PROFESSOR: So let's build on this concept of diffusion of virions in droplets to understand how we would expect a size dependent infectivity of virions in different sized droplets.

So an important concept in epidemiology that we will come to later is the infectivity, which is the probability that if a virion is transferred that it actually causes an infection in the host.

That can be further broken down into a product of two probabilities.

The first is that if the virus has escaped from the droplet, it actually causes an infection.

And that's perhaps something which is roughly constant.

It has to do with the physiology of the host.

But then there is the escape of the virion from the droplet.

And as we've already discussed, that's a strongly size dependent quantity.

And from very large droplets, it's very difficult in a mucus droplet, especially, for the virion to diffuse out in a reasonable amount of time.

And in fact, virions are typically found to have a period of deactivation where after a certain amount of time, they are no longer viable and able to basically cause further infection.

And so if we assume there's a certain time t, or tau v for the virus deactivation, then we can ask ourselves if the virus has had a chance to escape or not as a function of size.

So basically, to solve this problem, we think of the droplet here.

And we actually want to solve a diffusion problem where C here is the concentration of viruses in the domain.

D is the diffusivity of the viruses.

And this is the [INAUDIBLE] equation in the sphere, which is the diffusion equation.

And our boundary conditions are that C of R and 0, the initial condition is 0.

And then at R and t, it's going to be one.

So basically what we're imagining here is that we're trying to figure out the C will be the concentration viruses that has left the system actually.

So what we have is if we look as a function of the radius, of the radius of this thing is R, capital R. So in that distance, we have this constant-- what I'm calling concentration here is just going to jump up to one.

And then it's going to diffuse inward like this.

OK, and then eventually the final state is that it's entirely basically one everywhere.

And that's when basically the probability of removal has hit every part of the drop and all of the virus has been removed.

So the C is a time dependent fraction of the virus, the virions in the droplet, which had been removed at time t.

So this spherical diffusion equation can be solved analytically in various ways.

But there's not a simple closed form solution to this problem.

And what we're really interested in here is just a rough approximation of what the solution might look like.

So let's pull out an approximation for this.

So I'll sketch the droplet again here.

Now at early times, when there hasn't been a chance for the viruses, the virions to diffuse very far.

Then only those which are close to the boundary actually have a chance of leaving.

That's this initial boundary earlier that I sketched here, which is working its way in.

So why don't we sketch the central region and give that a distance delta, which is the boundary layer thickness.

So basically this outer annulus has been-- is really where virions had a chance to leave.

And that's where c is jumping to one.

And from-- if this were just a plane with a semi-infinite diffusion towards the center, so in other words, this delta is much less than R, capital R, the radius, then it's almost like diffusion from a planar source.

And then we actually know that this distance as well approximated by square root of 2 DT.

So that just comes from solving the diffusion equation in one dimension leads to that scaling of the diffusion layer thickness.

So that's this thickness of this blue region as it goes that way is delta.

And it scales as it's approximated by square root of 2DT.

And now let's ask ourselves then what is this concentration here?

Well, what I'm really interested in actually is this escape probability PE.

And that's going to be the integral of CDV over the volume.

So this is the integral over all the R's that are less than capital R. So basically inside the drop of this concentration field.

So that contrary field starts at 0 and eventually goes to 1.

And that base is giving me this total escape probability.

So to calculate this integral of the concertation field, I basically have a domain at the outside here with the concept of this concentration variable is near one and a central region where it's C approximately zero.

And here C is equal to one on the boundary.

This variable I've defined here.

So therefore, I can write that this PE is, roughly speaking, if we think of just what is the volume of that spherical annulus, that would be-- and relative to the total volume-- that would be r-cube minus R minus delta cube divided by r-cube.

So each of the volumes has a 4/3 pi, which I've canceled off.

So this is basically the volume of the total sphere minus the volume in the inner sphere.

So that's just the volume of the shell.

Then I normalize it properly here.

So this is one minus delta over r parentheses cubed.

And if I now-- and I have this expression here.

So now I have at least an approximation for what this might look like.

We can also further say that this approximation here was valid for the delta B much less than r.

And when that's the case, then I also can say that this quantity is small.

So at early times that's small.

And I can expand.

All right, this is 1 minus.

And then 1 minus something cubed, where that something is small, is 1 minus 3 times that something.

That's basically a tailor expansion.

So that when I work this out, the ones cancel.

And I get three delta over R. So what we find is that this PE, which we're trying to calculate, has two limits that are easy to calculate.

One of them is this 3 delta over R. And if that's our delta, then we get 3 square root of 2 DT times R.

And specifically, the p is defined up to a certain time tau v. So I'll now replace t with tau v because that is my timescale for virus deactivation.

And so this would be in the case where this quantity is-- basically, this ratio here is much less than one.

And then in the opposite limit where this diffusion has completely spanned the particle and is getting much bigger than R, then this obviously has to tend to 1.

OK, now, I can write down a function that makes this transition right about when this thing is of order one in a variety of ways.

One way we could do that would be to write that PE is approximately given by 1 minus the exponential of minus this quantity.

So minus 3 square root of 2 d tau v divided by R.

And you can see there we have a-- there's sort of-- you could either write this in terms of a time where the critical time is-- so we could write this-- just to get more insight into it, we could write PE is approximately 1 minus e to the minus tau v over some timescale-- I'll call it tau d for diffusion-- where we see here that tau d is R squared over-- and then it's-- To bring inside the square root, this 3 becomes 9.

And then times 2 is 18.

So 18D.

Now, you may recall from our last calculation, the average first passage time in the sphere calculated exactly was R squared over 15D.

So this very simple calculation is clearly giving us roughly the right order of magnitude for that time.

But we're actually not interested so much in writing this in terms of time.

We'd actually like to write in terms of radius.

So I can also write PE is 1 minus E to the minus R.

I'll call it maybe Rd for diffusion over R where Rd is basically all this stuff, 3 root 2 d tau v. OK, so this is maybe another useful way to write that.

And what does this function look like as a function of R, this one right here?

So maybe if I sketch that out, I'll look at this a little bit more carefully.

Let's plot this.

So as a function of R, here is this Rd, this critical size.

When we are smaller than that critical size, then basically we have that PE.

The escape probability, essentially, is very close to 1, OK, because then we have-- that's basically just what we were just arguing.

It's this limit right here.

But then it's a function that when it gets much larger than our d, then it decays as we suggested here as sort of 1 over R.

So it's actually a fairly slow decay in the long run.

So basically, there's this limit here.

And I just wanted to get to this picture.

Just to point out that even though there are obviously physiological characteristics having to do with the way the a virion would actually get into a host cell and whether they would get infected, but a lot of those properties should be independent of the delivery of the virion in a droplet.

It's really more once the virion gets out, there's some process.

But what this calculation shows is that we would expect a fairly strong dependence of the infectivity on the size of the drop.

Well, in particular, if we calculate this Rd.

We'll have some idea that droplets that are smaller than that are highly infectious because every virion in those droplets can get out and infect the host cell.

Whereas if the virus is-- the droplet is much bigger than that, then you have this problem where this dead region in the middle.

And those virions are not going to be able to get out in a reasonable amount of time, which is set by this tau v.

So for example, a tau v for SARS COV-2, the coronavirus, is estimated to be anywhere from one hour.

There was one study in aerosol droplets finding that kind of decay.

But another study found that after 16 hours, it was still viable.

So there's not quite a consensus forming yet.

But it may be a time on the order of hours, certainly days, over which the virion needs to get out of the droplet in order to be able to cause infection.

And this calculation shows you that as a result, you would expect a size dependent diffusivity-- or excuse me, a size dependent infectivity.

And roughly speaking, if we plug-in the numbers, these are the aerosol droplets.

And these are the large drops.

We've already done that.

That was our previous calculation based on this time here, which is what I'm calling tau d here, which corresponds to this, is also pretty close to what we call tau 0.

That was the-- well, that was the longest escape time, actually what I call, I think, tau bar actually, which was R squared over 15d.

That was the average escape time.

So basically, we've already shown that that average escape time starts to become days or even months when we get to large drops.

But for the aerosol droplets in mucus anyway, this timescale is of order minutes to hours, which is reasonable.

And you would expect those to be very infectious droplets.