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Module 2: Mathematical Models of Infectious Diseases SISMID 2024

Basics of SIR models

Review of key points from day 1

Review of basic compartmental models

- S, I, and R represent the number of individuals currently susceptible, infected, and recovered
- Contact process quantifies the rate at which susceptibles and infecteds interact
- Transmission parameter: β is rate of contact * probability of infection given contact. High β = more transmission
- Higher recovery rate, γ = shorter duration of infection

Heterogeneity in disease transmission

Using foot-and-mouth disease as a motivating example

Learning Objectives

- Understand how heterogeneity can present in disease systems
- Understand how and when to use multi-class SIR models
- Understand how and when to use multi-class SIR models with transitions

between classes

Heterogeneity in disease systems

- Foot-and-mouth disease (FMD)
 - Caused by the FMD virus (FMDV)
 - Affects multiple species of mammals (including cows, sheep, goats, pigs)
 - Can cause blisters around the hooves and mouth and spontaneous abortions
 - Reduces milk yield
 - ~\$3 billion USD of economic impact in India alone

Heterogeneity in FMD

Where does heterogeneity appear in the case of FMD?

- Pathogen: FMDV affects species differently
- Host: animals have different lifespans and behaviours
- Policy: some countries vaccinate cows, others also vaccinate pigs
- Environment: Contact rates within and between species can differ based on

how animals are kept

Heterogeneity in FMD



- FMDV is highly transmissible in pigs compared to other species
- Pigs tend to have a shorter lifespan in animal husbandry contexts (1 year or less)
- Pigs are not always vaccinated in FMD control programs



- Cattle are more susceptible to FMD compared to other species

- Cattle can live up to 14 years in some animal husbandry contexts (e.g., in India)

 Cattle are almost always vaccinated in FMD control programs

- Recovery:

••	
$\frac{dS}{dt} = \delta N - \beta S I \qquad - \delta S$	$\frac{dS}{dt} = \delta N - \beta S I \qquad - \delta S$
$\frac{dI}{dt} = \beta SI - \gamma_{ij}I - \alpha I - \delta I$	$\frac{dI}{dt} = \beta SI - \gamma_{\textcircled{a}}I - \alpha I - \delta I$
$\frac{dR}{dt} = \gamma_{ij}I - \delta R$	$\frac{dR}{dt} = \gamma_{\bigcirc}I \qquad -\delta R$

- Disease severity:

••			
$\frac{dS}{dt} = \delta N - \beta S I \qquad \qquad - \delta S$	$\frac{dS}{dt} = \delta N - \beta S I \qquad - \delta S$		
$\frac{dI}{dt} = \beta SI - \gamma I - \alpha \mathbf{w} I - \delta I$	$\frac{dI}{dt} = \beta SI - \gamma I - \alpha_{\textcircled{o}}I - \delta I$		
$\frac{dR}{dt} = \gamma I - \delta R$	$\frac{dR}{dt} = \gamma I - \delta R$		

- Lifespan:

••			
$\frac{dS}{dt} = \delta_{ij}N - \beta SI \qquad - \delta_{ij}S$	$\frac{dS}{dt} = \delta_{\textcircled{o}}N - \beta SI \qquad - \delta_{\textcircled{o}}S$		
$\frac{dI}{dt} = \beta SI - \gamma I - \alpha I - \delta_{ij}I$	$\frac{dI}{dt} = \beta SI - \gamma I - \alpha I - \delta_{\textcircled{a}}I$		
$\frac{dR}{dt} = \gamma I - \delta \mathbf{v} R$	$\frac{dR}{dt} = \gamma I - \delta_{\mathfrak{W}}R$		

- Contact and transmissibility:



How do we model those differences?

- 1. Make 2 separate models
- 2. Make one model with both species

🠷 and 🐮 are different!

How do we model those differences?

1. Make 2 separate models

Why is this a bad idea?

2. Make one model with both species



How do we model those differences?

- 1. Make 2 separate models
- 2. Make one model with both species \checkmark

$$\frac{dS_{ij}}{dt} = \delta_{ij}N_{ij} - (\beta_{ij}I_{ij}I_{ij} + \beta_{ij}I_{ij})S_{ij} - \delta_{ij}S_{ij}$$

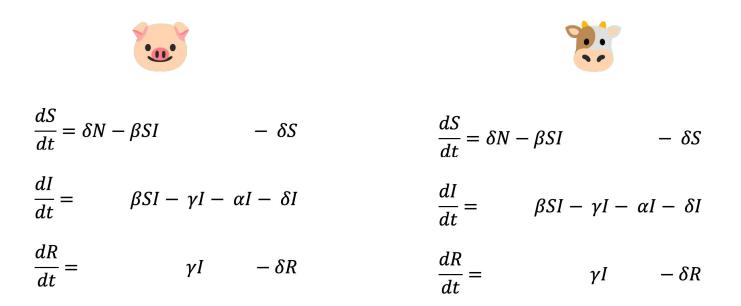
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$$\frac{dI_{ij}}{dt} = (\beta_{ij}I_{ij}I_{ij} + \beta_{ij}I_{ij})S_{ij} - \gamma_{ij}I_{ij} - \alpha_{ij}I_{ij} - \delta_{ij}I_{ij}$$

$$\frac{dI_{ij}}{dt} = (\beta_{ij}I_{ij}I_{ij} + \beta_{ij}I_{ij})S_{ij} - \gamma_{ij}I_{ij} - \alpha_{ij}I_{ij} - \delta_{ij}I_{ij}$$

$$\frac{dR_{ij}}{dt} = \gamma_{ij}I_{ij} - \delta_{ij}R_{ij}$$

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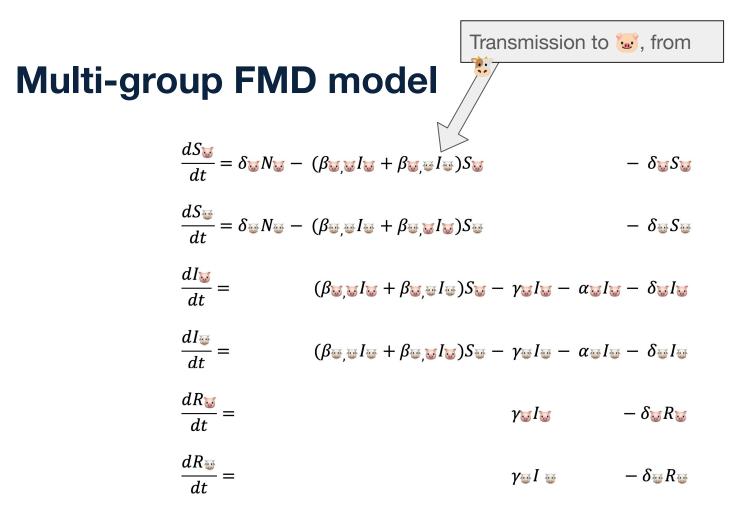
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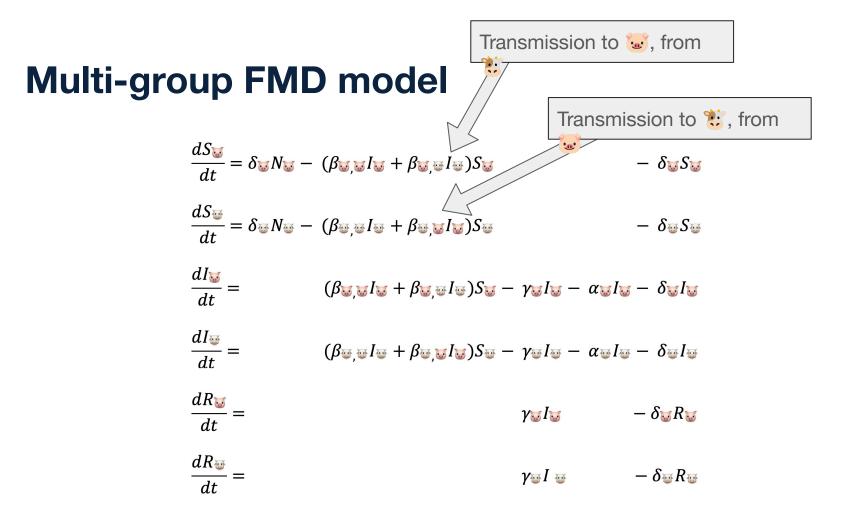
$$\frac{dI_{ij}}{dt} = (\beta_{ij}I_{ij}I_{ij} + \beta_{ij}I_{ij})S_{ij} - \gamma_{ij}I_{ij} - \alpha_{ij}I_{ij} - \delta_{ij}I_{ij}$$

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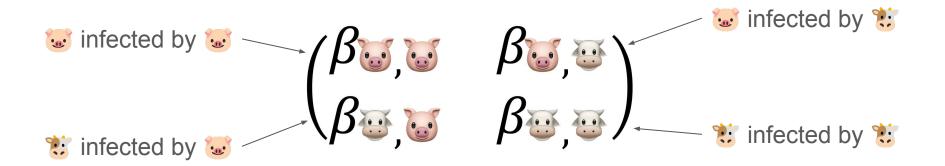
$$\frac{dR_{ij}}{dt} = \gamma_{ij}I_{ij} - \delta_{ij}R_{ij}$$

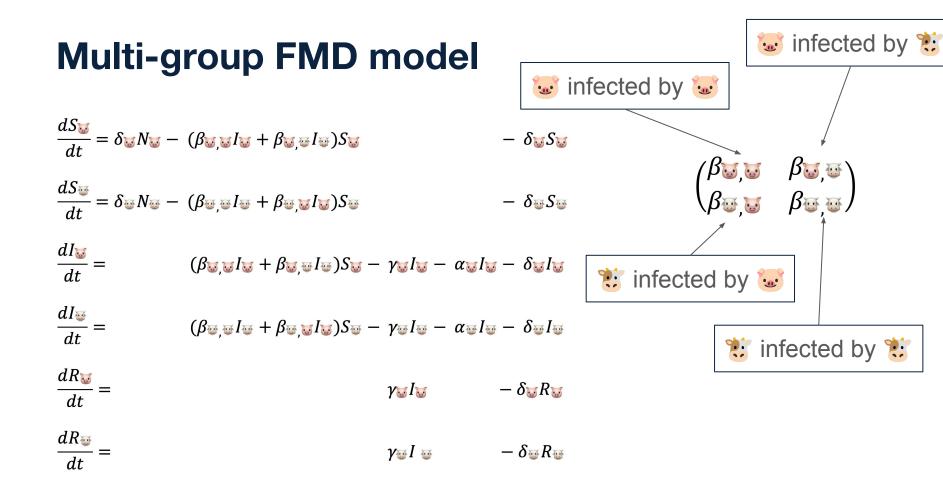
$$\frac{dR_{ij}}{dt} = \gamma_{ij}I_{ij} - \delta_{ij}R_{ij}$$





Instead of having a single β term for transmission, and a single I term for one infected population, we use a *mxm* matrix of β values for *m* different populations in our model.





FMD doesn't just

affect pigs and

cows. Can also

infect goats, sheep,

and buffalo.

$$\begin{array}{c} \beta_{{\scriptscriptstyle {\scriptstyle {\scriptstyle \lor}}},{\scriptscriptstyle {\scriptstyle \lor}}} & \beta_{{\scriptscriptstyle {\scriptstyle \lor}},{\scriptscriptstyle {\scriptstyle \ominus}}} \\ \beta_{{\scriptscriptstyle {\scriptstyle \ominus}},{\scriptscriptstyle {\scriptstyle \lor}}} & \beta_{{\scriptscriptstyle {\scriptstyle \ominus}},{\scriptscriptstyle {\scriptscriptstyle \ominus}}} \end{array} \end{array}$$

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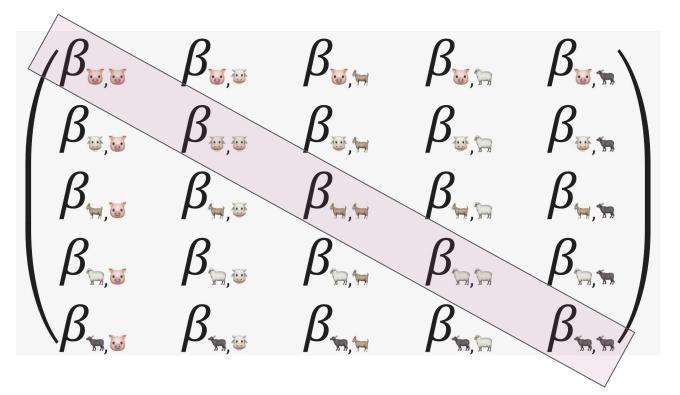


When you have additional complexity in your system, matrices allow you to add complexity to your model without rewriting equations.



Transmission within groups is on the diagonal of the matrix, and transmission between groups is on the off-diagonal.

What happens if off-diagonal values are 0?



Let's interpret this matrix together. In which pair of species does the highest transmission occur? Lowest transmission?

$$\begin{pmatrix} \beta_{\underline{w},\underline{w}} = 1 & \beta_{\underline{w},\underline{w}} = 0.3 & \beta_{\underline{w},\underline{w}} = 0.1 & \beta_{\underline{w},\underline{w}} = 0.2 & \beta_{\underline{w},\underline{w}} = 0.3 \\ \beta_{\underline{w},\underline{w}} = 50 & \beta_{\underline{w},\underline{w}} = 15 & \beta_{\underline{w},\underline{w}} = 5 & \beta_{\underline{w},\underline{w}} = 10 & \beta_{\underline{w},\underline{w}} = 15 \\ \beta_{\underline{w},\underline{w}} = 10 & \beta_{\underline{w},\underline{w}} = 3 & \beta_{\underline{w},\underline{w}} = 1 & \beta_{\underline{w},\underline{w}} = 2 & \beta_{\underline{w},\underline{w}} = 3 \\ \beta_{\underline{w},\underline{w}} = 20 & \beta_{\underline{w},\underline{w}} = 6 & \beta_{\underline{w},\underline{w}} = 2 & \beta_{\underline{w},\underline{w}} = 6 \\ \beta_{\underline{w},\underline{w}} = 60 & \beta_{\underline{w},\underline{w}} = 18 & \beta_{\underline{w},\underline{w}} = 6 & \beta_{\underline{w},\underline{w}} = 12 & \beta_{\underline{w},\underline{w}} = 18 \end{pmatrix}$$

Let's interpret this matrix together. Based on this information, which animal transmits the most FMD? Which animal is the most susceptible to FMD?

$$\begin{pmatrix} \beta_{\underline{w},\underline{w}} = 1 & \beta_{\underline{w},\underline{w}} = 0.3 & \beta_{\underline{w},\underline{w}} = 0.1 & \beta_{\underline{w},\underline{w}} = 0.2 & \beta_{\underline{w},\underline{w}} = 0.3 \\ \beta_{\underline{w},\underline{w}} = 50 & \beta_{\underline{w},\underline{w}} = 15 & \beta_{\underline{w},\underline{w}} = 5 & \beta_{\underline{w},\underline{w}} = 10 & \beta_{\underline{w},\underline{w}} = 15 \\ \beta_{\underline{w},\underline{w}} = 10 & \beta_{\underline{w},\underline{w}} = 3 & \beta_{\underline{w},\underline{w}} = 1 & \beta_{\underline{w},\underline{w}} = 2 & \beta_{\underline{w},\underline{w}} = 3 \\ \beta_{\underline{w},\underline{w}} = 20 & \beta_{\underline{w},\underline{w}} = 6 & \beta_{\underline{w},\underline{w}} = 2 & \beta_{\underline{w},\underline{w}} = 6 \\ \beta_{\underline{w},\underline{w}} = 60 & \beta_{\underline{w},\underline{w}} = 18 & \beta_{\underline{w},\underline{w}} = 6 & \beta_{\underline{w},\underline{w}} = 12 & \beta_{\underline{w},\underline{w}} = 18 \end{pmatrix}$$

Pause and reflect

- Models can have multiple groups
- Groups can be constructed in different ways
- Capturing transmission between groups is important
 - No transmission between groups means we can just make individual models
 - (What value(s) do the off-diagonal elements of the beta matrix have in this case?)

Can individuals change groups?

So far we've looked at groups where individuals will never change group affiliation over time. Cows will stay cows, pigs will stay pigs, etc.

Can you think of some groupings of a population that are not fixed? i.e., where individuals can be in one group at one time, and another group at another time?

Can individuals change groups?

This question is driven by the biology of the system.

In the Indian context: stray cattle exist, and many stray cattle used to be managed cattle.

Stray cattle move around in different ways compared to managed cattle and have a higher death rate.

We wanted to know whether including stray cattle explicitly in our model improved our model fit. There are two parts to adding stray cattle to the model. One is to add the transition from managed to stray, and another is the addition of stray as a group (along with i i i i i).

Transition rates between classes

Key assumptions:

- 1. Managed cattle can become stray cattle
- 2. Stray cattle CANNOT become managed cattle

In the case of cattle, they are moving at a rate π from managed cattle to unmanaged cattle. *NB: we'll practice this concept in the R session today*

However, this transition is directional, as stray cattle cannot become managed cattle in our model. The rate of movement of stray cattle to managed cattle is therefore 0.

$$\frac{dS_{\varpi}}{dt} = \delta_{\varpi} N_{\varpi} - (\beta_{\varpi, \varpi} I_{\varpi} + \beta_{\varpi, \varpi} I_{\varpi}) S_{\varpi} - \delta_{\varpi} S_{\varpi} - \pi S_{\varpi}$$

$$\frac{dS_{\varpi}}{dt} = (\beta_{\varpi, \varpi} I_{\varpi} + \beta_{\varpi, \varpi} I_{\varpi}) S_{\varpi} - \delta_{\varpi} S_{\varpi} + \pi S_{\varpi}$$

$$\frac{dI_{\varpi}}{dt} = (\beta_{\varpi, \varpi} I_{\varpi} + \beta_{\varpi, \varpi} I_{\varpi}) S_{\varpi} - \gamma_{\varpi} I_{\varpi} - \alpha_{\varpi} I_{\varpi} - \delta_{\varpi} I_{\varpi} - \pi I_{\varpi}$$

$$\frac{dI_{\varpi}}{dt} = (\beta_{\varpi, \varpi} I_{\varpi} + \beta_{\varpi, \varpi} I_{\varpi}) S_{\varpi} - \gamma_{\varpi} I_{\varpi} - \alpha_{\varpi} I_{\varpi} - \delta_{\varpi} I_{\varpi} + \pi I_{\varpi}$$

$$\frac{dR_{\varpi}}{dt} = \gamma_{\varpi} I_{\varpi} - \delta_{\varpi} R_{\varpi} - \pi R_{\varpi}$$

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 $\frac{dS_{\textcircled{\tiny{\tiny{\odot}}}}}{dt} = \delta_{\textcircled{\tiny{\tiny{\odot}}}} N_{\textcircled{\tiny{\tiny{\odot}}}} - (\beta_{\textcircled{\tiny{\tiny{\boxdot}}},\textcircled{\tiny{\tiny{\odot}}}} I_{\textcircled{\tiny{\boxdot}}} + \beta_{\textcircled{\tiny{\tiny{\boxdot}}},\textcircled{\tiny{\textcircled{\textcircled{}}}}} I_{\textcircled{\tiny{\textcircled{}}}}) S_{\textcircled{\tiny{\textcircled{}}}}$ $-\delta_{\overline{\oplus}}S_{\overline{\oplus}}-\pi S_{\overline{\oplus}}$ $\frac{dS_{m}}{dt} =$ $(\beta_{\underline{m}},\underline{m}I_{\underline{m}} + \beta_{\underline{m}},\underline{\omega}I_{\overline{\omega}})S_{\underline{m}}$ $-\delta_{\nabla}S_{\nabla} + \pi S_{\Theta}$ $\frac{dI_{\textcircled{w}}}{dt} =$ $(\beta_{\overline{\Theta},\overline{\Theta}}I_{\overline{\Theta}}+\beta_{\overline{\Theta},\overline{\Sigma}}I_{\overline{\Sigma}})S_{\overline{\Theta}}-\gamma_{\overline{\Theta}}I_{\overline{\Theta}}-\alpha_{\overline{\Theta}}I_{\overline{\Theta}}-\delta_{\overline{\Theta}}I_{\overline{\Theta}}-\pi I_{\overline{\Theta}}$ $\frac{dI_{m}}{dt} =$ $(\beta_{tra} tra I_{tra} + \beta_{tra} \blacksquare I_{\boxdot})S_{tra} - \gamma_{tra}I_{tra} - \alpha_{tra}I_{tra} - \delta_{tra}I_{tra} + \pi I_{\boxdot}$ $\frac{dR_{\textcircled{}}}{dt} =$ $-\delta_{\overline{\Theta}}R_{\overline{\Theta}}|-\pi R_{\overline{\Theta}}$ γ⊕I⊕ $\frac{dR_{m}}{dt} =$ $-\delta_{\Im}R_{\Im} + \pi R_{\odot}$ $\gamma_{m}I_{m}$

 π = rate of becoming stray

 $\frac{dS_{\textcircled{\tiny{\tiny{\odot}}}}}{dt} = \delta_{\textcircled{\tiny{\tiny{\odot}}}} N_{\textcircled{\tiny{\tiny{\odot}}}} - (\beta_{\textcircled{\tiny{\tiny{\boxdot}}},\textcircled{\tiny{\tiny{\odot}}}} I_{\textcircled{\tiny{\boxdot}}} + \beta_{\textcircled{\tiny{\tiny{\boxdot}}},\textcircled{\tiny{\textcircled{\textcircled{}}}}} I_{\textcircled{\tiny{\textcircled{}}}}) S_{\textcircled{\tiny{\textcircled{}}}}$ $-\delta_{\overline{\oplus}}S_{\overline{\oplus}}-\pi S_{\overline{\oplus}}$ $\frac{dS_{m}}{dt} =$ $(\beta_{\underline{m}},\underline{m}I_{\underline{m}} + \beta_{\underline{m}},\underline{\omega}I_{\overline{\omega}})S_{\underline{m}}$ $-\delta_{\nabla}S_{\nabla} + \pi S_{\Theta}$ $\frac{dI_{\textcircled{w}}}{dt} =$ $(\beta_{\overline{\Theta},\overline{\Theta}}I_{\overline{\Theta}}+\beta_{\overline{\Theta},\overline{\Sigma}}I_{\overline{\Sigma}})S_{\overline{\Theta}}-\gamma_{\overline{\Theta}}I_{\overline{\Theta}}-\alpha_{\overline{\Theta}}I_{\overline{\Theta}}-\delta_{\overline{\Theta}}I_{\overline{\Theta}}-\pi I_{\overline{\Theta}}$ $\frac{dI_{m}}{dt} =$ $(\beta_{tra} tra I_{tra} + \beta_{tra} \blacksquare I_{\boxdot})S_{tra} - \gamma_{tra}I_{tra} - \alpha_{tra}I_{tra} - \delta_{tra}I_{tra} + \pi I_{\boxdot}$ $\frac{dR_{\textcircled{}}}{dt} =$ $-\delta_{\overline{\Theta}}R_{\overline{\Theta}}|-\pi R_{\overline{\Theta}}$ γ⊕I⊕ $\frac{dR_{m}}{dt} =$ $-\delta_{\Im}R_{\Im} + \pi R_{\odot}$ $\gamma_{m}I_{m}$

 π = rate of becoming stray

$$\frac{dS_{\overline{w}}}{dt} = \delta_{\overline{w}} N_{\overline{w}} - (\beta_{\overline{w}}, \overline{w} I_{\overline{w}} + \beta_{\overline{w}}, \overline{w} I_{\overline{w}}}) S_{\overline{w}} - \delta_{\overline{w}} S_{\overline{w}} - \pi S_{\overline{w}}$$

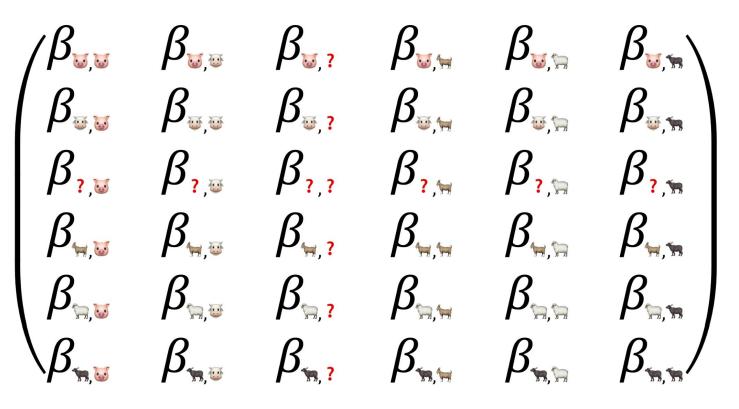
$$\frac{dS_{\overline{w}}}{dt} = (\beta_{\overline{w}}, \overline{w} I_{\overline{w}} + \beta_{\overline{w}}, \overline{w} I_{\overline{w}}}) S_{\overline{w}} - \delta_{\overline{w}} S_{\overline{w}} + \pi S_{\overline{w}}$$

$$\frac{dI_{\overline{w}}}{dt} = (\beta_{\overline{w}}, \overline{w} I_{\overline{w}} + \beta_{\overline{w}}, \overline{w} I_{\overline{w}}}) S_{\overline{w}} - \gamma_{\overline{w}} I_{\overline{w}} - \alpha_{\overline{w}} I_{\overline{w}} - \delta_{\overline{w}} I_{\overline{w}} + \pi I_{\overline{w}}$$

$$\frac{dI_{\overline{w}}}{dt} = (\beta_{\overline{w}}, \overline{w} I_{\overline{w}} + \beta_{\overline{w}}, \overline{w} I_{\overline{w}}}) S_{\overline{w}} - \gamma_{\overline{w}} I_{\overline{w}} - \alpha_{\overline{w}} I_{\overline{w}} - \delta_{\overline{w}} I_{\overline{w}} + \pi I_{\overline{w}}$$

$$\frac{dR_{\overline{w}}}{dt} = \gamma_{\overline{w}} I_{\overline{w}} - \delta_{\overline{w}} R_{\overline{w}} - \pi R_{\overline{w}}$$

Can individuals change groups?



Impact of stray cattle on model accuracy

- We found that adding stray cattle to our FMD model did, in fact increase accuracy.
- However, the increase in accuracy was small

Year	RMSE (S-)	RMSE (S+)	r (S-)	r (S+)
2017	0.627	0.625	0.230	0.234
2018	0.661	0.658	0.379	0.375
2019	0.686	0.683	0.527	0.527
2020	0.715	0.713	0.428	0.430

- Conclusion: at the levels of stray cattle seen in India, we do not need to explicitly include them in our modelling!

Link to poster: https://scholarsphere.psu.edu/resources/ebe9cf79-b9d8-4342-a8e4-584040f9ab6d

Directional vs. non-directional transitions

Can you think of some other situations where individuals only change groups in a directional way?

- Åging (unless you're Éenjamin Button)
- Life stages in animals

What about transitions that are non-directional?

- Risk groups in STI settings (using a condom vs. not using a condom)
- Socioeconomic status
- Number of contacts

Remember, in public health/policy, we are often discussing interventions that may move individuals from one group to another group.

Review

Use the worksheet at the link below to review concepts from the heterogeneity lecture:

https://forms.gle/NUkMGicmrTBA7TGP6