Model

```
function dydt = model(t, y , params)
    s = y(1); %sensitive bacteria
    r = y(2); %resistant bacteria
    b = y(3); %immune cells
    a1 = y(4);  % INH
    a2 = y(5);  % ZPA

    % PARAMETERS
    beta_S = 1.1;     % Growth rate of sensitive bacteria
    beta_R = 0.9;     % Growth rate of resistant bacteria (with fitness cost)
    eta = 0.6;        % Immune killing rate
    k = 0.4;          % Immune cell proliferation rate

    % For INH (antibiotic 1)
    alpha1 = params.alpha1;    % Mutation rate due to INH
    d1 = params.d1;          % Death rate due to INH

    % For ZPA (antibiotic 2)
    alpha2 = params.alpha2;    % Mutation rate due to ZPA
    d2 = params.d2;          % Death rate due to ZPA

    mu1 = 0.08;        % Clearance rate for INH
    mu2 = 0.04;       % Clearance rate for ZPA

    % DE
    total_bac = s + r; % Total bacteria
```

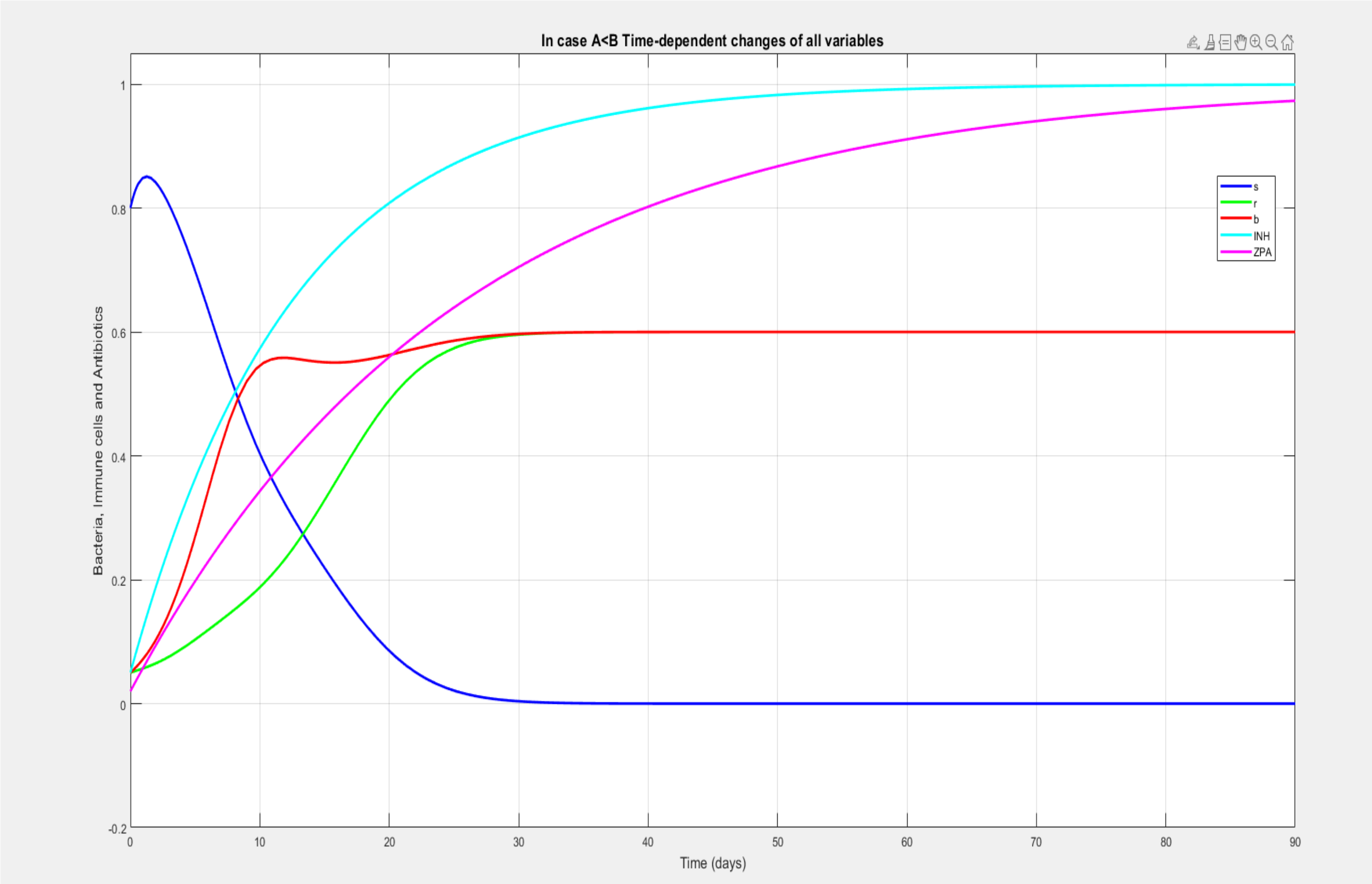
```
% Sensitive bacteria
% ds/dt = β_S * s * (1 - s - r) - η * s * b - s * Σ(α_i + d_i)*a_i

growth_s = beta_S * s * (1 - total_bac);
immune_kill_s = eta * s * b;
antibiotic_effect_s = s * ((alpha1 + d1) * a1 + (alpha2 + d2) * a2);

ds = growth_s - immune_kill_s - antibiotic_effect_s;

% Resistant bacteria
% dr/dt = β_R * r * (1 - s - r) - η * r * b + s * Σ(α_i)*a_i

growth_r = beta_R * r * (1 - total_bac);
immune_kill_r = eta * r * b;
mutation_gain = s * (alpha1 * a1 + alpha2 * a2);

dr = growth_r - immune_kill_r + mutation_gain;

% Immune cells
% db/dt = k * b * (1 - b/(s + r))

db = k * b * (1 - b / total_bac);

% Antibiotic concentrations
% da_i/dt = μ_i * (1 - a_i)

da1 = mu1 * (1 - a1);
da2 = mu2 * (1 - a2);
```

```
    % OUTPUT
    dydt = [ds; dr; db; da1; da2];
end
```

All variables (A<B)

```
tspan = [0 90];

s = 0.8; %sensitive bacteria
r = 0.05; %resistant bacteria
b = 0.05; %immune cells
a1 = 0.05;  % INH
a2 = 0.02;  % ZPA

% For INH (antibiotic 1)
params.alpha1 = 0.02;    % Mutation rate due to INH
params.d1 = 0.15;        % Death rate due to INH

% For ZPA (antibiotic 2)
params.alpha2 = 0.06;    % Mutation rate due to ZPA
params.d2 = 0.35;        % Death rate due to ZPA

y0 = [s  r  b  a1  a2];
[t,y] = ode45(@(t,y) model(t,y,params), tspan, y0);

s  = y(:,1);
r  = y(:,2);
b  = y(:,3);
```

```
a1 = y(:,4);
a2 = y(:,5);

% Plot
figure;
hold on; grid on; box on;

plot(t,s,'b','LineWidth',2)
plot(t,r,'g','LineWidth',2)
plot(t,b,'r','LineWidth',2)
plot(t,a1,'c','LineWidth',2)
plot(t,a2,'m','LineWidth',2)

xlabel('Time (days)','FontSize',12)
ylabel('Bacteria, Immune cells and Antibiotics','FontSize',12)
title('In case A<B Time-dependent changes of all variables','FontSize',13)

legend('s','r','b','INH','ZPA','Location','best')
ylim([-0.2 1.05])
xlim([0 90])
```



Bacteria Vs Immune

tspan = [0 90];

s = 0.8; %sensitive bacteria

r = 0.05; %resistant bacteria

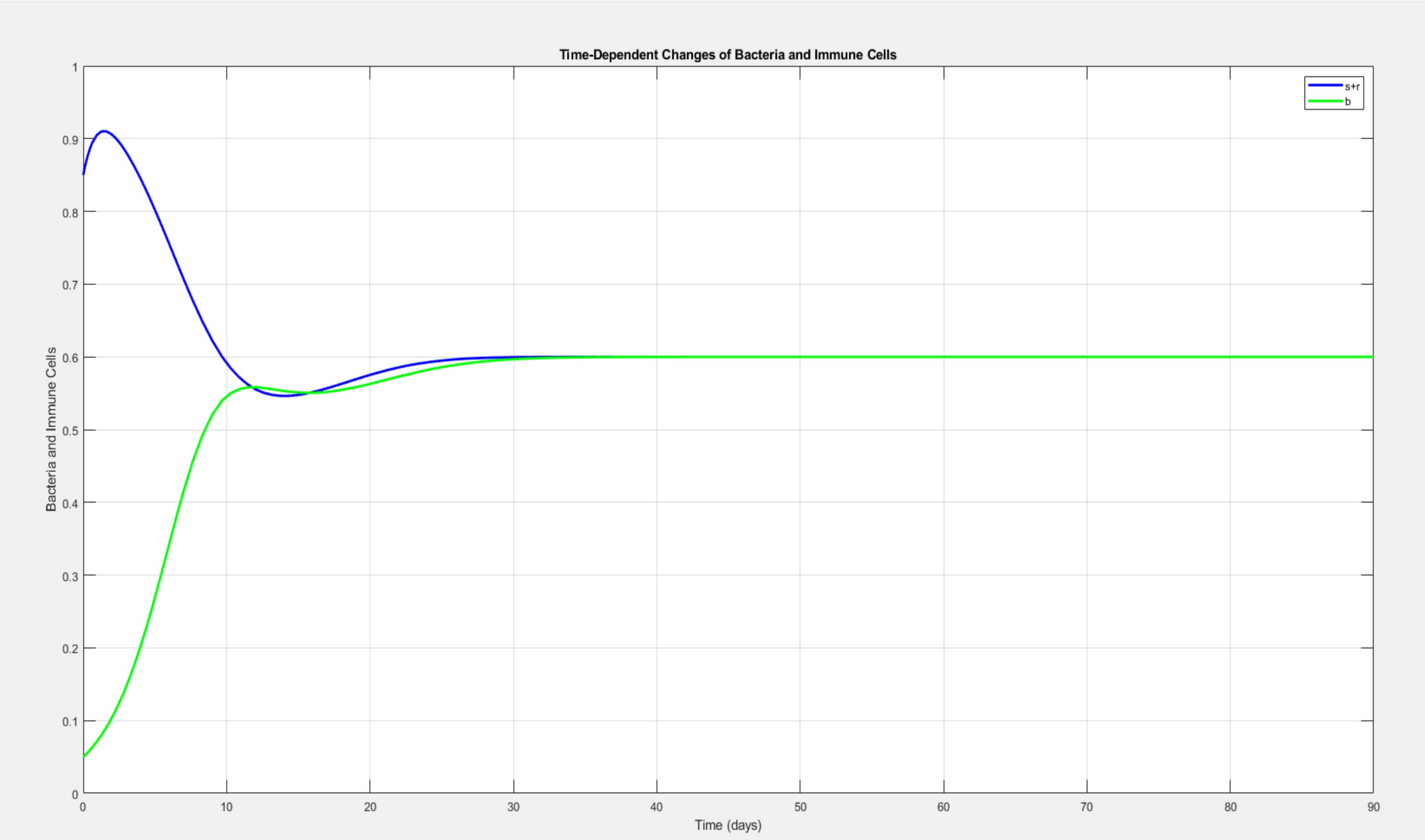
b = 0.05; %immune cells

a1 = 0.05; % INH

a2 = 0.02; % ZPA

% For INH (antibiotic 1)

```
params.alpha1 = 0.02;    % Mutation rate due to INH
params.d1 = 0.15;         % Death rate due to INH

% For ZPA (antibiotic 2)
params.alpha2 = 0.06;    % Mutation rate due to ZPA
params.d2 = 0.35;         % Death rate due to ZPA

y0 = [s  r  b  a1  a2];
[t,y] = ode45(@(t,y) model(t,y,params), tspan, y0);

figure
plot(t, y(:,1)+y(:,2),'b','LineWidth',2)   % s+r
hold on
plot(t, y(:,3),'g','LineWidth',2)          % b
xlabel('Time (days)')
ylabel('Bacteria and Immune Cells')
title('Time-Dependent Changes of Bacteria and Immune Cells')
legend('s+r','b')
grid on
```



<u>All Variables (B<A)</u>

tspan = [0 90];

s = 0.8; %sensitive bacteria

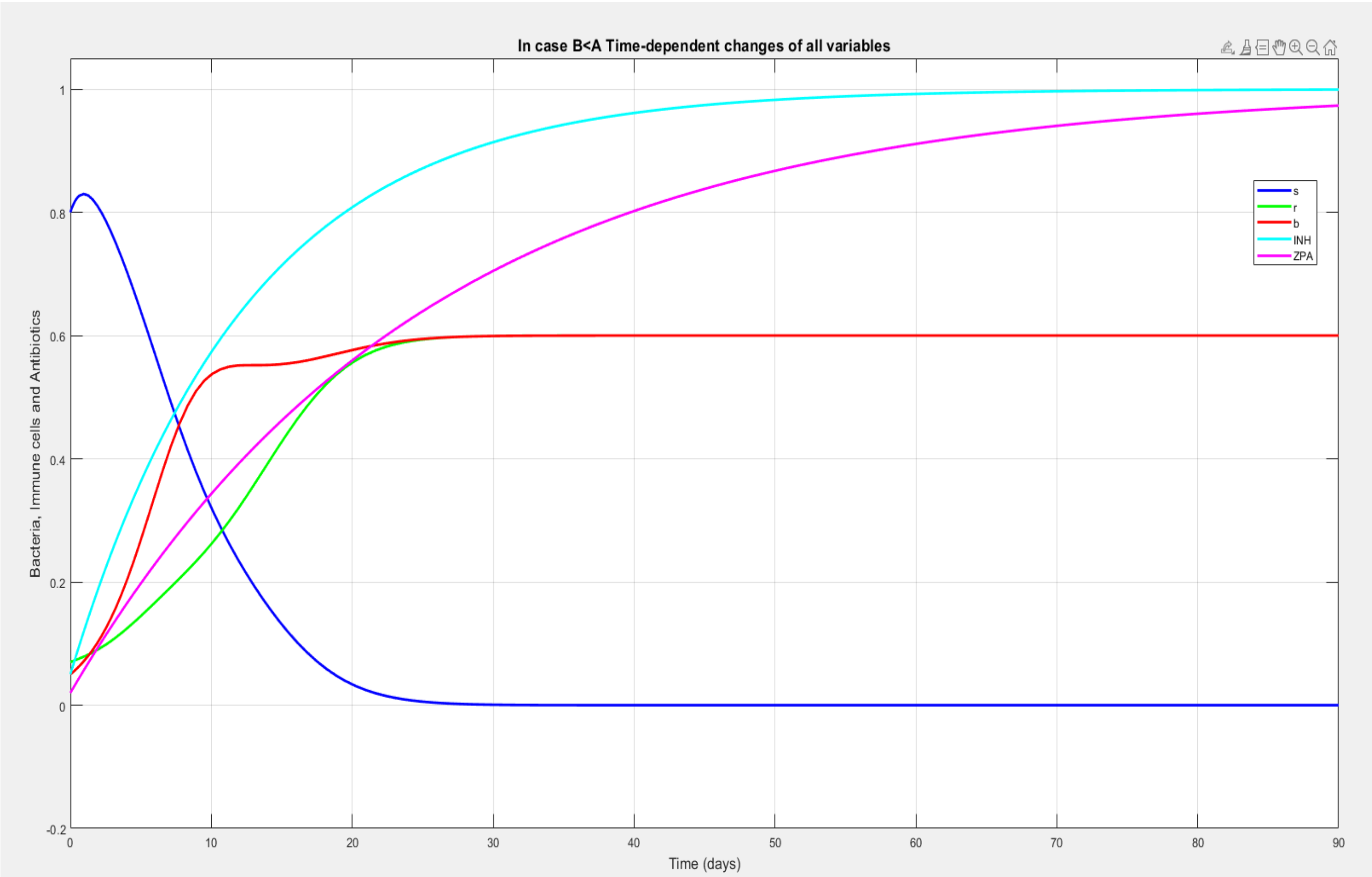
r = 0.07; %resistant bacteria

b = 0.05; %immune cells

a1 = 0.05; % INH

```
a2 = 0.02;  % ZPA

% For INH (antibiotic 1)
params.alpha1 = 0.06;    % Mutation rate due to INH
params.d1 = 0.35;        % Death rate due to INH

% For ZPA (antibiotic 2)
params.alpha2 = 0.02;    % Mutation rate due to ZPA
params.d2 = 0.15;        % Death rate due to ZPA

y0 = [s  r  b  a1  a2];
[t,y] = ode45(@(t,y) model(t,y,params), tspan, y0);

s  = y(:,1);
r  = y(:,2);
b  = y(:,3);
a1 = y(:,4);
a2 = y(:,5);

% Plot
figure;
hold on; grid on; box on;

plot(t,s,'b','LineWidth',2)
plot(t,r,'g','LineWidth',2)
plot(t,b,'r','LineWidth',2)
plot(t,a1,'c','LineWidth',2)
plot(t,a2,'m','LineWidth',2)
```

```
xlabel('Time (days)','FontSize',12)
ylabel('Bacteria, Immune cells and Antibiotics','FontSize',12)
title('In case B<A Time-dependent changes of all variables','FontSize',13)

legend('s','r','b','INH','ZPA','Location','best')
ylim([-0.2 1.05])
xlim([0 90])
```



Resistance VS Sensitive Bacteria

```
params.alpha1 = 0.06;   % Mutation rate due to INH
params.d1 = 0.35;       % Death rate due to INH
params.alpha2 = 0.02;   % Mutation rate due to ZPA
params.d2 = 0.15;       % Death rate due to ZPA

s = 0.8; %sensitive bacteria
r = 0.1; %resistant bacteria
b = 0.5; %immune cells
a1 = 1;  % INH
a2 = 1;  % ZPA



y0 = [s, r, b, a1, a2];

tspan = [0 90];

[t, y] = ode45(@(t,y) model(t, y, params), tspan, y0);

figure;
plot(y(:,1), y(:,2), 'b', 'LineWidth', 2);  % y(:,1)=s, y(:,2)=r
xlabel('Sensitive Bacteria');
ylabel('Resistant Bacteria');
title('Time-Dependent Changes of Bacteria ');
grid on;
```

```
hold on;
plot(y(1,1), y(1,2), 'ks', 'MarkerFaceColor', 'k'); % initial point
plot(y(end,1), y(end,2), 'ks', 'MarkerFaceColor', 'r'); % final point
```