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Regulating drug resistance: Evolution and the double-bind

Treatment of cancer cell populations with chemotherapeutic drugs is nearly always associated with the onset of resistance, where minor populations of cells escape from therapy and continue to proliferate and lead to cancer recurrence and subsequent treatment failure. Resistance is also a common issue in the ecology field, where insects become resistant to chemical pesticides after repeated treatments. However, unlike the oncology field, the ecologists have used other strategies to control insect populations. Specifically, by using biological agents such as predators, parasites, pathogens, and parasitoids control has been achieved without any resulting resistance. One possible mechanism for the success of such biological agents is an evolutionary double-bind, where in order to adapt to a given treatment an insect pays the high cost of becoming significantly less fit in comparison to the unadapted population. Here we present an Evolutionary Game Theory (EGT) model to investigate such a double-bind approach in the treatment of cancer. Specifically, we use EGT to better understand the use of combination chemotherapeutic strategies when mono-therapies ultimately always lead to drug resistance.