

An Agent-Based Modelling Framework for Tuberculosis Infection with Drug-Resistance

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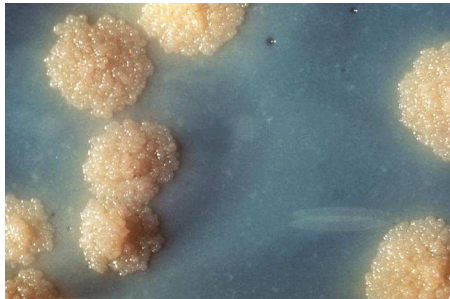
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Introduction

- TB is a disease caused by the *Mycobacterium tuberculosis*.



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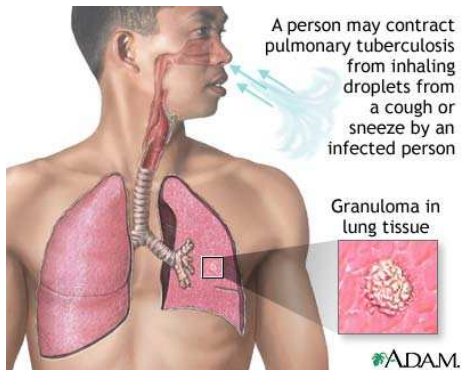


(Colony)

- Tuberculosis (TB) is a worldwide pandemic.

Introduction

- TB is spread through the air: cough, sneeze, or spit



- More than **2 billion** people are infected with TB bacilli.

Introduction

- Over 10 million new infections and deaths annually.
- There were an estimated 511,000 new MDR-TB cases in 2007.
- There is also TB (XDR-TB) occurs when resistance to second-line drugs develops.
- It is extremely difficult to treat XDR-TB.
- XDR-TB cases have been confirmed in more than 50 countries.

Susceptible and Latent individuals (X and L)

State	Description
X	susceptible (pathogen-free)
L_S	infected with S <u>only</u> (pathogen-harboured but not infectious)
L_R	infected with R <u>only</u>
L_{SR}	co-infected with <u>both</u> S and R pathogens

Table: Disease states. Note: S and R represents states related to drug sensitive and drug resistant pathogens, respectively.

Infectious individuals (T_S and T_R)

State	Description
T_S	active TB infectious with S pathogens only
T_R	active TB infectious with R pathogens only
T_{SR}^S	<u>co-infected</u> TB active with S pathogens only
T_{SR}^R	<u>co-infected</u> TB active with R pathogens only

Table: Disease states. Note: S and R represents states related to drug sensitive and drug resistant pathogens, respectively.

Effectively Treated (L^D)

State	Description
$L_S^{D_1}$	effectively treated S active TB
$L_R^{D_2}$	effectively treated R active TB
$L_{RS}^{D_1}$	effectively treated co-infected TB active with S pathogens only
$L_{RS}^{D_2}$	effectively treated co-infected TB active with R pathogens only

Table: Disease states. Note: D_1 and D_2 correspond to the treatment with the first and second drugs, respectively. Sensitive and resistant pathogens refer to drug sensitive and drug resistant, respectively.

Latent TB

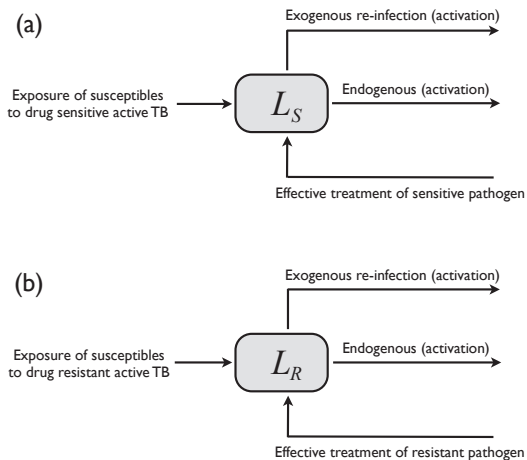


Figure: Influx and outflow of the latent states with S and R pathogens.

Active TB

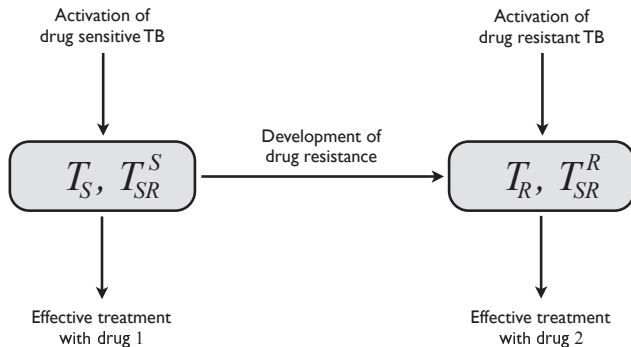
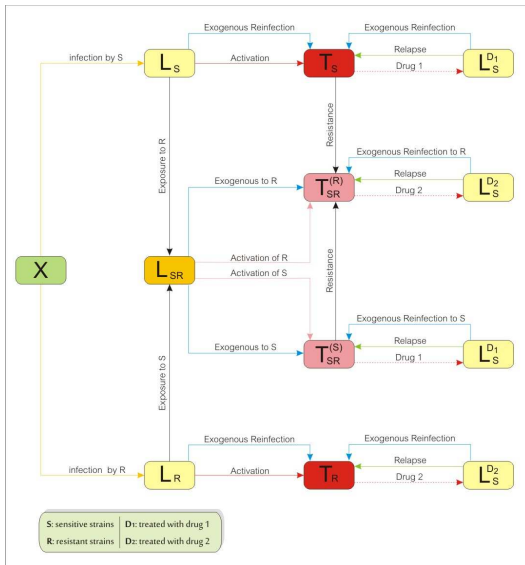


Figure: Influx and outflow of the active TB states with S and R pathogens.

Agent-Based Model for TB



Lattice and Neighborhood

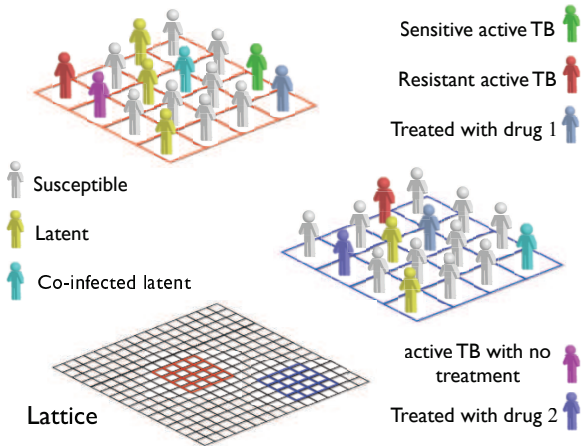


Figure: Schematic diagram of the lattice environment in the ABM model.

Contagion and Emergence of Drug Resistance

- Contagion: Only T_S , T_R , T_{SR}^S , T_{SR}^R are source of infection.
- Activation: Latent individuals may undergo endogenous activation.
- Relapse: reactivated during latency (already treated).
- Exogenous Re-infection: reactivation influenced by re-exposure to another active TB.
- Drug Resistance: treatment failure with drug 1.

Numerical Implementation

- At $t = 0$, only X and T_S individuals in the lattice.
- Transition: $X \rightarrow L_S$:

$$P_S = 1 - (1 - \beta_S)^{K_S}$$

- β_S is the baseline infectivity of the S strain.
- K_S is the number of neighbours having active TB.
- The system evolves during 200 years.
- Antibiotics (D_1 and D_2) are introduced with P_{treat} probability.
- We monitor the spread of disease for 25 years following the start of treatment.

Exogenous Re-infection=ON & Relapse=ON

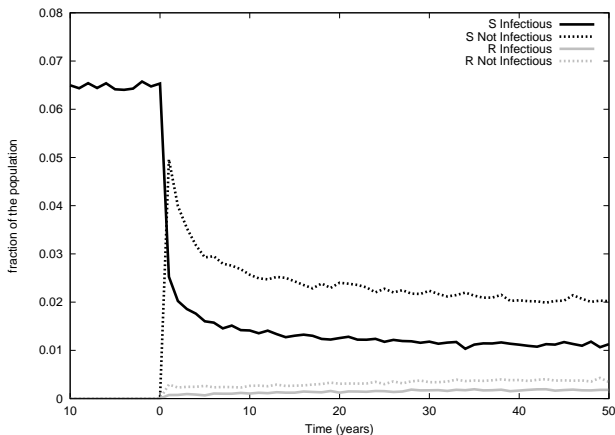


Figure: Solid black: S infectious; Dashed black: S not infectious; Solid grey: R infectious; Dashed grey: R not infectious.

Exogenous Re-infection=ON & Relapse=OFF

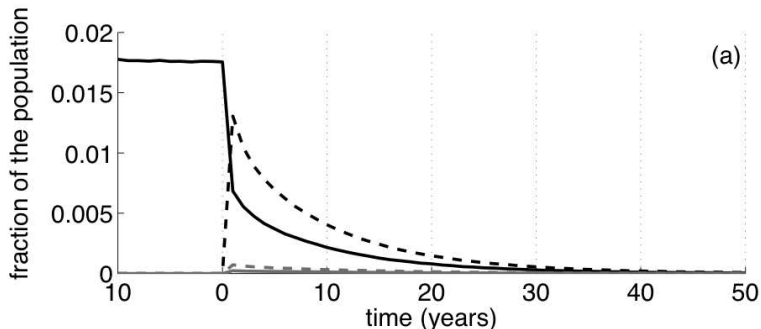


Figure: Solid black: S infectious; Dashed black: S not infectious; Solid grey: R infectious; Dashed grey: R not infectious.

Exogenous Re-infection=OFF & Relapse=ON

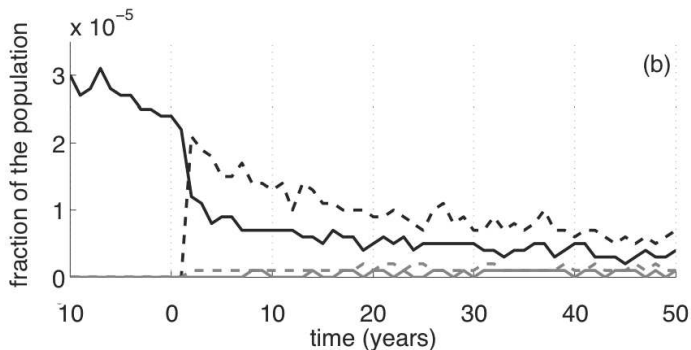


Figure: Solid black: S infectious; Dashed black: S not infectious; Solid grey: R infectious; Dashed grey: R not infectious.

Exogenous Re-infection=OFF & Relapse=OFF

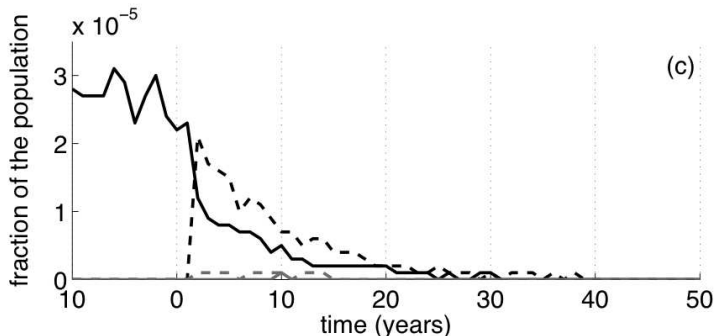
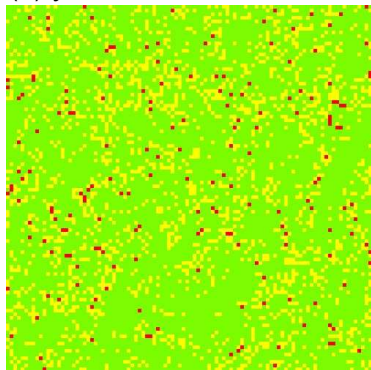


Figure: Solid black: S infectious; Dashed black: S not infectious; Solid grey: R infectious; Dashed grey: R not infectious.

Snapshot of the Lattice. Relapse = ON

(a) year 0, start of treatment



(b) year 25 following treatment

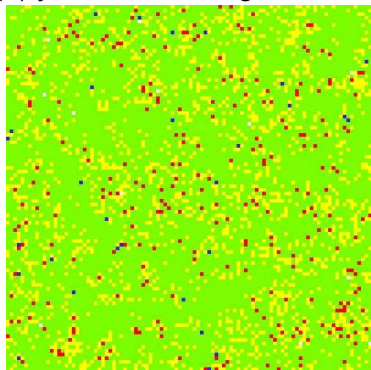
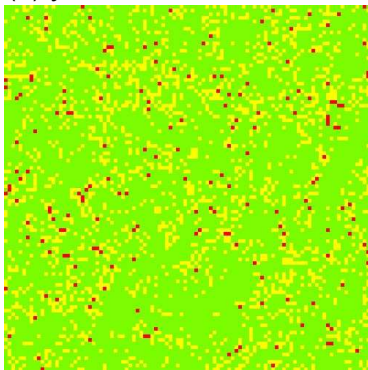


Figure: Colours: susceptible (green), latent (yellow), active TB with the sensitive strain (red), active TB with the resistant strain (blue), and effectively treated (white).

Snapshot of the Lattice. Relapse = OFF

(a) year 0, start of treatment



(b) year 25 following treatment

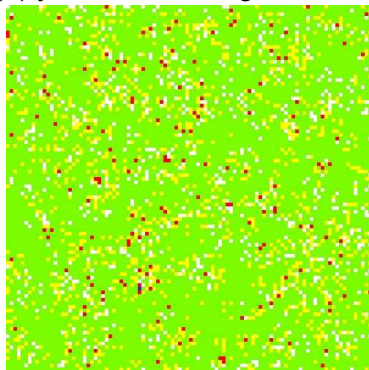


Figure: Colours: susceptible (green), latent (yellow), active TB with the sensitive strain (red), active TB with the resistant strain (blue), and effectively treated (white).

Discussion and Future Direction

- General framework to study of complex TB dynamics.
- Two strains of the pathogen: drug sensitive and drug resistant.
- Treatment with two types of antimicrobial agents.
- Our model encapsulates mechanisms of exogenous re-infection and relapse.
- A more realistic model including: dynamical lattice, age, individuals' characteristics, and population demographics.

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