Supplementary Material: Network-based prediction of drug combinations with quantum annealing

Diogo Ramos
Faculdade de Ciências (FCUP), Universidade do Porto, Portugal

Bruno Coutinho
Institute of Communications and Navigation, German Aerospace Center (DLR), Weßling, Germany and Instituto de Telecomunicações (IT), Lisboa, Portugal

Duarte Magano*
Faculdade de Ciências (FCUP), Universidade do Porto, Portugal and 21strategies GmbH, Hallbergmoos, Germany
(Dated: December 23, 2025)

We have used the **human protein-protein interactome** compiled by Cheng, Kovács & Barabási (Nat Commun, 2019) [1] available in Supplementary Data 1, which contains 243,603 protein-protein interactions connecting 16,677 proteins. The interactome was mapped to official gene symbols and Entrez IDs as described by Cheng *et al.* using GeneCards. The original data was collected from Rolland *et al.* [2] and Rual *et al.* [3], and from an unpublished CCSB dataset.

The **Drug-target interactions** were taken from Cheng, Kovács & Barabási (Supplementary Data 2), which aggregates DrugBank, the Therapeutic Target Database (TTD), PharmGKB, ChEMBL, BindingDB and the IUPHAR/BPS Guide to PHARMACOLOGY [1, 4–9] and reviewed in the UniProt database [10].

More details on data preprocessing and filtering can be found under the Method section in Reference [1].

Disease-gene associations were obtained from the BioSNAP 'DG-AssocMiner' dataset (Stanford SNAP Biomedical Network Dataset Collection) [11], downloaded from `https://snap.stanford.edu/biodata/datasets/10012/10012-DG-AssocMiner.html` on 4 October 2024. The dataset contains 21,357 associations from 519 diseases to 7,294 gene nodes.

The disease-specific validated **Drug Combinations** dataset was constructed by intersecting the multi-drug combinations reported in the Continuous Drug Combination Database (CDCB) [12] with drug-disease associations compiled by Guney *et al.* [13]. A disease-combination pair was retained only if (i) the combination appears in CDCB as a verified multi-drug combination, and (ii) every drug in that combination is associated with the disease in Guney *et al.* — i.e., we required exact agreement between the set of drugs in the combination and the set of drugs associated with the disease. Applying this overlap and selection rule yields disease-combination pairs spanning 35 distinct diseases with at least one combination, 136 unique drugs, and 287 unique disease-combination pairs, 234 of which are constituted by two drugs, 40 are combinations of three drugs, and 13 of four or more drugs. The resulting dataset is publicly available in the associated project repository: `https://github.com/dmrapk/Drug-Combinations-using-Quantum-Annealers`.

[1] F. Cheng, I. A. Kovács, and A.-L. Barabási, Nature Communications **10**, 1197 (2019).
[2] T. Rolland *et al.*, Cell **159**, 1212 (2014).
[3] Rual, Jean-François, *et al.*, Nature **437**, 1173 (2005).
[4] V. Law *et al.*, Nucleic Acids Research **42**, D1091 (2013).
[5] F. Zhu *et al.*, Nucleic Acids Research **40**, D1128 (2012).
[6] T. Hernandez-Boussard *et al.*, Nucleic Acids Research **36**, D913 (2008).
[7] A. Gaulton *et al.*, Nucleic Acids Research **40**, D1100 (2012).
[8] T. Liu, Y. Lin, X. Wen, R. N. Jorissen, and M. K. Gilson, Nucleic Acids Research **35**, D198 (2007).
[9] A. J. Pawson *et al.*, Nucleic Acids Research **42**, D1098 (2014).
[10] UniProt Consortium, Nucleic Acids Research **47**, D506 (2019).
[11] M. Zitnik, R. Sosič, S. Maheshwari, and J. Leskovec, BioSNAP Datasets: Stanford biomedical network dataset collection, `http://snap.stanford.edu/biodata` (2018).
[12] G. Shtar, L. Azulay, O. Nizri, and et al., Scientific Data **9**, 263 (2022).

---

* Corresponding author address: duarte.magano@fc.up.pt

[13] E. Güney, J. Menche, M. Vidal, and A.-L. Barabási, Nature Communications **7**, 10331 (2016).