Theory of Infectious Disease

Homework 2

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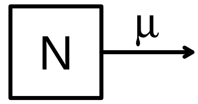
In this lesson, you'll derive some of the key expressions for compartmental models, from the probabilistic point of view. Specific exercises for you are indicated **in boldface**.

Residence time in a compartment

In the context of compartmental models, the following diagram has a specific meaning.



It means that the *occupancy* of the compartment, i.e., the number of individual hosts within it, at any time, is N. Each of these individuals has a risk, or *hazard*, μ, of leaving the compartment. This hazard is a rate: it has units of inverse time.

What does this mean? Let T be the amount of time a host spends inside the compartment, the *residence time*. T is a random variable. How is it distributed?

To answer this, we'll derive an equation for, $\mathbb{P}[T \le t]$, the cumulative distribution function for T. First, notice that

$$\begin{aligned}\mathbb{P}[T \le t + \Delta t] &= \mathbb{P}[T \le t] + \mathbb{P}[t < T \le t + \Delta t] \\ &= \mathbb{P}[T \le t] + \mathbb{P}[T \le t + \Delta t \mid T > t]\, \mathbb{P}[T > t]\,.\end{aligned}$$

Why?

Therefore

$$\mathbb{P}[T \le t + \Delta t] - \mathbb{P}[T \le t] = \Big(1 - \mathbb{P}[T \le t]\Big)\, \mathbb{P}[T \le t + \Delta t \mid T > t]\,.$$

Now, the *memoryless* property of compartmental models comes into play. Since every host in the compartment is identical, there is no sense in which one host has been in the compartment longer than any other. In fact, each individual host's history is completely forgotten once it enters the compartment. Therefore, the probability that a host leaves the box at time t cannot depend on how long that host has been in the box. It follows that

$$\mathbb{P}[T \le t + \Delta t \mid T > t] = \mathbb{P}[T \le \Delta t]\,.$$

Now, if Δt is small, the last expression is approximately proportional to Δt. The proportionality constant is, by definition, μ.

Putting this all together, we have

$$\mathbb{P}[T \le t + \Delta t] - \mathbb{P}[T \le t] = \Big(1 - \mathbb{P}[T \le t]\Big)\, \mu\, \Delta t + o(\Delta t),$$

where the $o(\Delta t)$ term is something that is small relative to Δt, at least when Δt is small. Dividing the last equation through by Δt and taking the limit as $\Delta t \to 0$, we obtain the differential equation

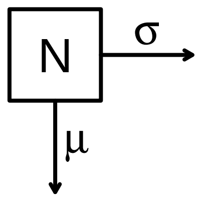
$$\frac{\mathrm{d}}{\mathrm{d}t}\mathbb{P}[T \le t] = (1 - \mathbb{P}[T \le t])\, \mu.$$

Solve this to obtain $\mathbb{P}[T \le t] = 1 - e^{-\mu\, t}$**.** This shows that T is exponentially distributed with rate μ. Sometimes we write $T \sim \mathrm{Expon}(\mu)$ as shorthand for this statement.

Work out the probability density function, $f_T(t)$**, of** T**.**

Multiple hazards

When there are multiple arrows leading out of a compartment, it means that there are multiple ways an individual host can exit. Each of these is associated with its own hazard. For example, consider the following diagram.



Here, the total hazard, $\sigma + \mu$, is the hazard of leaving by either route. By the same logic as before, $T \sim \text{Expon}(\sigma + \mu)$.

How are we to think about the choice of *which* route an individual host will take? It turns out that we can reason about this *competing hazards* situation by imagining that each exit route has its own independent, exponentially distributed residence time. Specifically, let's suppose that $T_\sigma \sim \text{Expon}(\sigma)$ is the time associated with the first route and $T_\mu \sim \text{Expon}(\mu)$ is that associated with the second.

Show that $\min(T_\sigma, T_\mu) \sim \text{Expon}(\sigma + \mu)$**. Accomplish this by convincing yourself that**

$$1 - \mathbb{P}[\min(T_\sigma, T_\mu) \le t] = \mathbb{P}[\min(T_\sigma, T_\mu) > t] = \mathbb{P}[T_\sigma > t]\,\mathbb{P}[T_\mu > t]\,.$$

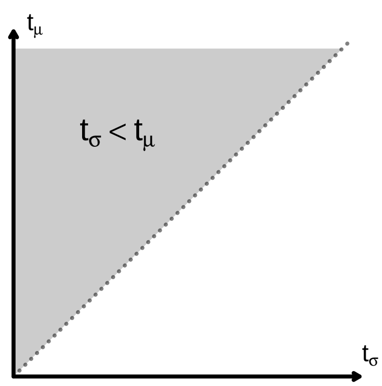
Thus one can think of the two-exit situation by imagining that for each host, each exit "door" will open at a random time, independently of the other. The host leaves by whichever door opens first. This extends to the multiple-exit situation straightforwardly.

What is the probability that a host leaves by the first door? To know this, we just need to find $\mathbb{P}[T_\sigma < T_\mu]$. The joint probability density of (T_σ, T_μ) is

$$f_{T_\sigma, T_\mu}(t_\sigma, t_\mu) = \sigma\,\mu\,e^{-\sigma\,t_\sigma - \mu\,t_\mu}.$$

We integrate this density over the appropriate region:

$$\mathbb{P}[T_\sigma < T_\mu] = \int_{t_\sigma < t_\mu} f_{T_\sigma, T_\mu}(t_\sigma, t_\mu)\,\mathrm{d}t_\sigma \mathrm{d}t_\mu = \int_0^\infty \int_0^{t_\mu} \sigma\,\mu\,e^{-\sigma\,t_\sigma - \mu\,t_\mu}\,\mathrm{d}t_\sigma \mathrm{d}t_\mu.$$

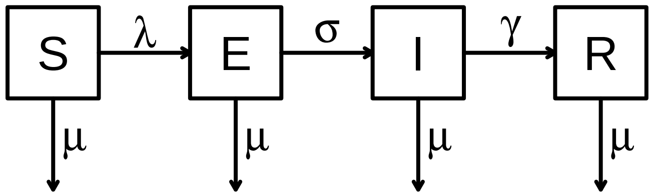


Evaluate this integral to show that

$$\mathbb{P}[T_\sigma < T_\mu] = \frac{\sigma}{\sigma + \mu}.$$

Chains of compartments

We can link the basic motifs studied above into complicated diagrams, wherein individuals enter one box upon leaving another. For example, the following diagram caricatures a permanently immunizing infection with a latent period.



What is the chance that an individual host is in the latent class, given that it was infected t units of time ago? In other words, what is $\mathbb{P}[T_E > t]$, where T_E is the residence time of the E compartment?

Show that $\mathbb{P}[t < T_E] = e^{-(\sigma+\mu)\,t}$**.**

What is the probability that an individual host, infected t units of time ago, is infectious? To work this out, we need to account for all the possible ways this host could have come from S to I, including the amount of time spent in E and allowing for the possibility of death while still in E.

Show that the probability a host is in the I box given that it spent $s < t$ **units of time in the E compartment is**

$$e^{-(\gamma+\mu)\,(t-s)}\,\left(\frac{\sigma}{\sigma+\mu}\right)\,(\sigma+\mu)\,e^{-(\sigma+\mu)\,s}\,\mathrm{d}s$$

Accomplish this in three steps:

1. Show that the probability the host spent between s and $s + \mathrm{d}s$ units of time in the E box is

$$(\sigma+\mu)\,e^{-(\sigma+\mu)\,s}\,\mathrm{d}s.$$

2. Recall that the probability the host went into the I box after leaving the E box is $\sigma/(\sigma+\mu)$.
3. Show that the probability the host has not yet left the I box is $e^{-(\gamma+\mu)\,(t-s)}$.

Now we can sum the above expression over all possible values of s to obtain the desired probability:

$$\int_0^t \sigma\,e^{-(\sigma+\mu)\,s}\,e^{-(\gamma+\mu)\,(t-s)}\,\mathrm{d}s.$$

Evaluate this integral and show that it agrees with Eq. 3.12 in Keeling & Rohani.

What happens when $\sigma = \gamma$**?**