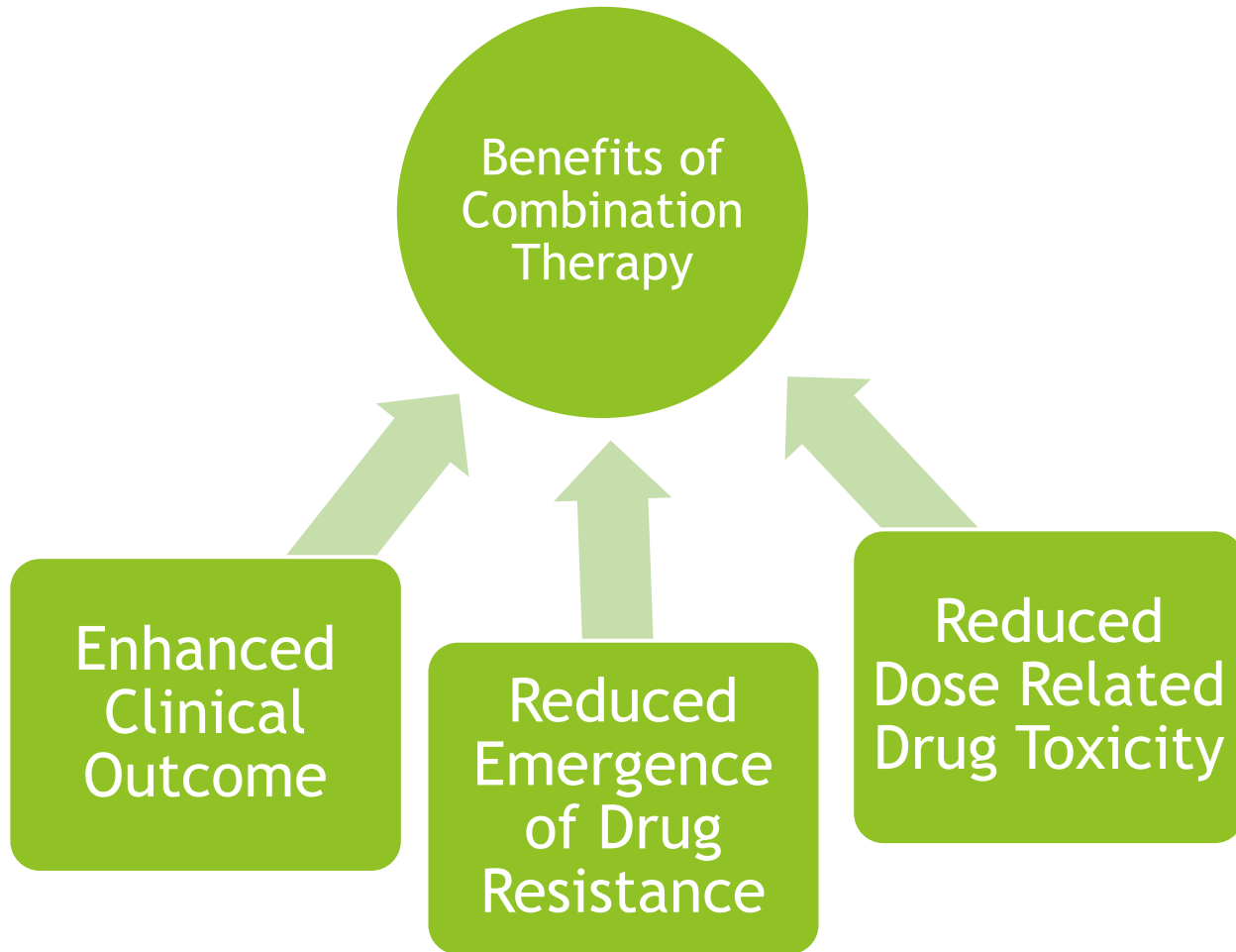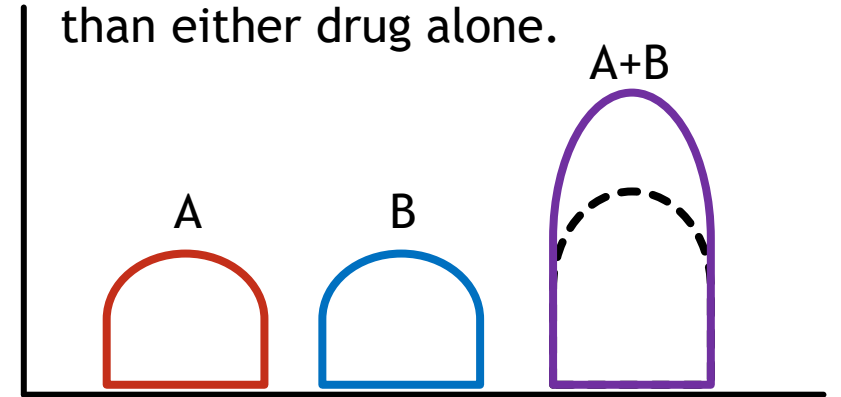# Advancing Research through Computing 2021

Ron Nafshi

Predicting the Effects of Drug Combinations Using Probabilistic Matrix Factorization

# Combination therapies are increasingly used to treat disease, but discovering them requires a lot of resources

Benefits of Combination Therapy

Enhanced Clinical Outcome

Reduced Emergence of Drug Resistance

Reduced Dose Related Drug Toxicity

The combination of drugs A and B has a greater therapeutic effect than either drug alone.

A   B   A+B

Testing all possible 2-drug combinations is costly and inefficient. Computation can help.
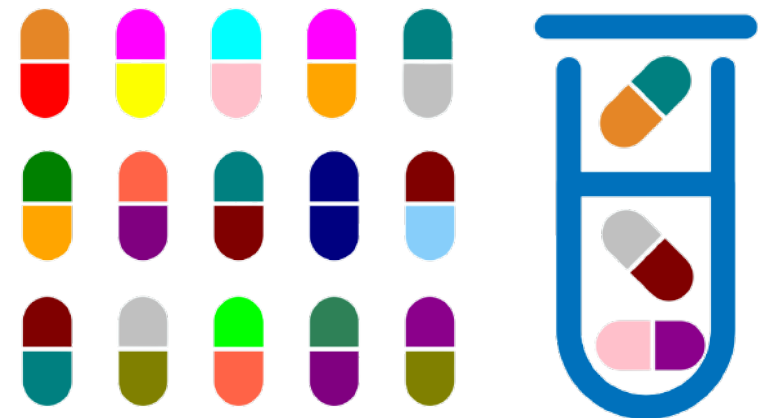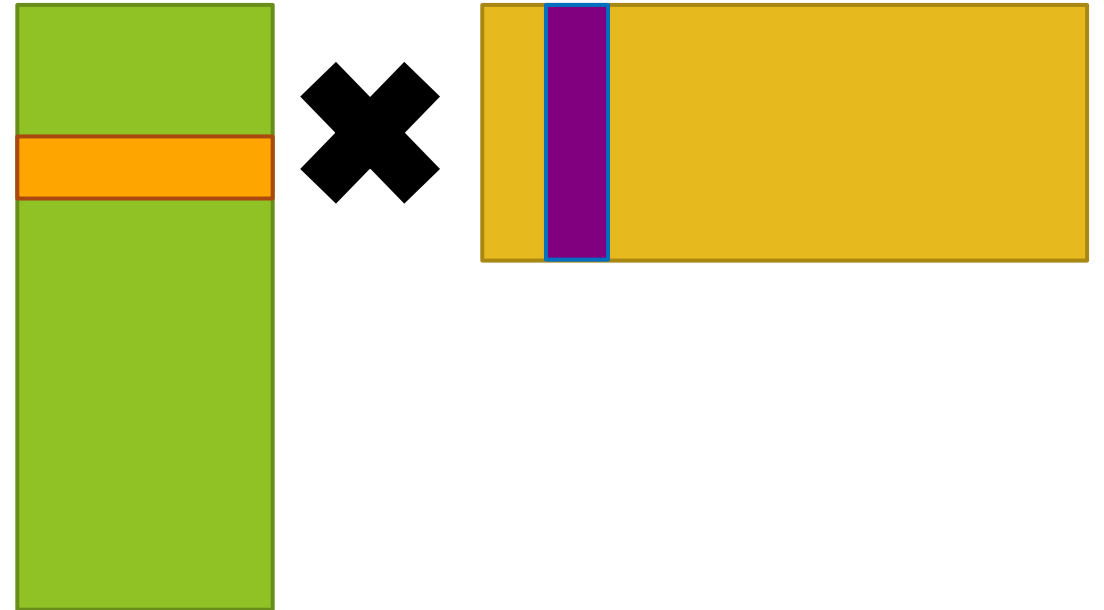
Probabilistic Matrix Factorization (PMF) can impute missing efficacies for drug combinations

$$\mathbf{M}_{ij} = \mathbf{A}_i \mathbf{B}_j^T$$

Drug Effect

- ➢ We can express the matrix as the product of two low-rank matrices of latent factors, and then estimate them using gradient descent.
- ➢ For very large datasets, using low-rank approximations greatly decreases computational time

PMF reduces experimental burden by 58%

➢ We investigate the effects of the starting set of accuracy

Individual Efficacy

Topology

PMF as ComboScore Cutoff Increases
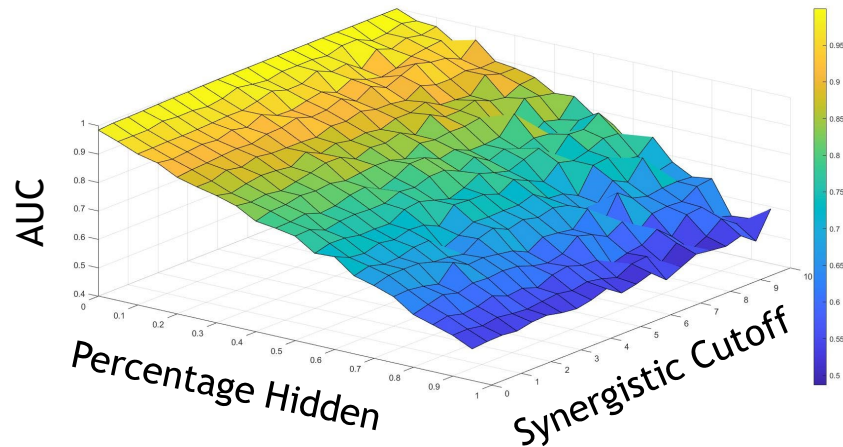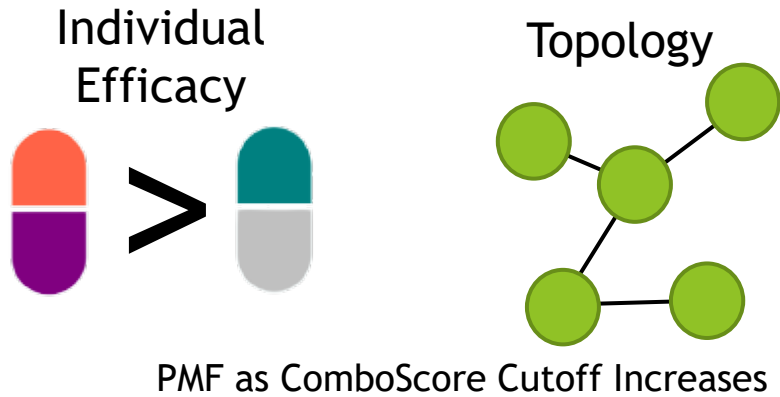
➢ PMF is robust to changes in node identity and topology and predicts all elements with equal accuracy.
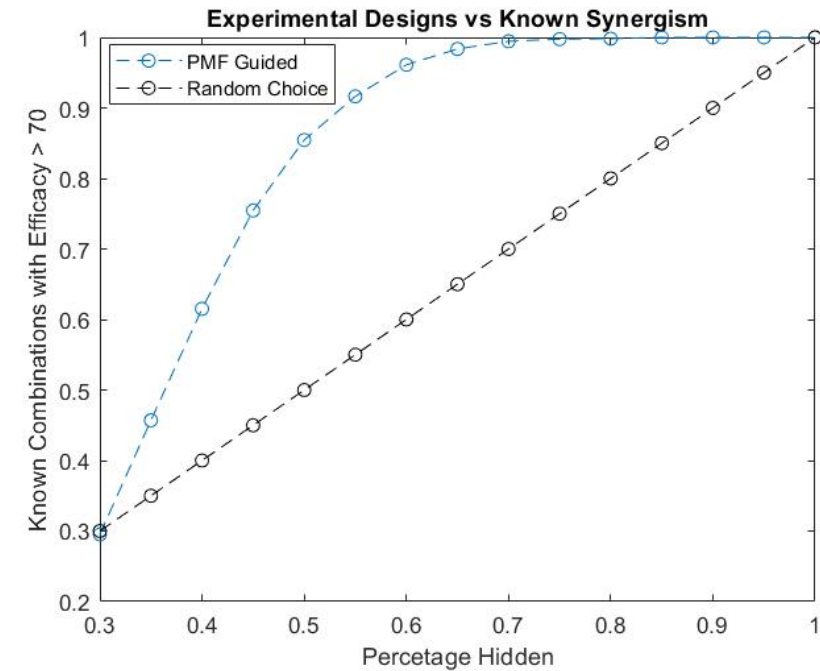
Conclusions

➢ A guided assay can identify 95% of all efficacious combinations while testing 60% of all available combinations.
  ➢ Much greater than random chance.
➢ Since the accuracy of PMF does not change depending on node identity or topology, PMF guided assays could expedite current drug synergism assays.