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A GAME-THEORETIC MODEL OF MONKEYPOX TO ASSESS POTENTIAL VACCINATION STRATEGIES

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Introduction

- Monkeypox virus (MPXV) is a rare zoonotic *Orthopoxvirus* that causes monkeypox (MPX), a disease endemic to the Democratic Republic of the Congo and Nigeria.
- There are likely less than 10000 cases of MPX worldwide. In 2003, 47 cases were reported in USA and in 2018, 3 cases reported in UK.
- Common symptoms of MPX, though relatively milder than smallpox, include fever, severe headaches, skin lesions, and myalgia
- The case fatality rate is over 10%.
- A smallpox vaccine is an effective prevention against MPX.
- Administration of the smallpox vaccine has ceased since the disease's eradication in 1980, resulting in lowered immunity against *Orthopoxviruses* in general.
- We analyze a game theoretical model of MPX with voluntary smallpox vaccinations.

MPX overview

- MPX is capable of being transmitted amongst rodents, and primates.
- The majority of reported human cases originate from an interaction with an infected animal.
- We consider only a moribund rope squirrel (*Funisciurus anerythrus*) and sun squirrels (*Heliosciurus rufobrachium*) .
- The incubation period for the virus ranges from 5 to 21 days.
- MPX infection is split into 2 distinct phases: the invasion period (fever, lymphadenopathy, intense asthenia, severe headaches, and myalgia) and the skin eruption period (rash and fluid filled blisters, the number vary from a few to thousands across the body).

Scheme of MPX transmission

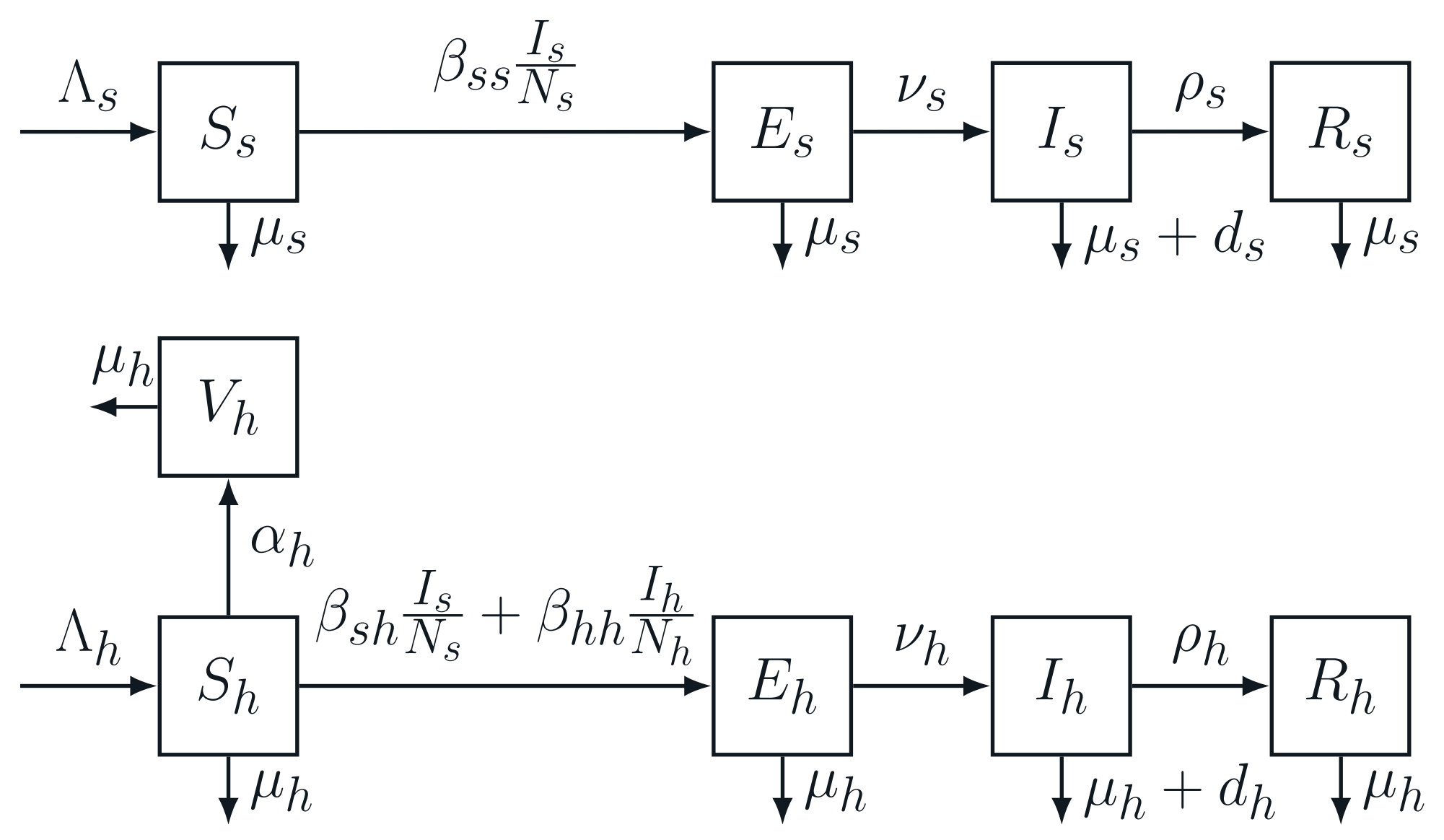

Fig. 1: Susceptible (S), Exposed (E), Infectious (I), Recovered (R), Vaccinated (V). h - humans, s - squirrels. The rates are explained in Table 1.

ODE model of MPX transmission

$$\frac{dS_s}{dt} = \Lambda_s - \left(\mu_s + \beta_{ss}\frac{I_s}{N_s}\right) S_s$$
$$\frac{dE_s}{dt} = \beta_{ss}\frac{I_s}{N_s}S_s - (\mu_s + \nu_s)\, E_s$$
$$\frac{dI_s}{dt} = \nu_s E_s - (\mu_s + d_s + \rho_s) I_s$$
$$\frac{dR_s}{dt} = \rho_s I_s - \mu_s R_s$$
$$\frac{dS_h}{dt} = \Lambda_h - \left(\mu_h + \frac{\beta_{sh} I_s}{N_s} + \frac{\beta_{hh} I_h}{N_h} + \alpha_h\right) S_h$$
$$\frac{dV_h}{dt} = \alpha_h S_h - \mu_h V_h$$
$$\frac{dE_h}{dt} = \left(\beta_{sh}\frac{I_s}{N_s} + \beta_{hh}\frac{I_h}{N_h}\right) S_h - (\mu_h + \nu_h) E_h$$
$$\frac{dI_h}{dt} = \nu_h E_h - (\mu_h + d_h + \rho_h) I_h$$
$$\frac{dR_h}{dt} = \rho_h I_h - \mu_h R_h$$

Symbol	Meaning	Value
Λ_h	Human birth rate	0.0328
Λ_s	Squirrel birth rate	2
μ_h	Human natural death rate	$1/60$
μ_s	Squirrel natural death rate	0.5
d_h	Human MPX related death rate	3.12
d_s	Squirrel MPX related death rate	17.5
ρ_h	Human recovery rate	28.08
ρ_s	Squirrel recovery rate	12
ν_h	Human infection rate	30.42
ν_s	Squirrel infection rate	120
α_h	Vaccination rate	variable
β_{ss}	Squirrel-to-squirrel trans. rate	40
β_{sh}	Squirrel-to-human trans. rate	0.05
β_{hh}	Human-to-human trans. rate	32.85
C_V	Cost of vaccine	$\$4$
C_{MPX}	Cost of MPX infection	$\$100$

Table 1: Parameters of MPX dynamics. See preprint for the references.

Results - Equilibria of the dynamics

	Disease-free (ϵ^0)	Fully Endemic (ϵ^*)	Semi-endemic ($\epsilon^\dagger$)
N_s	$\frac{\Lambda_s}{\mu_s}$	$\frac{\Lambda_s \cdot \left(\frac{\mu_s+d_s+\rho_s}{\nu_s}+1+\frac{\rho_s}{\mu_s}\right)}{\mu_s \cdot \left(\frac{\mu_s+d_s+\rho_s}{\nu_s}\right)+d_s \cdot \left(1-\frac{1}{R_{0ss}}\right)+\mu_s+\rho_s}$	$\frac{\Lambda_s}{\mu_s}$
S_s	N_s^0	$N_s^* \cdot \frac{1}{R_{0ss}}$	$N_s^\dagger$
E_s	0	$\left(\frac{\mu_s+d_s+\rho_s}{\nu_s}\right) \cdot I_s^*$	0
I_s	0	$\frac{\Lambda_s-\mu_s N_s^*}{d_s}$	0
R_s	0	$\frac{\rho_s}{\mu_s} \cdot I_s^*$	0
N_h	$\frac{\Lambda_h}{\mu_h}$	see preprint	see preprint
S_h	$\frac{\mu_h}{\mu_h+\alpha_h} \cdot N_h^0$	$\frac{(\mu_h+\nu_h)\left(\frac{\mu_h+d_h+\rho_h}{\nu_h}\right) \cdot I_h^*}{\beta_{sh}\left(\frac{I_s^*}{N_s^*}\right)+\beta_{hh}\left(\frac{I_h^*}{N_h^*}\right)}$	$\frac{(\mu_h+d_h+\rho_h)(\mu_h+\nu_h)}{\nu_h \beta_{hh}} \cdot N_h^\dagger$
V_h	$\frac{\alpha_h}{\mu_h+\alpha_h} \cdot N_h^0$	$\frac{\alpha_h}{\mu_h} \cdot S_h^*$	$\left(\frac{\alpha_h}{\mu_h}\right) \cdot S_h^\dagger$
E_h	0	$\left(\frac{\mu_h+d_h+\rho_h}{\nu_h}\right) \cdot I_h^*$	$\left(\frac{\mu_h+d_h+\rho_h}{\nu_h}\right) \cdot I_h^\dagger$
I_h	0	$\frac{\Lambda_h-\mu_h N_h^*}{d_h}$	$\frac{\Lambda_h-\mu_h N_h^\dagger}{d_h}$
R_h	0	$\frac{\rho_h}{\mu_h} \cdot I_h^*$	$\frac{\rho_h}{\mu_h} \cdot I_h^\dagger$

Table 2: Three different equilibria of the MPX dynamics. The formulas for N_h^* and $N_h^\dagger$ are too long for the table and are given in manuscript. The disease-free equilibrium is (locally asymptotically) stable when $\mathcal{R}_{0ss} < 1$ and $\mathcal{R}_{0hh} < 1$. The endemic equilibrium is stable when $\mathcal{R}_{0ss} > 1$. The semi-endemic equilibrium is stable when $\mathcal{R}_{0ss} < 1$ and $\mathcal{R}_{0hh} > 1$.

$$\mathcal{R}_{0ss} = \beta_{ss} \cdot \frac{1}{\mu_s + d_s + \rho_s} \cdot \frac{\nu_s}{\mu_s + \nu_s}$$
$$\mathcal{R}_{0hh} = \beta_{hh} \cdot \frac{\mu_h}{\alpha_h + \mu_h} \cdot \frac{1}{\mu_h + d_h + \rho_h} \cdot \frac{\nu_h}{\mu_h + \nu_h}.$$

Results - Herd immunity and Nash equilibrium

- Herd immunity is impossible to achieve in the fully endemic equilibrium (due to the reservoir of MPX in squirrel population).
- In the semi-endemic equilibrium, one can achieve herd immunity when the vaccination rate reaches

$$\alpha_{HI} = \max\left\{0, \frac{\nu_h \beta_{hh} \mu_h}{(\mu_h + d_h + \rho_h)(\mu_h + \nu_h)} - \mu_h\right\}.$$

- The Nash equilibrium vaccination rate α_{NE} is given as a solution of $C_{notV}(\alpha_h) = C_V$ where

$$C_{notV}(\alpha_h) = C_{MPX} \cdot \left(\frac{\left(\beta_{sh}\frac{I_s}{N_s} + \beta_{hh}\frac{I_h}{N_h}\right)}{\left(\beta_{sh}\frac{I_s}{N_s} + \beta_{hh}\frac{I_h}{N_h}\right) + \mu_h}\right) \cdot \left(\frac{\nu_h}{\nu_h + \mu_h}\right).$$

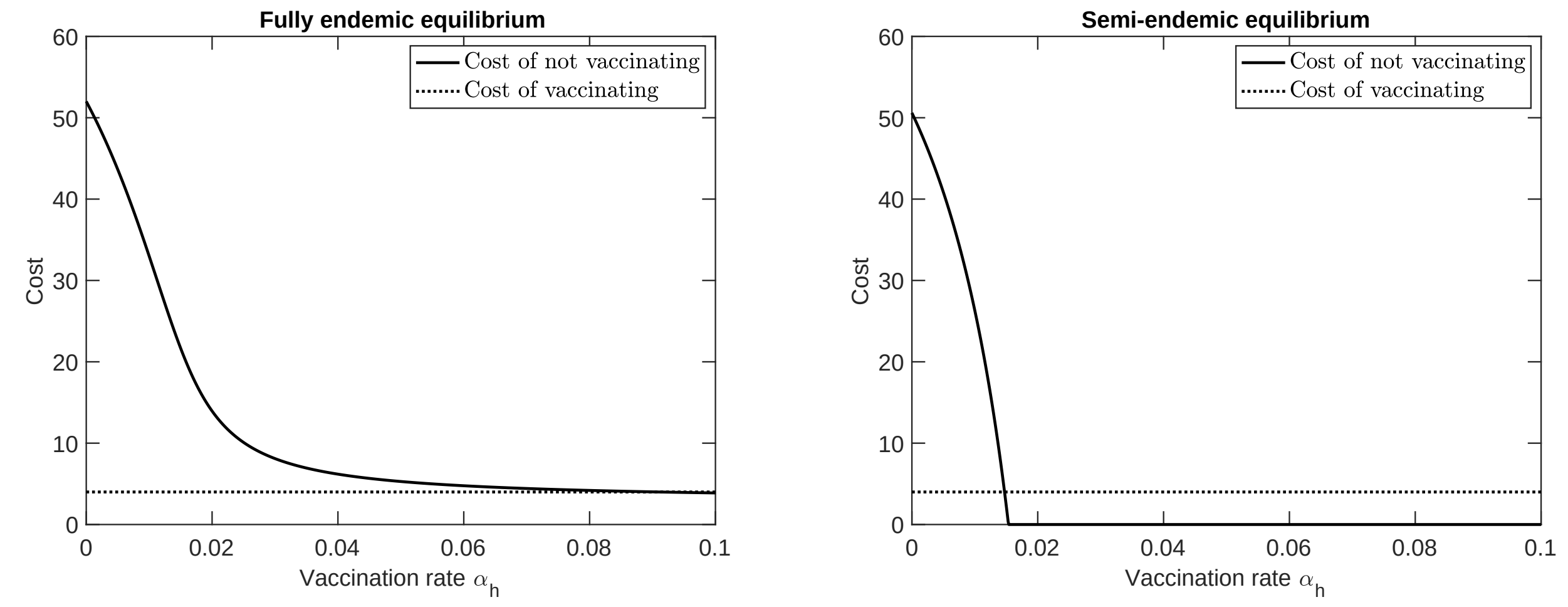

Fig. 2: Costs vs. Vaccination rate when the effective human-to-human transmission rate is high, $\beta_{hh} = 60$. Left: the fully endemic state. Right: the semi-endemic state ($\beta_{ss} = 30 < (\mu_s + d_s + \rho_s) \cdot \frac{\mu_s+\nu_s}{\nu_s}$). The same scenario occurs when $\beta_{sh} = 0$ and β_{ss} is arbitrary. All other parameters as in Table 1.

Conclusions

- We provided closed form formulas of the equilibrium states of the dynamics.
- We showed a potential existence of the previously neglected semi-endemic equilibrium, in which there is no infection in the animal population and the disease still persists in the human population.
- We demonstrated that α_{NE} is about 10 times more sensitive to parameters related to vectors than to a corresponding parameter related to humans. It is therefore important to provide accurate estimates.
- As cases of MPX become increasingly reported among humans, we hope that the models like ours may serve as a predictive tool to better study the spread of MPX.

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