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Cancer drug treatment is unnatural selection

Targeted drug treatment reduces the tumour volume, but there is almost always recurrence even under chronic treatment. We show that the tumour population is heterogenous. Then the drug treatment is a selection process, targeting specific subpopulations. If treatment is stopped, phenotypic drift causes reversion towards the original wild-type population.

Our model is a discrete population of cells, the individual equivalent of an ODE. The cells each have a distinct phenotype. This phenotype determines their fitness. The fitness changes under drug conditions: we define a fitness landscape for both drug and drug-free conditions.

Experimentation shows evidence of only partial reversion to wild-type. We extend the complexity of the fitness landscape to multiple fitness "wells". Reversion after drug treatment only fills one of the wells. The overall behaviour matches experimental observations.

Our model concept extends to considering alternative treatments. Temporal variation appears unhelpful but well-chosen combination therapies could be effective. This approach gives a quantitative predicrtion of treatment strategies.