PROFESSOR: So let's think of a specific virus, the coronavirus, including the case of interest today, which is the SARS-CoV-2 novel coronavirus.

So this virus comes in the form of virion, which is the capsid containing RNA, which is then going to infect a cell.

And the size of that virion is around 120 nanometer diameter, and it's nearly a perfect sphere.

Now, the size here of 120 nanometers compared to bacteria is about 1,000 times smaller than [some] bacteria.

So this actually has a very big implication in terms of how a virion can be spread from one organism to another.

So the bacteria, if you recall, are the size of several microns.

That's the scale of large droplets, which sediment -- or larger than that, they would begin to sediment out of the air.

And we can think about transmission through coughing.

Also, besides the fact that the virus is much smaller, it cannot swim.

So bacteria have various means of locomotion -- cilia, flagella, et cetera, whereas the virion essentially is a little hard sphere.

So how can a virion actually transmit itself?

Well, if we draw a droplet, which is released by respiration, then the virus is actually extremely small, at the scale of typical droplets that come from respiration, which, as we've discussed, have a typical, most probable size around half a micron, and then have mostly droplets that are larger than that.

So at that scale, if we think of this as a micron scale droplet, this little virus is extremely small.

It's like a little point, essentially.

And so a single droplet may contain a couple viruses, a couple virions.

And so in order for the virion to escape the droplet and make connection with a cell in a host, let's say it's been breathed in, and in the lungs, it's going to try to meet with some cell and begin to infect it.

Or conversely, if the virion is being shed and released from an infected cell and then needs to go into a droplet to then be exhaled and spread to somebody else, either way, the virion has to get in and out of this droplet.

And since it cannot swim, the only way can do it is by essentially a random walk or a diffusion process, where it's just bouncing around due to thermal fluctuations.

And eventually, at some point, it gets out.

So the diffusion process -- we can estimate the typical time to escape.

I'll write it this way -- [it] can be shown if the radius of the droplet is R, the average time for a randomly distributed and selected virion anywhere in this droplet, the time for it to escape is of order R squared over D, where D if the diffusivity.

And if you do a precise calculation for a sphere, then there's a factor of 15 here.

And so that is basically average escape time by diffusion.

So that gives you a sense of how quickly the virion is able to get out of the cell -- or out of the droplet, excuse me.

Now, how big is the diffusivity?

Well, the diffusivity of the virus, if you think of it just as a fluctuating sphere in a viscous medium, then we can use the Stokes-Einstein formula for the diffusivity, which is k_B*T, where k is Boltzmann constant and T is the temperature.

So k*T is the thermal energy of the fluctuations.

And that's divided by 6*pi times the radius of the virus, and then the viscosity of the liquid or fluid containing the droplet.

So essentially, this denominator here is the Stokes drag coefficient for a sphere fluctuating in a viscous medium.

So that's the diffusivity.

And if you figure out for the size of 120 nanometers, if we use the viscosity of water, if we assume the droplets are just water, then this is 3.6e-8 centimeters squared per second in water, where we use the viscosity of water.

But the droplets are not just water.

In fact, they cannot be.

As we've already discussed, water droplets at this size range would very quickly evaporate and disappear, or they would leave the virus essentially, a virion no longer contained in such a droplet.

So what's more typical is that the droplet in fact contains many macromolecules and is coming from mucus in the pharynx, in the vocal cords, coming from the lungs directly.

And mucus has a much higher viscosity.

So notice, here, we have the viscosity of the liquid coming in.

And if we take into account the fact that the viscosity of mucus relative to the viscosity of water is roughly -- it depends where the samples are taken and also what's the shear rate.

So we're talking about low shear rate.

These are sort of moving slowly.

The viscosity of mucus is dependent how quickly you're shearing it.

But if it's a low shear rate, then this is on the order of 1e3 to 1e5 at low shear rates.

And because the viscosity has that factor, the diffusivity is then divided by that factor.

So what that's telling us is instead of being around 1e-8 centimeters squared per second, we're really looking at more like 1e-11 1e-13 centimeters squared per second in mucus.

So we assume these are actually mucus droplets, which are not fully evaporating and are contained in aerosol form, then this is the kind of diffusivity.

And if we plug into this formula here, we can get a sense of what is the average time for the virion to actually escape.

So why don't we make a little table of that result.

So let's look at the radius.

First, let's consider here 0.5 microns, or 500 nanometers.

So that would be a 1-micron diameter droplet.

So that would be kind of a typical aerosol droplet coming from breathing.

Let's also consider larger droplets.

So let's look at 5 microns, which is kind of on the upper end of the aerosol range.

And then we could look at 50 microns.

And I should say this is R of the drop.

So the R here, just to be careful, is they R of the drop, as opposed to the R of the virus, which is R_v is half d, so that's 60 nanometers.

OK, so that's the diameter.

So this is the different size of the drops.

And just for comparison, let's look at water versus mucus.

And from mucus, why don't we take that the viscosity of the mucus is 1e4 times the viscosity of water?

So we just pick something kind of in the middle of this range.

OK, well, if we plug in then the numbers and we try to plot the average escape time that I've just written here, R^2/(15*D), then in water, this turns out to be about 5 milliseconds for an aerosol droplet.

So we know the aerosol droplets are evaporating quickly and also that a virus can diffuse out of it relatively quickly, because the water is not really that this.

Now, if we move in this direction, we're multiplying R by 10.

And notice, the time scale goes like R^2.

So there is a pretty strong size dependence.

So as we think of a 10 times larger droplet, it's 100 times longer time.

So that would be 500 milliseconds, or 0.5 seconds.

And if we go another factor of 10, that's another factor of 100 in time.

And if we convert seconds to minutes, it turns out to be around 8 minutes for a fairly large drop.

Now, what if we're in a mucus?

So now, we go in this direction.

The timescale goes like 1/D, and D goes like 1 over viscosity.

So the timescale is proportional to viscosity.

So we're getting this factor of 1e4.

That's a pretty big factor.

And so, for example, this 5 milliseconds for mucus can turn into 1 minute.

So from an aerosol droplet, which is sort of at the most probable size from respiration, which is on the order of a little bit below 1 micron, a typical virion would take about a minute to diffuse out of that droplet and infect a nearby cell or tissue.

Now, if we look at a little bit bigger droplets, this 1 minute, we multiply by 100, it's 100 minutes, which is on the order of 1.5 hours.

And what if we keep going another factor of 100?

That turns into around 7 days.

So if the virion is contained in one of the larger droplets that comes from coughing or sneezing, it could take it hours to days to escape from that droplet and have any chance of infecting a host cell.

So you can immediately see the problem for a virus in terms of transmitting is it can't swim.

It's extremely small.

And so it's not a good way to transmit itself to be sitting in a large droplet or a pool of liquid, imagine a pool of saliva or some phlegm that you've just coughed up, which is very common for bacterial transmission.

For a virus, it's much more difficult for a significant amount of virus to actually get out.

So if the virus is going to transmit itself, it makes a lot more sense to be in aerosol droplets.

And so it's really here, the aerosol droplets are the most infectious, because basically, the virus able to get out.

And based on this calculation, roughly speaking, if R of the droplet, which we're just calling R, if R is less than around 5 microns, those are the ones we would expect to be the most infectious.

And interestingly for SARS-CoV-2, recent experiments have sampled droplets from sick patients with COVID-19 at different sizes.

And it was found that the droplets that had a diameter less than about 4 microns were the most infectious and clearly you could see replication of the viral RNA in samples of those droplets, whereas larger droplets in this range here, kind of larger than a few microns, were less infectious.

And in fact, the virus was less able to replicate.

So it's kind of consistent with this physical argument.

So basically what we would probably say is that in this range, the virions are mostly trapped.

They have a hard time getting out of those droplets and can deactivate over time, because that's also happening.

They are believed to have a certain finite lifetime.

And so this is the case that the virions are trapped and deactivate in large drops or the fomites, which are infectious residues on surfaces that are left over from those droplets.

So this really shows us that our focus should be on looking at aerosol droplets for viral transmission.