Physics of Biological Systems
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Lecture – 13
Cell Signalling and Capture Probability of absorbing sphere

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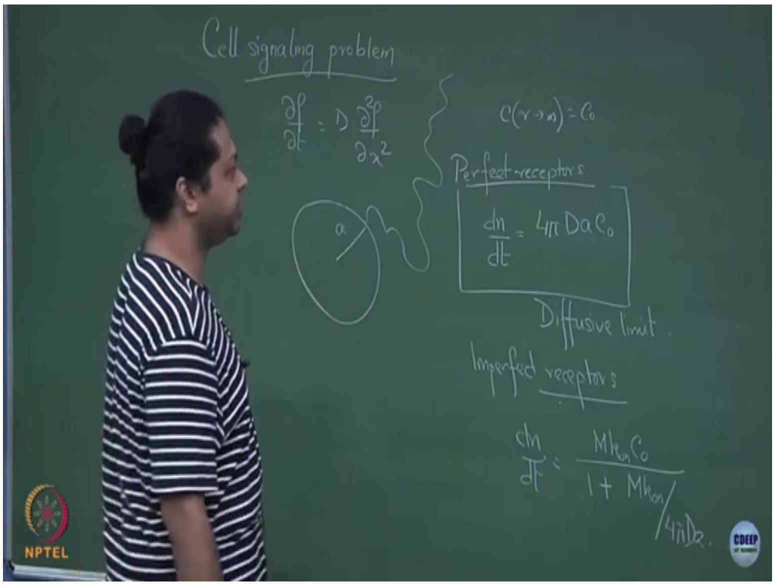

So, just to recap, what we were talking about is diffusion and in particular where we left off last class was the Cell Signaling Problem, right. So, we had the diffusion equation del rho del t is equal to D del 2 rho del x 2 and we solve it for the case of some chemicals getting absorbed onto the surface of a spherical cell. So, this was the cell signaling problem that I had the sphericals cell of radius a, and very far away as r tends to infinity there was some constant concentration.

And we asked what is the diffusion current. So, what is the current that we rate at which particles get absorbed onto this spherical surface and we came up with an answer which was dn dt that is the number of particles per time which was like 4 pi Da C, right. So, this was the case for perfect receptors. This was the case for perfect receptors, which means that whenever molecule performing random walk came onto the surface of the sphere it got absorbed without fail. So, all the receptors are 100 percent perfect and that give us this nice answer which is called the diffusive limit. This was the diffusive limit, right. So, this was like the fastest rate at which particles can get absorbed onto the surface of the spherical cell.

We then did imperfect preceptors, we then did imperfect receptors where there was some rate k on at which these chemicals got absorbed and in that case we got some dn dt which was I think M k on C naught by 1 plus something which was M k on by 4 pi Da, ok. And we showed that in the limit that k on was very large, so the receptors approach this perfect receptor limit, we go back to this perfect receptor result. Ordinarily this is less this rate is lower than this perfect receptors, but as k on becomes higher you approach that limit. And if k on was very small that nothing gets absorbed and the concentration is basically C naught throughout.

So, we will use this number this diffusive limit of 4 pi Da C naught, as a sort of rule of thumb to estimate how fast diffusion happens or this sort of cell signaling happens the rate at which this happens. So, (Refer Time: 03:42) just to clarify a couple of points with work this out for the spherical for the spherical cell, right. So, you could ask that how the shape affected. Sphere as we discussed is the easiest geometry to solve, but you can solve other, you can solve other geometries at least symmetrical geometries you can solve analytically.

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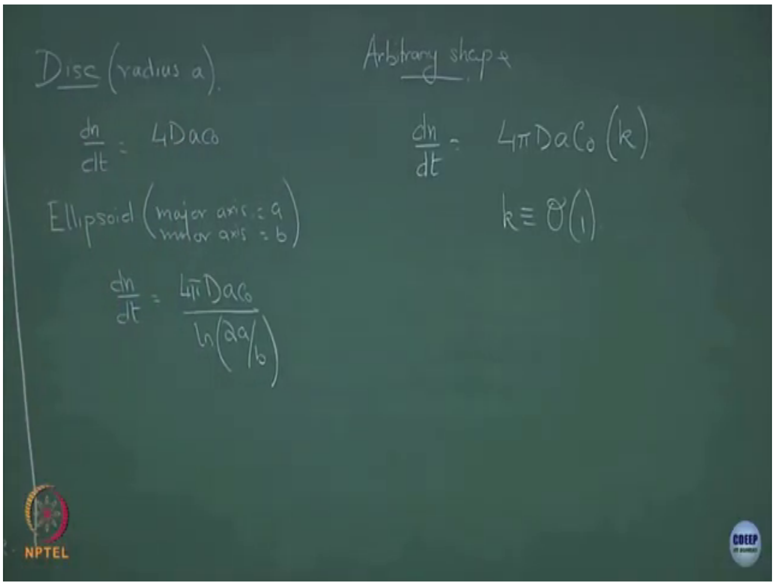

So, for example, if you take a disk I will not solve it, you can look up standard diffusion books or electricity books because ultimately the same as the Laplace equation. So, if we solve it for a disk shaped cell or of some radius a of some radius a then you would get a dn dt, you would get a dn dt of I think 4 Da C b. If on the other hand you were to do it for an ellipsoid, if you were to do it for an ellipsoid let say of major axis a, major axis a and minor axis b again you can solve this analytically and you would get dn dt is equal to 4 pi Da C naught divided by some log 2 a by b, ok.

So, you can try out all of these, these are not very difficult. But the main message is the following that what regardless of the geometry what you get on numbers which are of this order. So, for an arbitrary shape, for an arbitrary shape you could write this diffusion limited current, whether, so in the limit of perfect observers as something like whatever it was for this sphere 4 pi Da C naught times some factor, times some factor k with generally this k is of order 1, where generally this k is of order 1, ok. So, you will get some differences due to shape of course.

So, in that sense this k you can think of as like the capacitance, it encapsulates the geometry of the object, but it will not change the order of magnitude of the result mostly, unless you take a very. Unless you take something which is infinite in one direction and point like in another direction. For any reasonable things this will be of the order of 4 pi Da C naught. So, we will use this spherical result as sort of the benchmark and keep in mind that for an arbitrary shape you will have the effect of geometry, but that effect is generally not very strong, ok. So, that is number 1.

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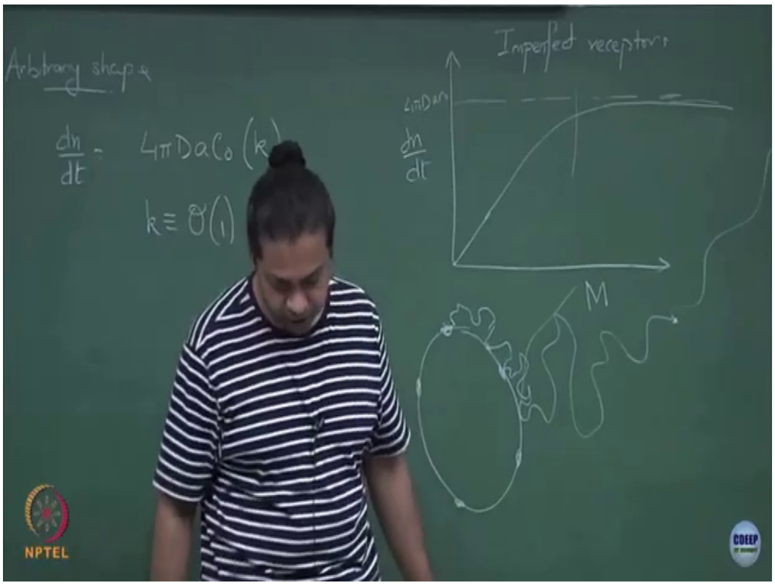

The other thing that we saw when we did this imperfect receptors was that if we plotted the current as a function of the number of receptors, if we plotted this dn dt so this was for the case of imperfect receptors, if we plot this dn dt is as a function of the number of receptors on the surface of the cell this M over here then for when M was small of course, it increases linearly almost with M. But as you increase keep increasing M more and more it is a it saturates to this diffusive limit. So, this is my 4 pi Da C naught. So, it saturates to that like this.

So, in this region if we increase M a lot you do not get a lot of increase in the rate at which particles are getting absorbed, ok. And we put in some numbers to that and we saw that in order to get half this maximum current the area coverage and the surface of the cell was roughly 0.001. So, the fraction of the area that was covered by these receptor, so 0.001.

So, even if you have a relatively sparse coverage on the surface of a cell, so here is my surface of the cell and I have some receptors on this. And let say these receptors are relatively sparse. So, they are quite well spaced on the surface of the cell. Even then the rate the current that you get that is very close to the theoretically maximum limit that you achieve, ok. And you can understand why this is in the sense that if I have a particle which is starting off here and its doing its random work and it hits some point on the surface of a sphere where there is no absorber, right.

It of course, it feels to get absorbed because there is an absorber here, but it does not immediately run away back to infinity, it will wander around somewhere on this close to the surface, maybe it wanders here, it hits this point there is no receptor here then at some point will hit one of the receptors and get absorbed.

So, as long as you have approached close enough to the surface the random walker will tend to spend some amount of time wandering near the near the surface and therefore, it will hit these absorbers even if they are relatively few number of them, ok. So, that is why you are relatively sparse coverage does quite well as far as the current is concerned, ok.

So, what I will try to spend today doing is to firm up this concept what is the probability. So, the question that we will ask is that if I take a random walker which has been released at some point at some radius whatever, what is the probability that it gets captured on the surface of a cell as opposed to the probability that it sort of escapes away to infinity. So, what we look at firstly is this captured probability, is this captured probability and then next we will look at what are the times that are involves. So, if I want to ask that, let say that it does get absorbed how fast is that process, so what are the time scales involved for this capture

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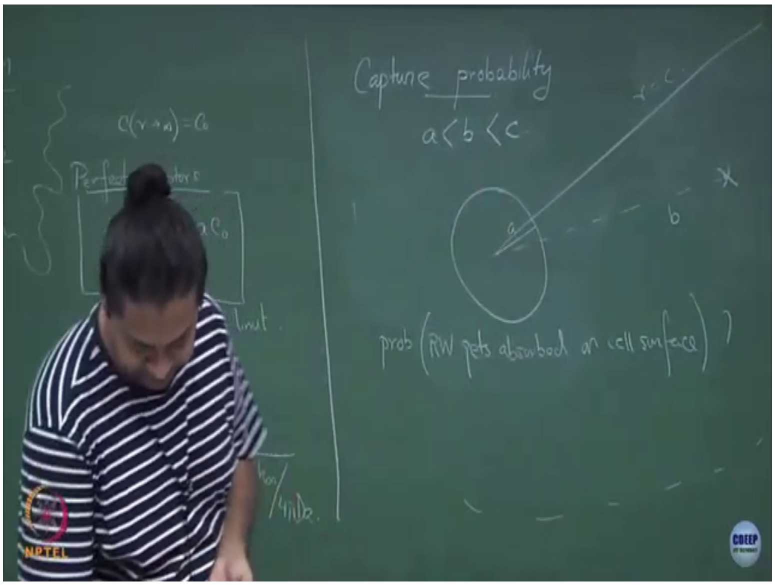

So, those are the two things that we will try to do today. At least for this part we will try to firm up this concept that how often does it visit the surface of the cell, once it is approach the vicinity of the cell itself, ok, all right. So, let me set up the problem. So, let say I have a spherical cell again. So, having discussed that shapes do not matter a lot I will go back to the sphere and I will keep using the sphere or maybe a one d (Refer Time: 10:30). So, here is my cell of radius a. I release a random walker at some radius a some radius away from itself which is let say b, ok.

So, here is my starting point for the random walker and I want to ask, so b is obviously greater than a, so b is greater than a. So, what I want to ask is what is the probability that the particle will be absorbed at r equal to a, so the surface of this cell is uniformly absorbing that is my assumption. So, I will ask what is the probability that this random walker released at r equal to b will get absorbed in the surface of the cell rather than wandering away to infinity ok. So, what is the probability that random walker gets absorbed on cell surface and for example, how would this probability change if I change the distance at which I release this random walk; so, how does this probability go as a function of b, ok, all right.

To do this I will first set up a similar problem. So, here is my cell here is my random walker let me say that I have another sphere at some radius c, ok. So, here is another sphere r equal to c which is also absorbing. So, I have let me say a less than b less than c, ok. a is the surface of the cell, b is the distance from which you are releasing the random walker, c is this outer sphere outer absorbing sphere that I have considered, ok.

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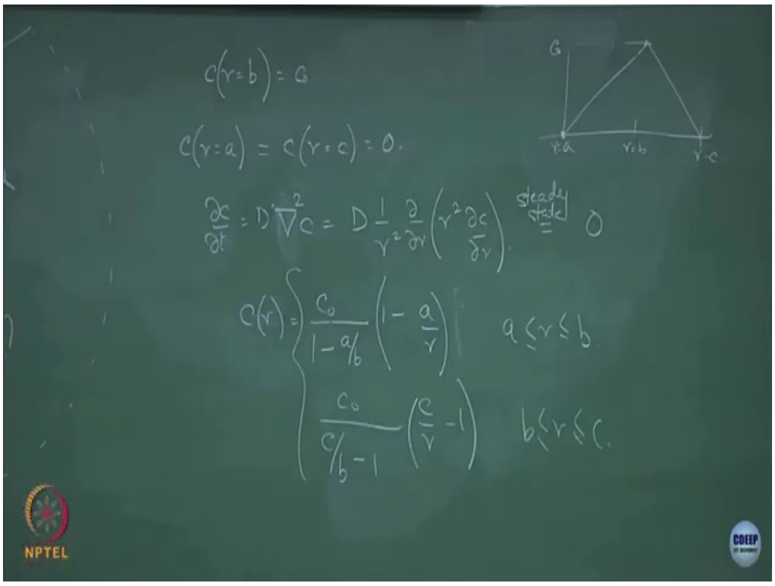

So, here at this radius at this radius b where I am releasing the random walker; let me say that I am maintaining a constant concentration. So, c at r equal to b is some c naught, and let me say that these two absorbers the cell and this outer sphere that I have considered they are both perfect absorbers which means that at the surface of the cell r equal to a and at this outer sphere r equal to c my concentration is 0, right everything gets absorbed.

So, now I want to solve the diffusion equation with these boundary conditions. So, I want to solve del c del t is equal to d del 2 c d Laplacian c, ok. Again this problem is spherical has I assume it just spherical symmetry, so I will write only the radial component of the Laplacian. So, this is 1 by r square del del r of r square del c del r, and I will solve for the concentration in the steady state limit again as before. So, this is going to be equal to 0 in the steady state. So, what will this; so, what will the c of r read? Anyone? We did this last class as well, right, it is a similar problem. How does the concentration profile look like? So, if at r equal to, this is r equal to a, let us say r equal to b and r equal to c, at r equal to a I know it is 0, at r equal to b I know it is some c naught, at r equal to c it is again 0. So, what how is the concentration profile look like?

Student: (Refer Time: 14:39).

Student: (Refer Time: 14:39).

Yes, it will go up and come down. In what form?

Student: (Refer Time: 14:43).

Hyperbola.

Student: (Refer Time: 14:47).

No, this is going to be linear. Again remember this is a Laplacian equation. It cannot have any Maximas or Minimas, like Griffiths, electromagnetic, electrostatics in fact, basic electrostatic. So, if you specify the boundary conditions the solution of the Laplace's equation is always the smoothest function that you can use to interpolate between the boundary conditions, right.

So, it will look something like that and then of course, you have to put in these boundary conditions. So, once we put in these boundary conditions let me just write it. So, what you have is c naught 1 minus a by b, 1 minus a by r for a less than equal to r less than equal to b and c naught c by b minus 1, c by r minus 1 for b less than r less than c, all right.

So, this is in the inner region between the cell and the source. This is in the outer region between the source and the outer sphere. So, if I put r equal to a then this goes to 0 as it should. If I put r equal to b then this 1 minus a by b and 1 minus a by b cancels, it goes to c naught, right and similarly for this outer region, ok. So, that is easy. So, at least for these 1D diffusion equation. So, you should always be able this effectively 1D equations you should always be able to solve for the solve for the concentration of the probability density. So, here is my, here is my concentration.

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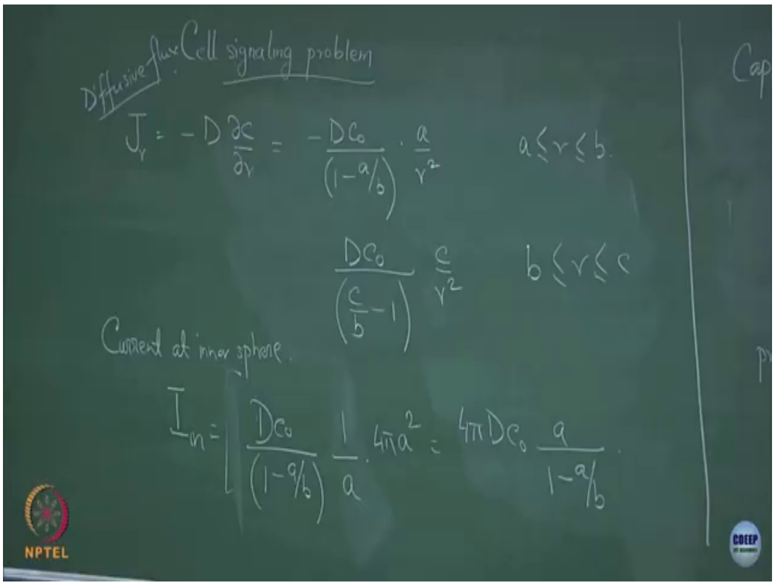

I can calculate the flux the radial flux. What is J in terms of the concentration? That is fixed law, right minus D del C by del r, right. J is minus D del C by del r, right. I have the concentrations therefore, I can calculate the fluxes. So, what does this read? Minus D del C del r. So, minus D C naught 1 minus a by b, a by r square, right, a by r square; this is again for the inner region. And for the outer region D C naught c by b minus 1 c by r square, ok. So, this is the current the diffusion current or the diffusion flux in these two regions, ok.

So, now, what I want to know is that what is the current; so, this was the flux this is the diffusive flux. Flux remember is number per unit area per unit time. So, if I want the current which is the number per time at the inner at the inner sphere let us say current at inner sphere, so that is the cell. What is the diffusive current? So, let me write it is I in. What is that going to be? This is going to be this flux into the area of the sphere, right, so 4 pi a square.

So, D C naught 1 minus a by b, a by r square into 4 pi a square, right. Now, so this is the current at any general r. This I should use at r equal to a, all right, so that means, that this will become 1 over a. So, if I do that this will become 1 by a that will cancel out that a, so 4 pi Da C naught. So, 4 pi D C naught, a by 1 minus a by b, ok. So, this is the number of particles per unit time that is coming and getting absorbed at the surface of this inner sphere.

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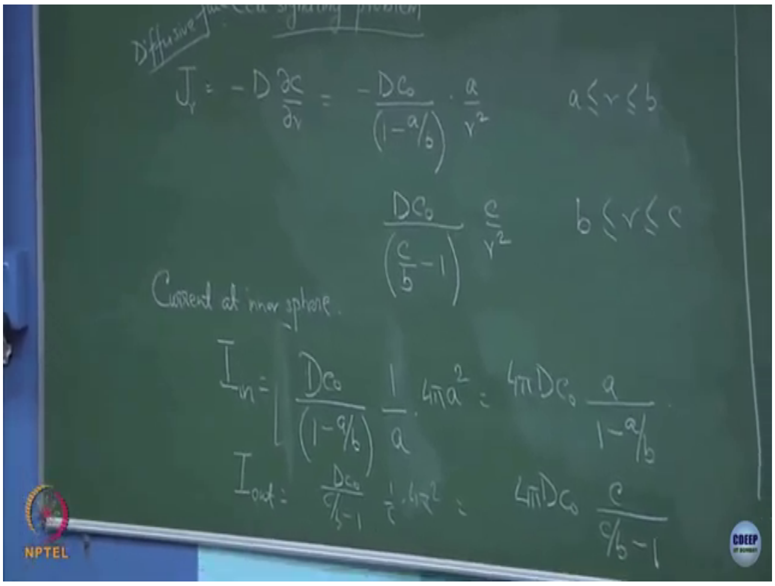

Similarly, you can find out what is the current at the outer sphere which is I out, which is I out. So, I substitute r equal to b over here and then the area is 4 pi b square. So, D C naught sorry I substitute r equal to c, the outer sphere is it c. So, c by b minus 1, 1 by c 4 pi c square. So, this is 4 pi 4 pi D C naught that is the same c by c by b minus 1, right. So, that is the number of particles per unit time that is getting absorbed at the outer sphere, ok. So, these are my two absorbers in the system. I have calculated the currents for each of this in the steady state, all right. So, now, if I want to therefore ask that what is the probability that a?

Student: (Refer Time: 20:58).

Yes.

Student: (Refer Time: 20:59) this c as a function of (Refer Time: 21:03).

Yes.

Student: This is 1 upon 2.

What is 1 upon r?

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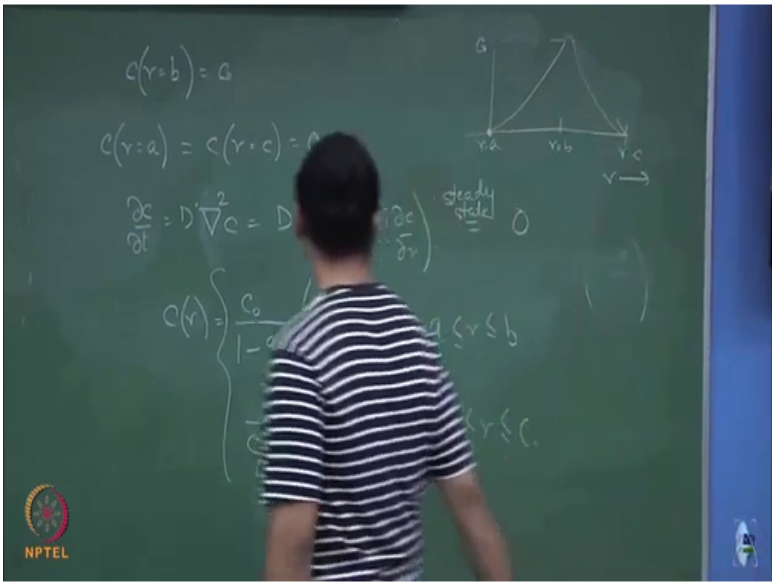

Yes, this axis is actually drawn wrongly. This is true indeed for Cartesian, but for spherical I should not draw it like this. (Refer Time: 21:40). So, this r square factors. So, once I have multiplied by these r squares it will become linear. So, in the Cartesian it is linear, in the in a curvilinear coordinate it would not minus (Refer Time: 21:51).

Student: If the (Refer Time: 21:52) it is coordinate.

No. So, this is let me see. This is r minus a by r and this let me not get into that, let me just plot this c as a function of r itself along the r axis. And you are right, this would not on the r axis it would not like this. That is my mistake thank you, ok. What was I saying? Right. The diffusion currents; so, I have this diffusive currents and on the inner and the outer spheres.

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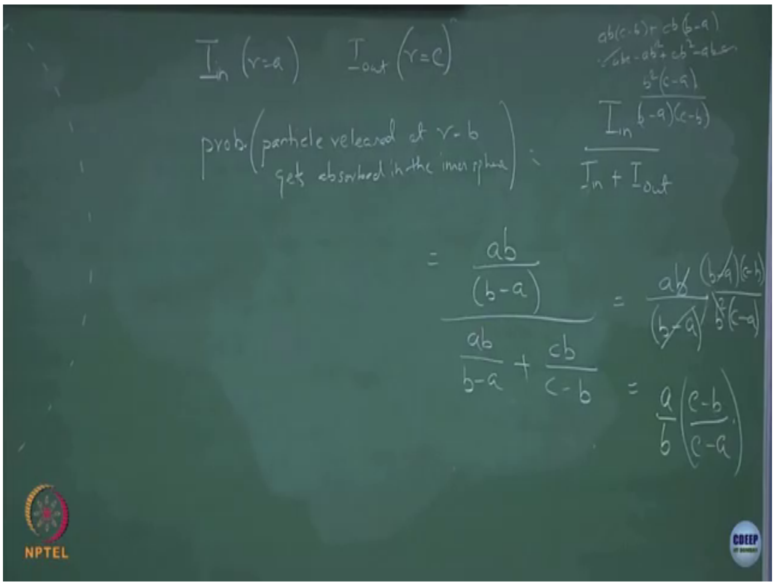

So, I have this I in which is the number of particles per unit time reaching this out inner sphere at r equal to a and I have this I out which is the number of particles per unit time reaching the outer sphere at r equal to c, right. So, then I can ask, now that I have these currents I can ask that what is the probability that a particle which I released here at r equal to b, that gets absorbed on the surface of the inner sphere as opposed to the outer sphere. So, what is the probability that particle released at r equal to b gets absorbed in the inner sphere? What is that probability if I know this I ins and I outs?

Student: (Refer Time: 23:48).

Yes.

Student: (Refer Time: 23:51).

Good. So, it will be I in by I in plus I out, right. I am releasing this particle, it is either getting absorbed here or there the number per unit time here is I in, the number per unit time there is I out. So, therefore, the probability that it is going to get absorbed on the inner sphere is that. And what is that? So, now, I can substitute for this. So, let me see. So, that 4 pi D C naught I do not bother about; so, ab upon b minus a divided by ab by b minus a plus cb by c minus b. What is this? Can somebody get simplify?

Yes, we yes. So, this is hopefully ab by b minus a into b minus a, c minus b by b square c minus a. So, this cancels, this cancels. So, this is a by b, c minus b divided by c minus a. Is that right? So, that is the probability that the particle gets absorbed on this inner sphere as opposed to this outer sphere and of course, the outer sphere is 1 minus this because the particle will have to get absorbed somewhere, ok, all right.

So, we started off with this problem that what is this, what is the probability that I if I release a particle here it will get absorbed on the surface as opposed to going away to infinity. So, I put in this sphere, if I am now interested in infinity I can take this radius of this outer sphere going to infinity, right. So, I can move this outer sphere all the way away to infinity, so the probability particle gets absorbed at r equal to a. Rather than one that to infinity rather than go off to infinity is going to be what? What is the limit of c tending to infinity? a over b, right.

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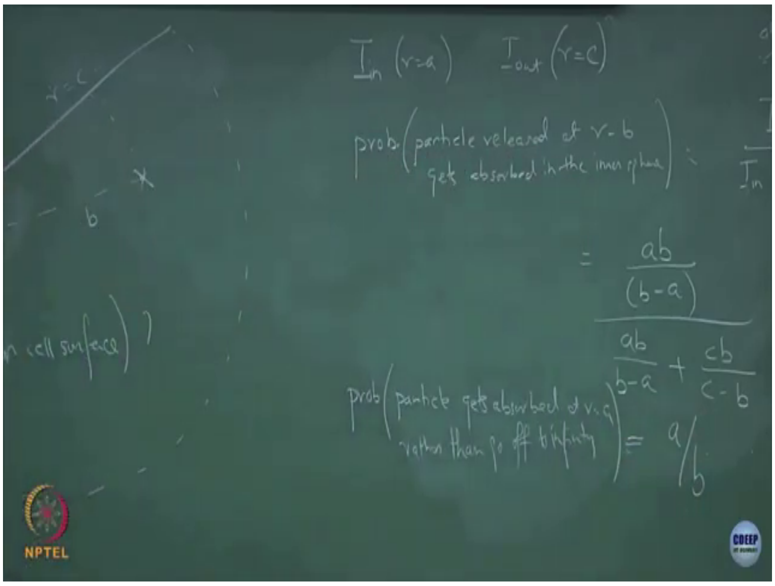

So, if I remove this outer sphere all the way away to infinity and the probability that this particle would get absorbed is a over b, ok. So, the further away you release this particle. Naively one might have thought that this probability might go off as down as 1 over b square because that is sort of the solid angle sort of argument that we generally think of, but it actually falls off as 1 over b, ok. So, that is the first part of this problem.

So, this is in some sense the probability of the captured probability that I release a particle here, the probability that it gets captured on the surface of a cell made up of this perfect absorbers is a over b, ok. So, the captured probability is a over b; so that.

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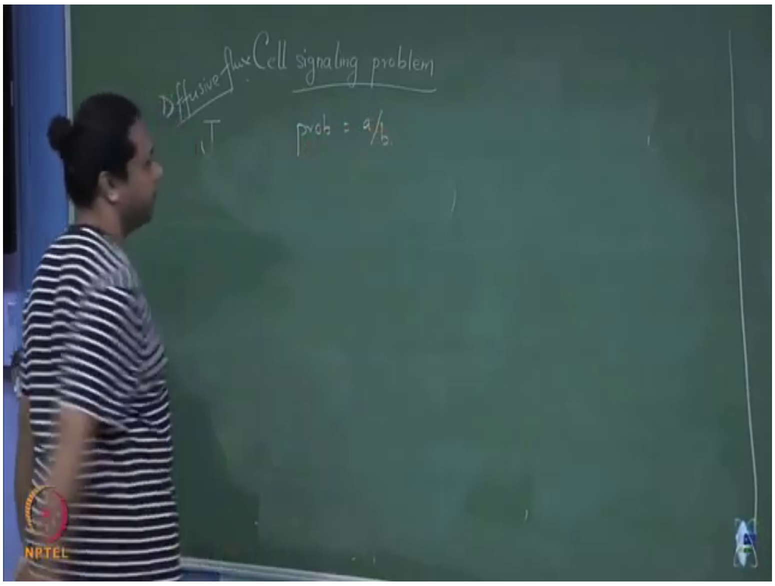

So, this probability is a by b.

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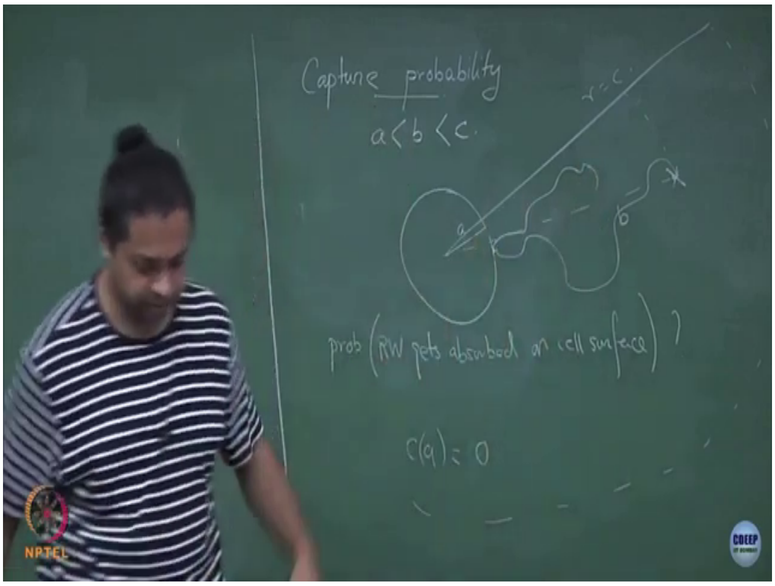

So, now, so remember this sphere was absorbing which is why I had c of a was equal to 0, right it is an it was an absorbing sphere. So, now let me change the problem a bit and make this a reflecting sphere, ok. So, if a particle comes in, if particle comes it hits here once it hits it would get reflected back and again do multiple it might come back again and so on, ok. So, let me now try to calculate this for this reflecting sphere.

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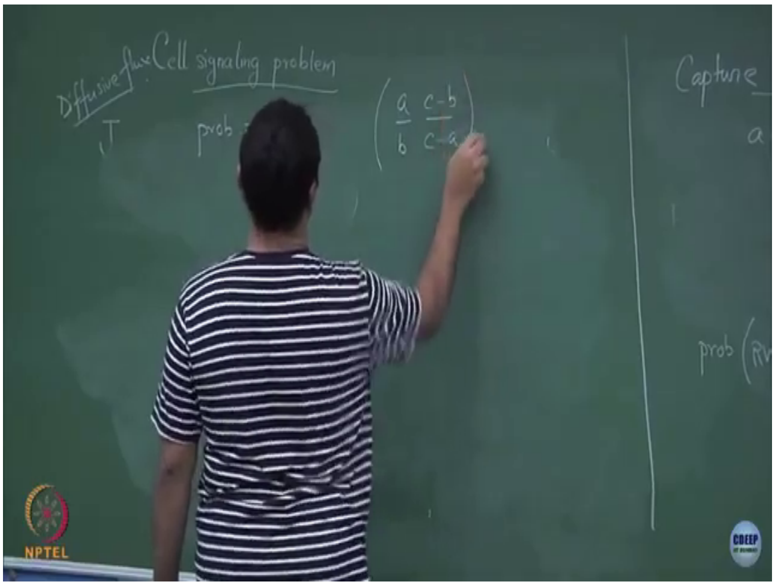

Let me write that result as well. The finite limit is a by b, c minus b by c minus a.