Using moment equations to understand heterogeneity

Definition

We want to write $Y_o(v; D)$ for **T**ype, **o**rder, **v**ariable, and **D**omain.

We define total as follows: $T_o(v; D) = \int v(a)^o D(a) da$. Since we're mainly interested with susceptibility for now, T_o is represents $T_o(.; S)$.

We define $M_i = T_i / T_0$. Then, M_1 is the mean susceptibility and $\kappa = \frac{M_2 M_0}{M_1^2} - 1$ is the squared coefficient of variance (CV).

SI example

We have $\dot{S}(a) = -\Lambda\sigma(a)S(a)$. Integrating gives us $\dot{T}_0 = -\Lambda T_1$. More generally, we have $\dot{T}_i = -\Lambda T_{i+1}$. Given that M_1 is the mean susceptibility, we can also write:

$$\dot{S} = -\Lambda M_1 S$$

Using M defined above, we also have the following equations: $\dot{M}_i = -\Lambda(M_{i+1} - M_i M_1)$.

Given that $M_2 = (1 + \kappa)M^2$ and assuming that κ stays constant, we can integrate the equation above to obtain the following equation:

$M = \hat{M}S^\kappa$, where $\hat{M}$ is the mean susceptibility of the susceptible population at a disease free equilibrium.

Idea 1 - $\kappa_i = \frac{M_i M_{i-2}}{M_{i-1}^2} - 1$

$$
\begin{aligned}
\dot{\kappa}_i &= \frac{M_{i-2}M_{i-1}\dot{M}_i + M_{i-1}M_i\dot{M}_{i-2} - 2M_{i-2}M_i\dot{M}_{i-1}}{M_{i-1}^3} \\
&= -\Lambda\frac{M_{i-2}M_{i-1}(M_{i+1} - M_iM_1) + M_{i-1}M_i(M_{i-1} - M_{i-2}M_1) - 2M_{i-2}M_i(M_i - M_{i-1}M_1)}{M_{i-1}^3} \\
&= -\Lambda\frac{M_{i-2}M_{i-1}M_{i+1} + M_{i-1}^2 M_i - 2M_{i-2}M_i^2}{M_{i-1}^3} \\
&= -\Lambda\frac{M_{i-2}(\kappa_{i+1} + 1)M_i^2 + M_{i-1}^2 M_i - 2M_{i-2}M_i^2}{M_{i-1}^3} \\
&= -\Lambda\frac{(\kappa_{i+1} - 1)M_{i-2}M_i^2 + M_{i-1}^2 M_i}{M_{i-1}^3} \\
&= -\Lambda\frac{(\kappa_{i+1} - 1)(\kappa_i + 1)M_i M_{i-1}^2 + M_{i-1}^2 M_i}{M_{i-1}^3} \\
&= -\Lambda\frac{(\kappa_{i+1}\kappa_i - \kappa_i + \kappa_{i+1})M_i}{M_{i-1}}
\end{aligned}
$$

Idea 2 - $\kappa_i = \frac{M_i}{M_{i-1}M_1} - 1$

$$\dot{\kappa}_i = \frac{M_{i-1}M_1\dot{M}_i - M_iM_1\dot{M}_{i-1} - M_iM_{i-1}\dot{M}_1}{M_{i-1}^2M_1^2}$$

$$= -\Lambda\frac{M_{i-1}M_1(M_{i+1} - M_iM_1) - M_iM_1(M_i - M_{i-1}M_1) - M_iM_{i-1}(M_2 - M_1^2)}{M_{i-1}^2M_1^2}$$

$$= -\Lambda\frac{M_{i-1}M_1M_{i+1} - M_iM_1M_i - M_iM_{i-1}M_2 + M_iM_{i-1}M_1^2}{M_{i-1}^2M_1^2}$$

$$= -\Lambda\frac{(\kappa_{i+1} + 1)M_iM_{i-1}M_1^2 - M_iM_1M_i - (\kappa_2 + 1)M_iM_{i-1}M_1^2 + M_iM_{i-1}M_1^2}{M_{i-1}^2M_1^2}$$

$$= -\Lambda\frac{(\kappa_{i+1} + 1)M_iM_{i-1}M_1 - (\kappa_i + 1)M_{i-1}M_iM_1 - \kappa_2 M_iM_{i-1}M_1}{M_{i-1}^2M_1}$$

$$= -\Lambda\frac{(\kappa_{i+1} + 1)M_i - (\kappa_i + 1)M_i - \kappa_2 M_i}{M_{i-1}}$$

$$= -\Lambda M_i\frac{\kappa_{i+1} - (\kappa_2 + \kappa_i)}{M_{i-1}}$$

$$= -\Lambda M_1(\kappa_i + 1)\{\kappa_{i+1} - (\kappa_2 + \kappa_i)\}$$

When $i = 2$, we have $\dot{\kappa} = -\Lambda M(\kappa + 1)(\kappa_3 - 2\kappa)$, where $\kappa = \kappa_2$. For gamma distribution, $\kappa_3 = 2\kappa$. Let's assume that $r = \kappa_3/\kappa$ stays constant. Then, we have $\dot{\kappa} = -\Lambda M(r - 2)(\kappa + 1)(\kappa)$. We can do this:

$$\frac{d\kappa}{dt} = \frac{d\kappa}{dS}\frac{dS}{dt}$$

$$-\Lambda M(r - 2)(\kappa + 1)(\kappa) = -\Lambda MS\frac{d\kappa}{dS}$$

$$(r - 2)(\kappa + 1)(\kappa) = S\frac{d\kappa}{dS}$$

$$\frac{(r - 2)}{S} = \frac{1}{\kappa(\kappa + 1)}\frac{d\kappa}{dS}$$

$$\int\frac{(r - 2)}{S}dS = \int\frac{1}{\kappa(\kappa + 1)}d\kappa$$

$$(r - 2)\log(S) = \log(\kappa) - \log(\kappa + 1) + C$$

We let the initial values $(S(0), \kappa(0)) = (1, \hat{\kappa})$, then we have $C = \log(\frac{\hat{\kappa}+1}{\hat{\kappa}})$. We can continue with the derivative:

$$\log(S^{r-2}) = \log(e^C\frac{\kappa}{\kappa + 1})$$

$$S^{r-2} = e^C\frac{\kappa}{\kappa + 1}$$

$$S^{r-2}(\kappa + 1) = e^C\kappa$$

$$S^{r-2} = (e^C - S^{r-2})\kappa$$

$$\kappa = \frac{S^{r-2}}{e^C - S^{r-2}}$$

How accurate is this?

Ex 1 - lognormal distribution

**Comparison of 3 simulations**   Linear equation:

$$r \approx (\hat{r} - 2)S + 2$$

- Heterogeneous model
- Approximated model: linear equation for κ_3/κ_2 coupled with approximated equation for κ
- Approximated model: constant κ

```
source("plotFunctions.R")
baseSim <- list(r.lnorm.het, r.lnorm.app1, r.lnorm.app2)
name <- c("Heterogeneous", "Approximation 1", "Approximation 2")
plotSim(baseSim, name)
```
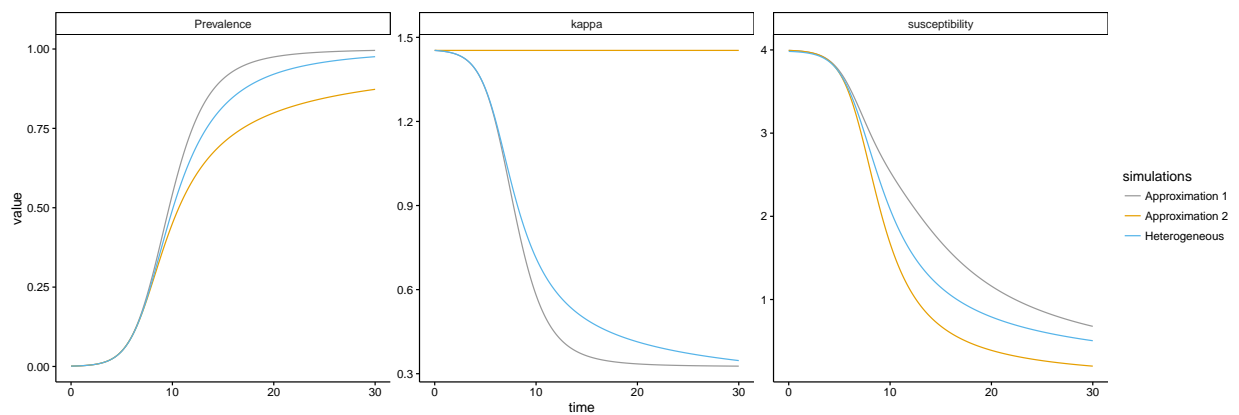

Linear extrapolation of the κ_3/κ_2 ratio approximates the prevalence trajectory better sice it matches the initial κ trajectory but it doesn't approximate κ so well near the equilibrium.... How does r vs S look like?

```
plot(cbind(totS, r= k3/k2), type = "l")
lines(cbind(totS,( k3[1]/k2[1] - 2)*totS + 2), col = 2)
```
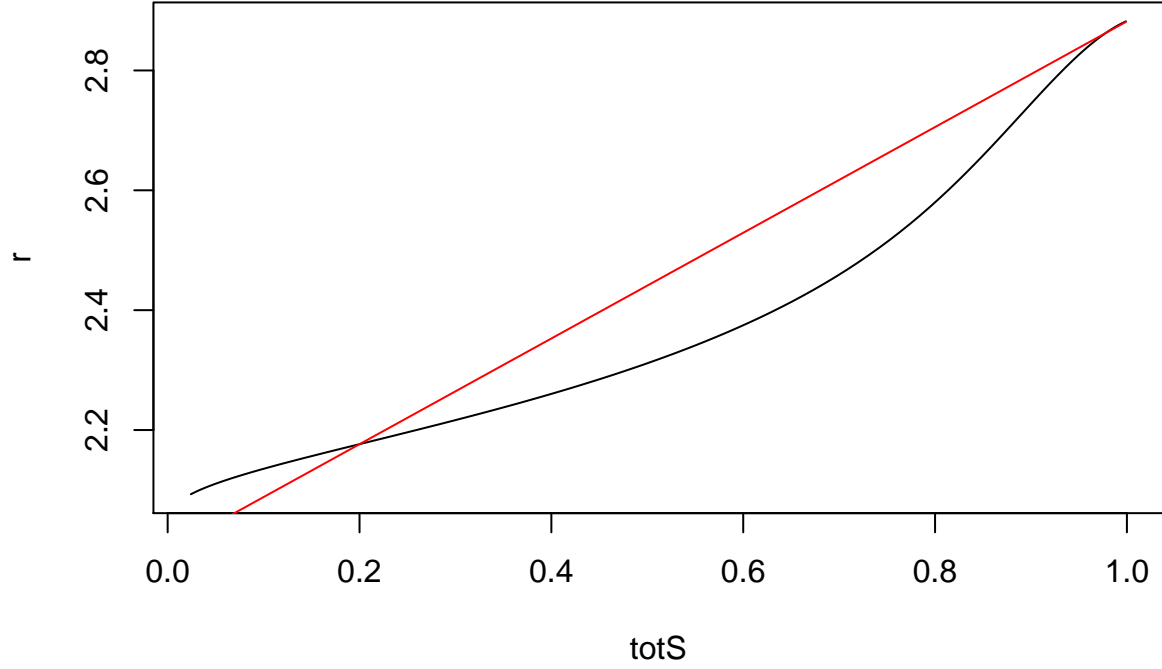
Can we get some understanding for κ_3/κ_2? Equation for $\dot{\kappa}$ shows us that the equilibrium value of $\kappa^* = \kappa_3/2$ but this might give us something else... Given that $\dot{\kappa}_3 = -\Lambda M(\kappa_3 + 1)(\kappa_4 - (\kappa_2 + \kappa_3))$, we can find the equation for the derivative of r:

$$\dot{r} = \frac{\dot{\kappa}_3 \kappa - \dot{\kappa} \kappa_3}{\kappa^2}$$

$$= -\Lambda M \frac{(\kappa_3 + 1)(\kappa_4 - (\kappa + \kappa_3))\kappa - (\kappa + 1)(\kappa_3 - 2\kappa)\kappa_3}{\kappa^2}$$

$$= -\Lambda M \frac{(\kappa_3 \kappa_4 - \kappa\kappa_3 - \kappa_3^2 + \kappa_4 - \kappa - \kappa_3)\kappa - (\kappa\kappa_3 - 2\kappa^2 + \kappa_3 - 2\kappa)\kappa_3}{\kappa^2}$$

$$= -\Lambda M \frac{(\kappa\kappa_3\kappa_4 - \kappa^2\kappa_3 - \kappa\kappa_3^2 + \kappa\kappa_4 - \kappa^2 - \kappa\kappa_3) - (\kappa\kappa_3^2 - 2\kappa^2\kappa_3 + \kappa_3^2 - 2\kappa\kappa_3)}{\kappa^2}$$

$$= -\Lambda M \frac{\kappa\kappa_3\kappa_4 - \kappa^2\kappa_3 - \kappa\kappa_3^2 + \kappa\kappa_4 - \kappa^2 - \kappa\kappa_3 - \kappa\kappa_3^2 + 2\kappa^2\kappa_3 - \kappa_3^2 + 2\kappa\kappa_3}{\kappa^2}$$

$$= -\Lambda M \frac{\kappa\kappa_3\kappa_4 + \kappa^2\kappa_3 - 2\kappa\kappa_3^2 + \kappa\kappa_4 - \kappa^2 + \kappa\kappa_3 - \kappa_3^2}{\kappa^2}$$

$$= -\Lambda M(\kappa_4 r + \kappa_3 - 2\kappa_3 r + \frac{\kappa_4}{\kappa_3}r - 1 + r - r^2)$$

$$= -\Lambda M(\frac{\kappa_4}{\kappa_3}\kappa r^2 + \kappa r - 2\kappa r^2 + \frac{\kappa_4}{\kappa_3}r - 1 + r - r^2)$$

$$= -\Lambda M((\frac{\kappa_4}{\kappa_3}\kappa - 2\kappa - 1)r^2 + (\frac{\kappa_4}{\kappa_3} + \kappa + 1)r - 1)$$

or... we can do this...

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$$\dot{r} = \frac{\dot{\kappa}_3}{\kappa} - \frac{\dot{\kappa}\kappa_3}{\kappa^2}$$
$$= -\Lambda M(\kappa_3 + 1)(\frac{\kappa_4}{\kappa_3}r - (1 + r)) + \Lambda M(\kappa + 1)(r - 2)r$$

SIS example

Here is a simple SIS model: $\dot{S}(a) = \mu(N(a) - S(a)) - \Lambda\sigma(a)S(a)$, where $N(a)$ is the initial distribution of the susceptible individuals in a disease free equilibrium. We are going to define $T_o(N) = T_o(v; N)$. For this model, we have $\dot{T}_i = \mu(T_i(N) - T_i) - \Lambda T_{i+1}$. Using chain rule, we can also get an equation for $M = M_1$:

$$\dot{M}_i = \frac{\dot{T}_i}{T_0} - \frac{\dot{T}_0 T_i}{T_0^2}$$
$$= (\mu(T_i(N)/T_0 - M_i) - \Lambda M_{i+1}) - \mu(M_i T_0(N)/T_0 - M_i) + \Lambda M_i M_1$$
$$= \mu(M_i(N) - M_i)\frac{T_0(N)}{T_0} - \Lambda(M_{i+1} - M_i M_1)$$
$$= \mu(M_i(N) - M_i)/T_0 - \Lambda\kappa_{i+1}M_i M_1$$

Can we get some understanding for κ?

$$\dot{\kappa}_i = \frac{M_{i-1}M_1\dot{M}_i - M_i M_1\dot{M}_{i-1} - M_i M_{i-1}\dot{M}_1}{M_{i-1}^2 M_1^2}$$
$$= \mu\frac{M_{i-1}M_1(M_i(N) - M_i) - M_i M_1(M_{i-1}(N) - M_{i-1}) - M_i M_{i-1}(M_1(N) - M_1)}{M_{i-1}^2 M_1^2 T_0}$$
$$- \Lambda M_1(\kappa_i + 1)\{\kappa_{i+1} - (\kappa + \kappa_i)\}$$
$$= \mu\frac{M_{i-1}M_1 M_i(N) - M_i M_1 M_{i-1}(N) - M_i M_{i-1}M_1(N) + M_1 M_{i-1}M_i}{M_{i-1}^2 M_1^2 T_0}$$
$$- \Lambda M_1(\kappa_i + 1)\{\kappa_{i+1} - (\kappa + \kappa_i)\}$$
$$= \mu\frac{M_{i-1}M_1 M_i(N) - M_i M_1 M_{i-1}(N) - M_i M_{i-1}M_1(N)}{M_{i-1}^2 M_1^2 T_0}$$
$$+ \mu\frac{\kappa_i + 1}{T_0} - \Lambda M_1(\kappa_i + 1)\{\kappa_{i+1} - (\kappa + \kappa_i)\}$$
$$= \mu\frac{(\kappa_i(N) + 1)M_{i-1}(N)M_1(N) - (\kappa_i + 1)M_1 M_{i-1}(N) - (\kappa_i + 1)M_{i-1}M_1(N)}{M_{i-1}M_1 T_0}$$
$$+ \mu\frac{\kappa_i + 1}{T_0} - \Lambda M_1(\kappa_i + 1)\{\kappa_{i+1} - (\kappa + \kappa_i)\}$$
$$= \mu\frac{(\kappa_i(N) + 1)M_{i-1}(N)M_1(N)}{M_{i-1}M_1 T_0} - \mu\frac{(\kappa_i + 1)M_{i-1}(N)}{M_{i-1}T_0} - \mu\frac{(\kappa_i + 1)M_1(N)}{M_1 T_0}$$
$$+ \mu\frac{\kappa_i + 1}{T_0} - \Lambda M_1(\kappa_i + 1)\{\kappa_{i+1} - (\kappa + \kappa_i)\}$$
$$= \frac{\mu}{T_0}\left(\frac{(\kappa_i(N) + 1)M_{i-1}(N)M_1(N)}{M_{i-1}M_1} - \frac{(\kappa_i + 1)M_{i-1}(N)}{M_{i-1}} - \frac{(\kappa_i + 1)M_1(N)}{M_1} + \kappa_i + 1\right)$$
$$- \Lambda M_1(\kappa_i + 1)\{\kappa_{i+1} - (\kappa + \kappa_i)\}$$

When $i = 2$, we have

$$\dot{\kappa} = \frac{\mu}{T_0}\left(\frac{(\kappa(N) + 1)M_1(N)^2}{M_1^2} - 2\frac{(\kappa + 1)M_1(N)}{M_1} + \kappa + 1\right) - \Lambda M_1(\kappa + 1)(\kappa_3 - 2\kappa)$$

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