of ratings/activity values  $R_{ij}$
- Accuracy function: Lift
- Wanted: *a model that generalizes well to data for a new target wrt to the accuracy function*

# The Lift

- $a$  = number of actives in general
- $N$  = number of molecules
- $a_s$  = number of actives at a given thr.
- $N_s$  = number of molecules at a given thr.
- $\text{Lift} = 100 \cdot \frac{a_s/N_s}{a/N}$

# Testing hypotheses

- Given a multi-target dataset
- For each target:
  - TrainValidSet = OtherTData [ + DataFromThisT ]
  - TestSet = TheRestOfDataFromThisT
- Two cases:
  1.  $t\text{fraction} = 0$ , is Lift > 100?
  2.  $t\text{fraction} > 0$ , is Lift > single-target Lift?

# Neural Network Approach

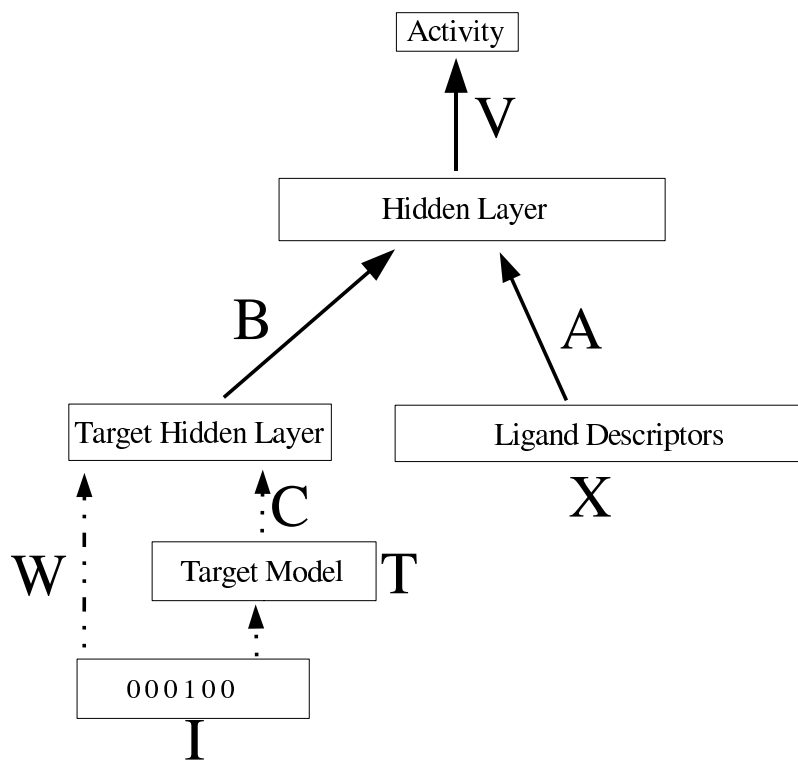


Figure 1: Collaborative Filtering Neural Network

# Kernel Approach

- What if we defined two kernels:

1.  $K_X(x_i, x_k)$

2.  $K_T(t_j, t_m)$

- and combined them?

- Correct way of doing it:

$$K[(x_i, t_j), (x_k, t_m)] = K_X(x_i, x_k) \cdot K_T(t_j, t_m)$$

- Tensor product in the feature space
- Kernels: identity, gaussian, correlation, quadratic, polynomial, etc.

# JRank

- Kernel Perceptron Ranker
- A set of learned parameters for each pair:

$$F((x_{new}, t_{new}); \alpha) = \sum_{i,j} \alpha_{i,j} K([(x_{new}, t_{new}), (x_i, t_j)])$$

- A set of learned thresholds used for ordinal regression (by binning F)
- Standard perceptron algorithm, updates when the bin is wrong
- Step-size of the update  $\propto$  how wrong

# Support Vector Machine

- Interpret dataset as classification problem
- Can then use the standard SVM routines:

$$W(\alpha) = \sum \alpha_i - \frac{1}{2} \sum_{i,j} \alpha_i \alpha_j y_i y_j K[(\mathbf{x}, \mathbf{t})_i, (\mathbf{x}, \mathbf{t})_j]$$

- Problem 1: explosion in number of datapoints
- Problem 2: *quadratic* optimization problem
- Problem 3: choice of kernels limited

# Target selection

- Problem: VERY BIG dataset
- Select “related” targets by “direct activity correlation”

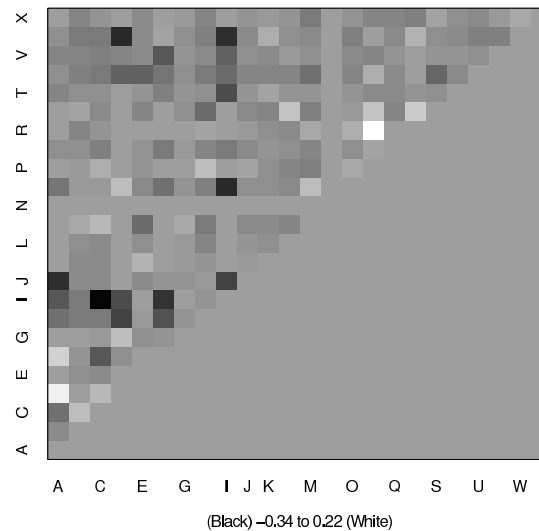
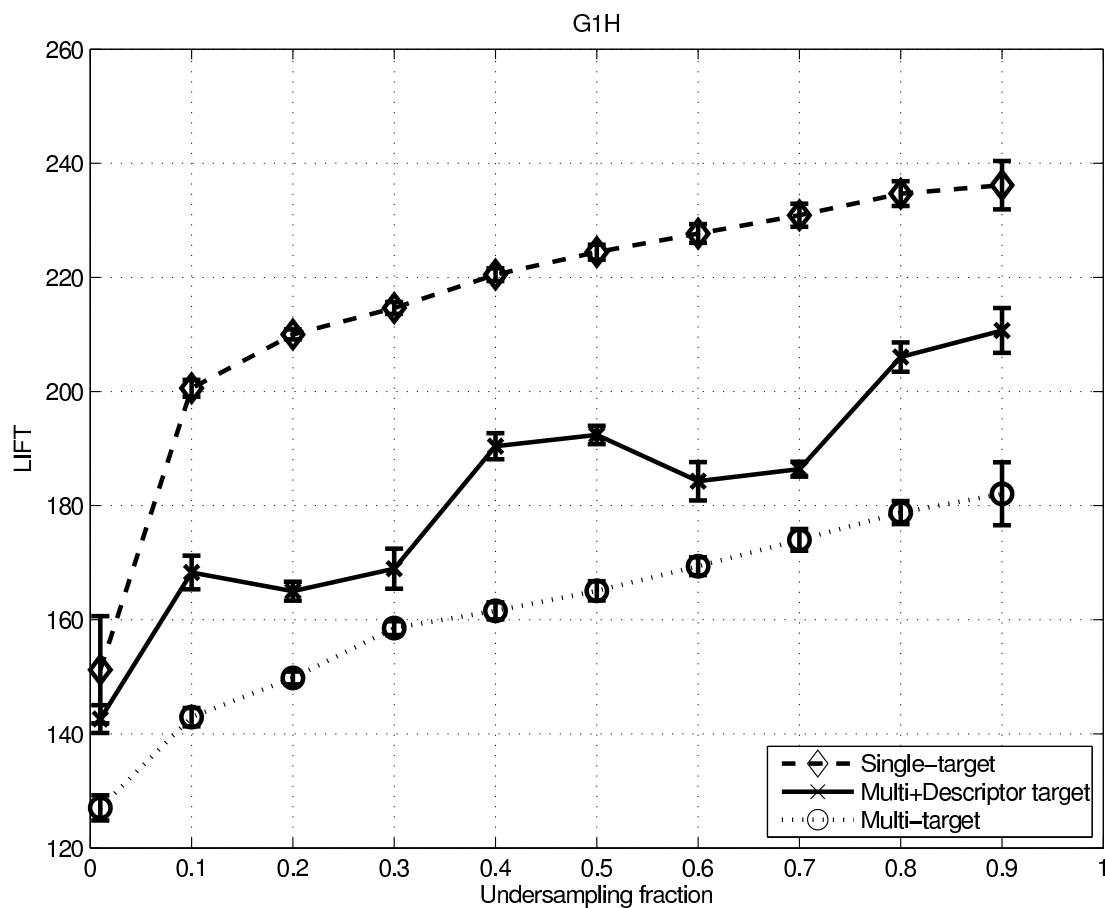
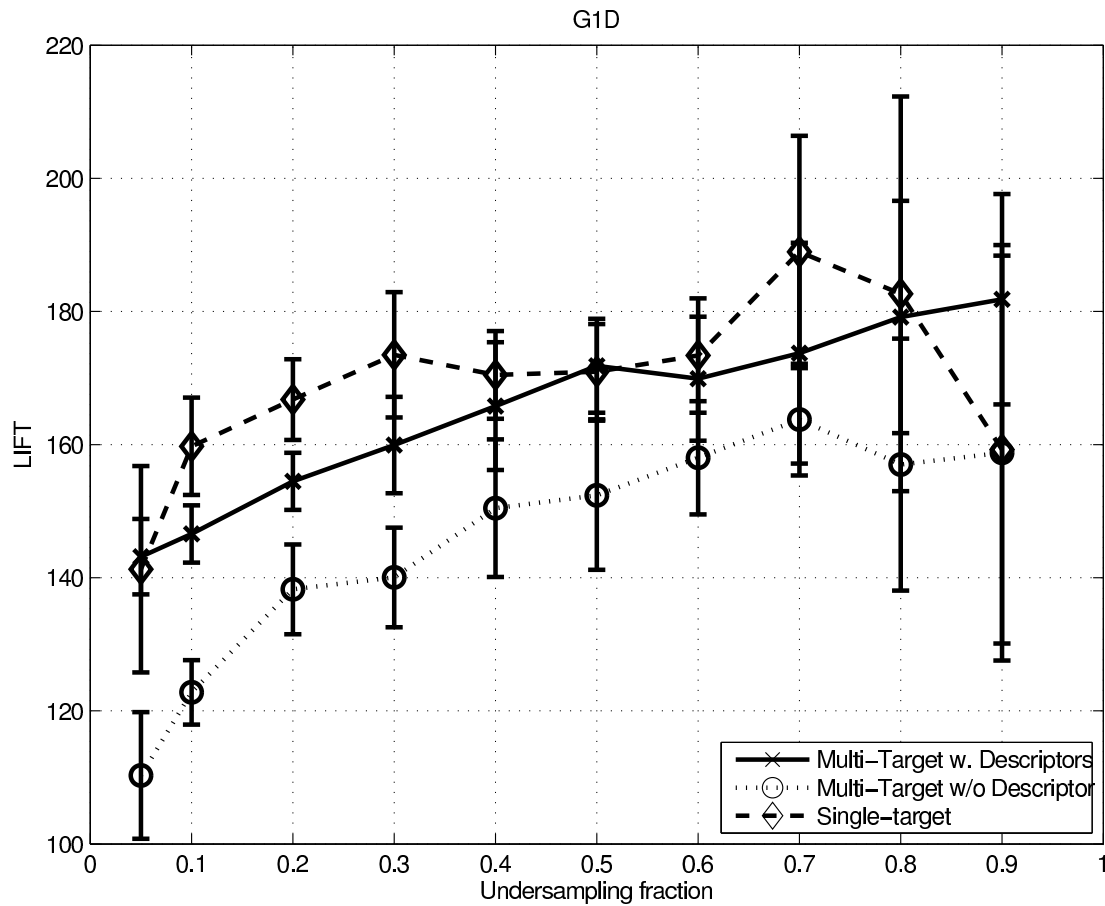


Figure 2: Pairwise Correlation of Biological Activity

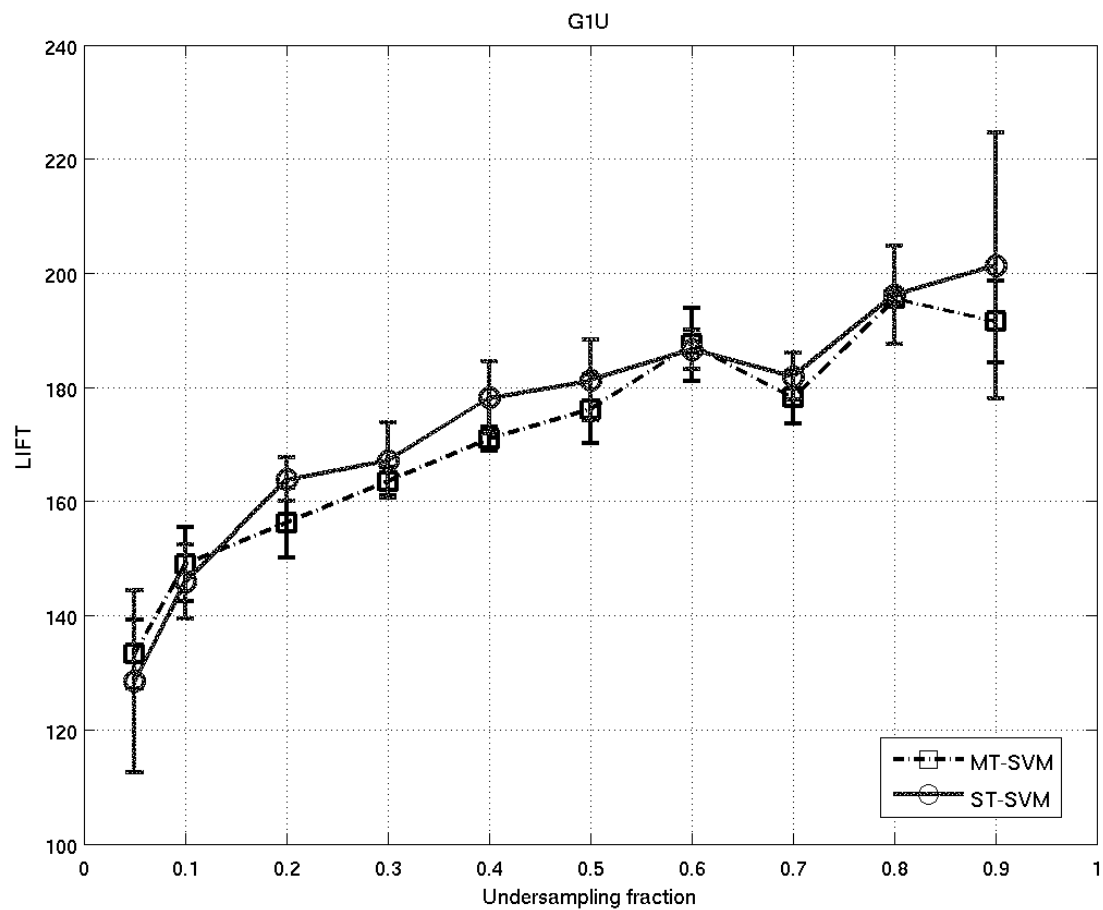
# Experimental Results – NNet



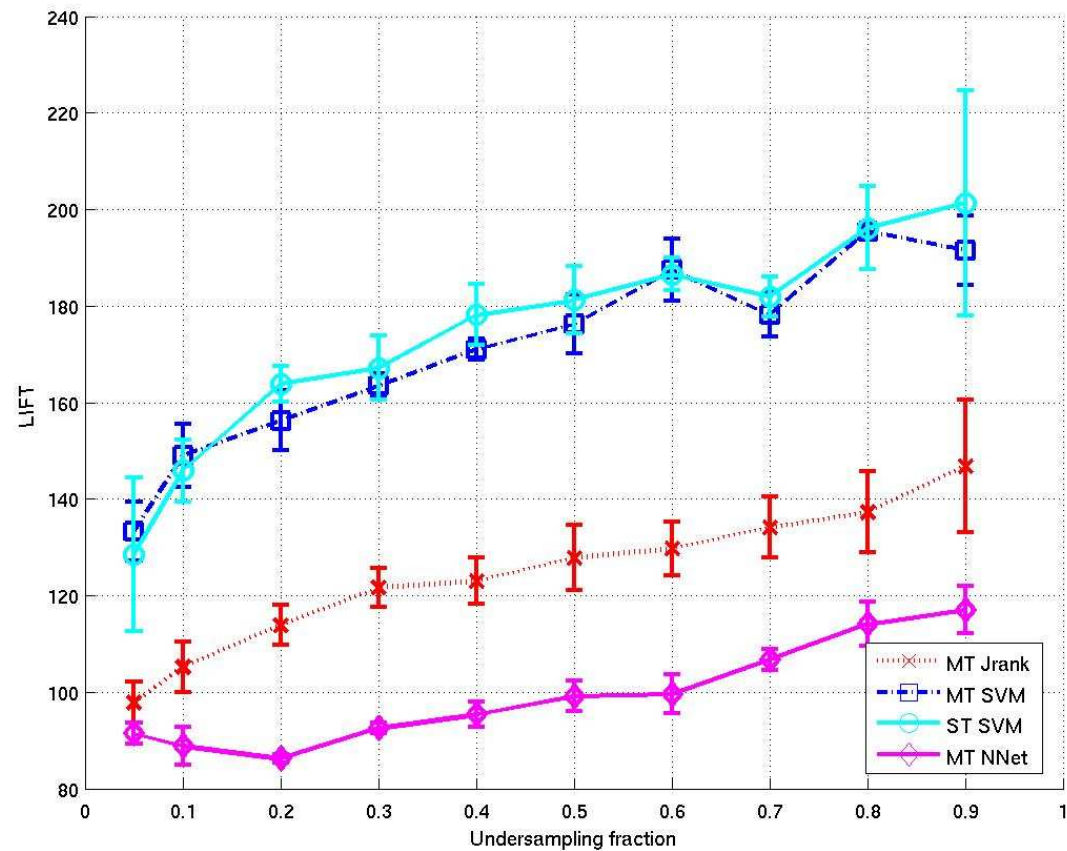
# Experimental Results – JRank



# Experimental Results – SVM

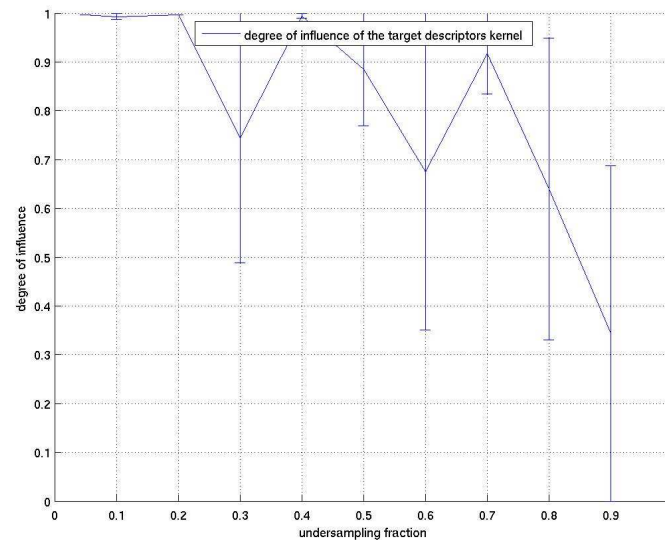


# Experimental Results – Comparison



# Experimental Results V

- $t_{\text{fraction}} = 0$ : 3 out of 7 targets with Lifts = 130...160
- NNet & JRank: lifts are close to 100
- Degree of influence



# Discussion



- MT NNet and MT JRank don't work as expected
- MT SVM works as well as ST SVM (which is state-of-the-art)
- Encouraging fact: at  $t_{\text{fraction}}=0$  Lifts are  $> 100$
- Means “inductive transfer” is happening!
- Need to find better way to exploit it



# Future Work



- Other target descriptors + more targets
- Better NNet
- Better kernels
- Ordinal regression with SVM, other SVM approaches



# Conclusions

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- Collaborative filtering
- Learning a new task
- Drug discovery
- Virtual screening, new target
- NNets, JRank, SVMs

# *The Conclusion*

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*It's all about the Benjamins!*  
(with apologies to Puff Daddy)

# References

- Rich Caruana, "Multitask Learning." *Machine Learning*, vol. 28(1), pp. 41–75, 1997.
- Jonathan Baxter, "A Bayesian/Information Theoretic Model of Learning to Learn via Multiple Task Sampling." *Machine Learning*, vol. 28(1), pp. 7–39, 1997.
- Jonathan Baxter, "A Model of Inductive Bias Learning.", *J. Artif. Intell. Res. (JAIR)*, vol. 12, pp. 149–198, 2000
- Theodoros Evgeniou and Massimiliano Pontil, "Regularized multi-task learning". *KDD 2004*, pp. 109–117
- Justin Basilico and Thomas Hofmann, "Unifying collaborative and content-based filtering." *ICML 2004*.