

**Computational Systems Biology**  
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**Indian Institute of Technology – Madras**

**Lecture - 78**  
**Lab: Gene Deletions**

So welcome to today's lab session.


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Computational Systems Biology  
Lab: Gene Deletions

- ▶ Single Reaction Deletion
- ▶ Minimal Reactome

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We will look at gene deletions, we will look at single reaction or single gene deletion and we will also look at how do we build up the minimal reactome for a given organism. So what is the least set of reactions or what is the smallest set of reactions that need to carry a flux for an organism to survive and this has interesting off-shoots from the synthetic lethality analysis that we were talking about a few videos earlier.

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## Gene Deletions



- Find deletions that “break” ATP maintenance
- What is the minimal medium components required for a given model to grow?
- Explore FSEOF strategies for over-producing pyruvate in *E. coli* model...



So let us continue with some lab exercises in constraint based modelling. So can we now identify gene deletions that break the ATP maintenance flux. So do we get infeasible solution and so on, let us explore that and for any given model how would you identify the minimum set of medium components for it to grow. Look for example what are the essential amino acids or something like that.

And can you explore FSEOF strategies for over producing say pyruvate in *E. coli* model, it maybe growth associated likely but let us just figure out if we can come with FSEOF strategies. So let us try to solve these.

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## Gene Deletions

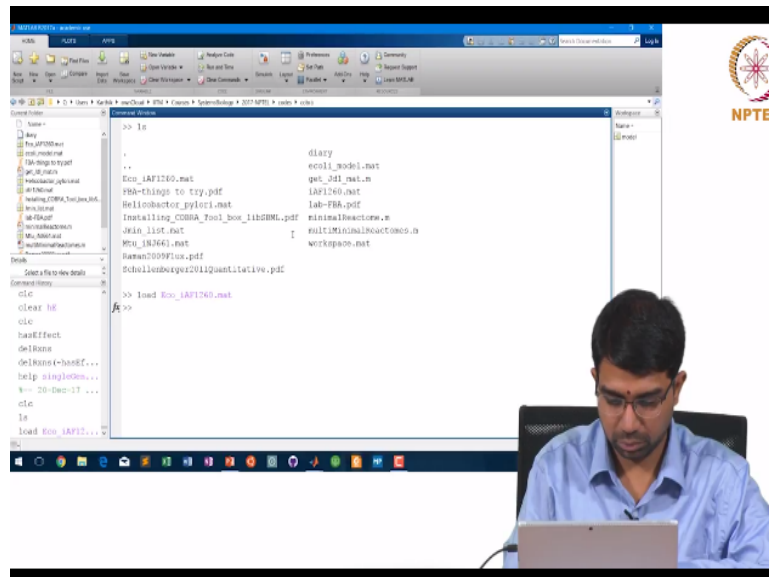


- Identify single lethals in the *E. coli* core model
  - [singleGeneDeletion](#)
- Identify double lethals in the *E. coli* core model
  - Using [doubleGeneDeletion](#)
- Find out a 4-5 gene deletion that is non-lethal
- Try this for multiple models
- Also check out [deleteModelGenes](#)
- What would be the minimal non-essential reaction set in a given model?



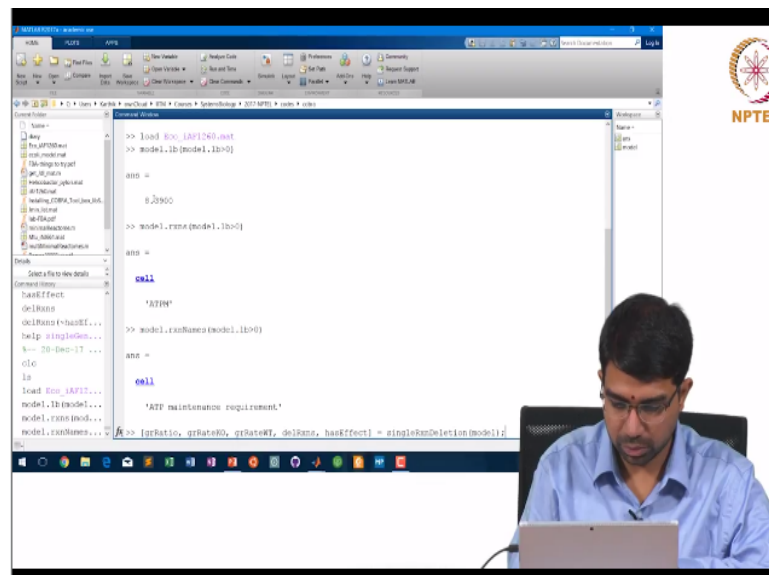
In addition, we can also revisit some of these which we were looking at in the previous lab session.

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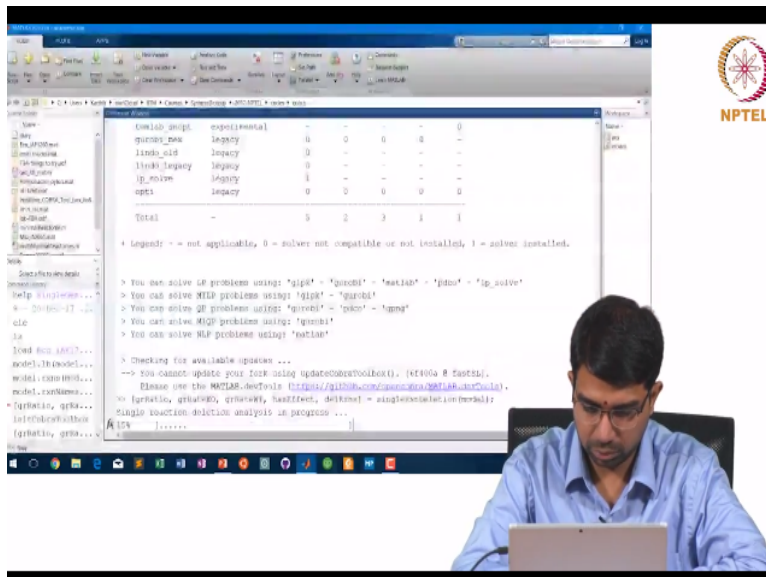


So if you see there is only 1 lb which is  $> 0$ , everything else is 0 or less and that corresponds to ATP maintenance just 8.39. “**Professor - student conversation starts**” So if we just keep on deleting reactions and see whether they will fit (()) (02:46) becomes 0 or not. There is probably one way to look at it because I do not think single gene deletion will directly show you that.

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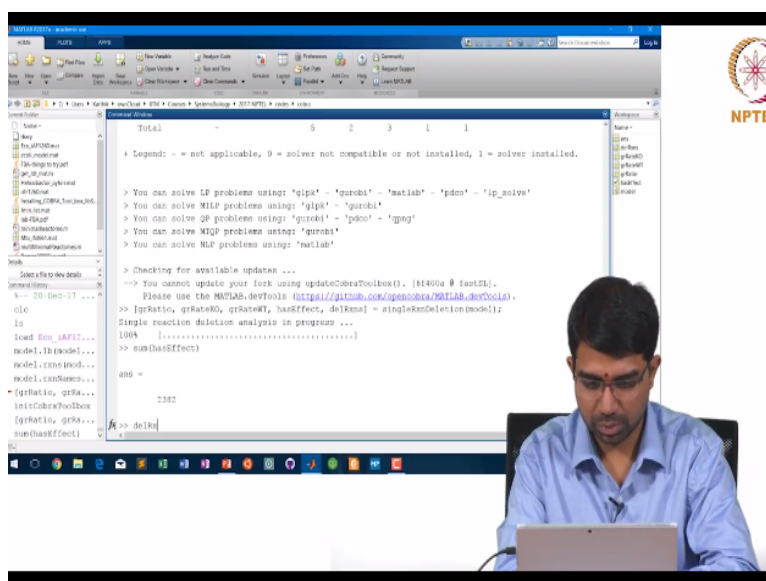
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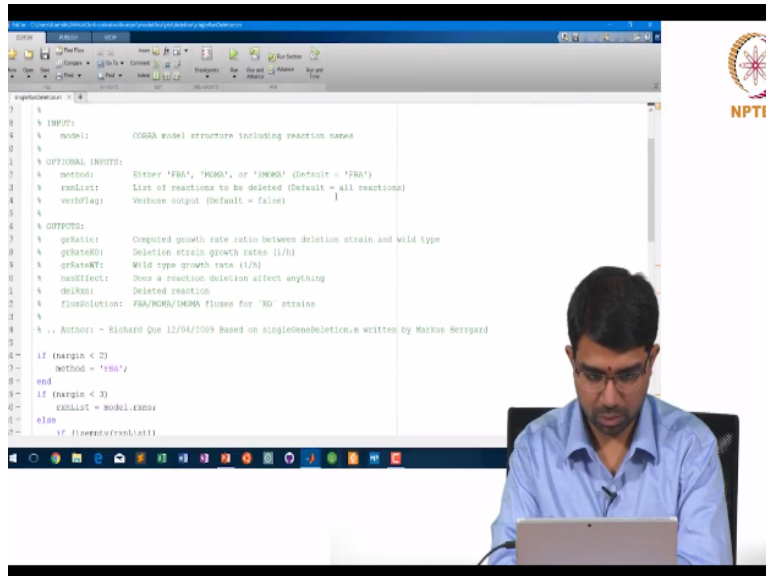
So how are you going about it. So have you already looked delete model genes in those commands. So try to find minimal genome right, by doing the delete model genes that is another exercise you can try out. So delete model genes that will delete (()) (04:58). That is how you will instead of putting the constraints by yourself you look through some genes and you delete them one by one or whatever.

(()) (05:10) if we make a subset of all the things (()) (05:12) 2 power number of things right. You do not want to try all the subsets, you incrementally go deleting genes. If it dies you undo it and you redo that kind of thing. Yeah, so this has affect us like fully one, it is the older version of single reaction deletion.

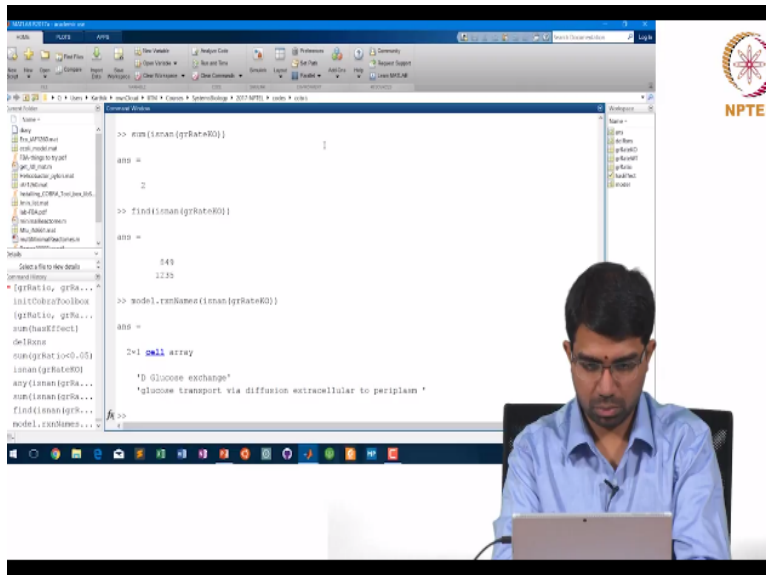
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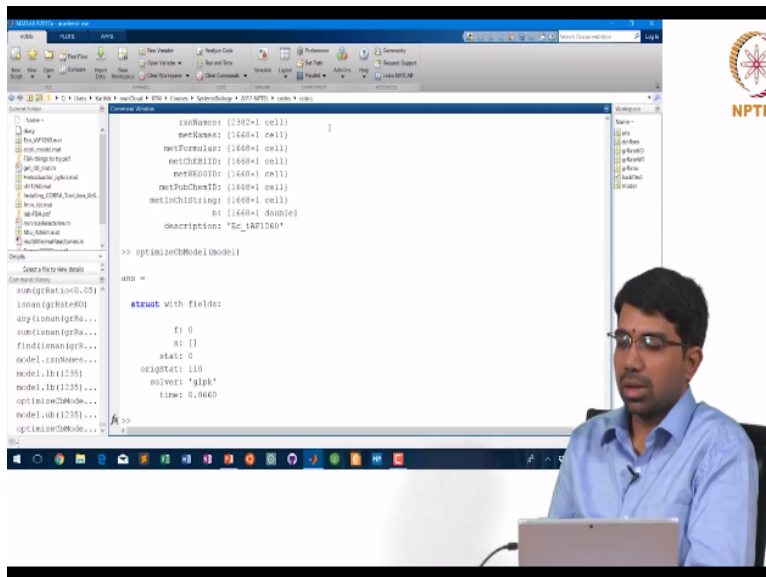


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In incremental deletion, so you are talking about incremental deletion for finding the minimal gene onset right, for ATP we cannot use deletion for finding the whether (()) (08:43).

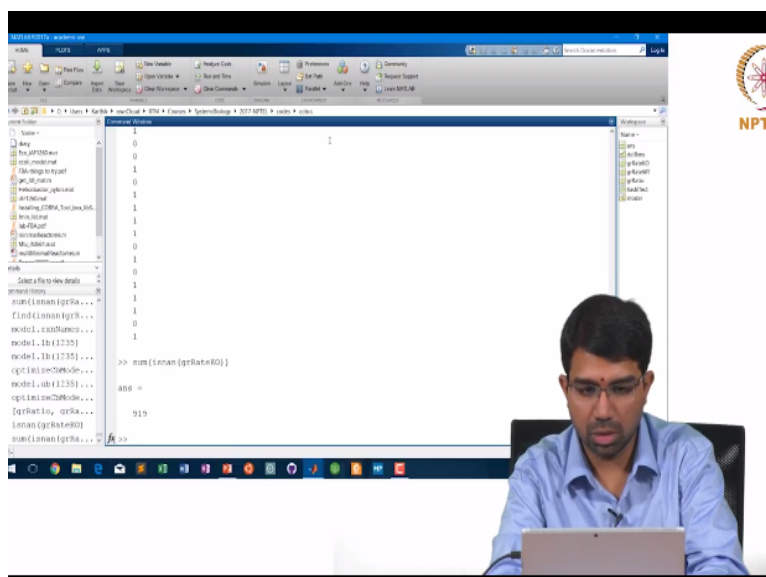
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You can try random sets and see if it happens with single reaction deletion it does not seem to happen, I do not know about single gene deletion, maybe you should try because I distinctly remember that being an issue. Here (()) (08:59) number of gene subset will come. They are possible, but I am just asking you to explore, I not, see only if you have to evaluate all possible subsets right.

You can basically just simulate some subsets some fraction of genes. For every subject we have to check whether that the biomass is whether the cell is growing or not for every subset, yeah, so you are asking us to like find the first subset which, something like that.

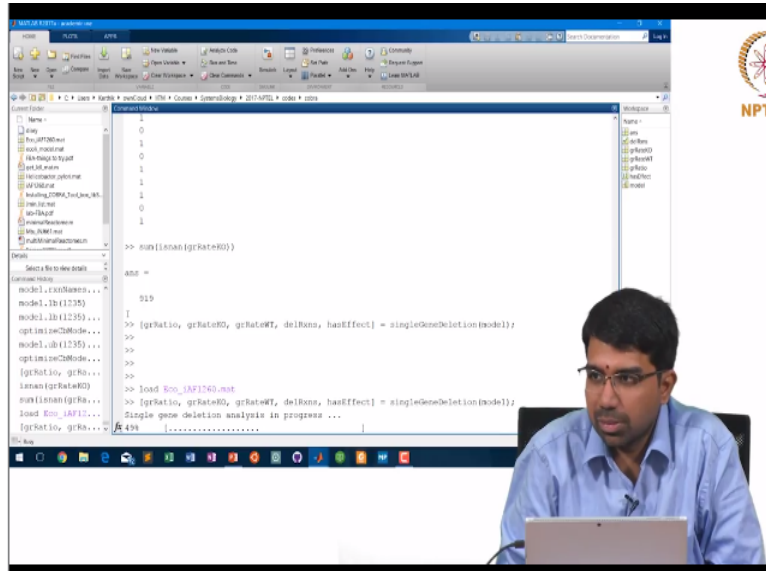
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There is several gene deletions that give you nans. We have to optimise the model and see whether that gene deletion is (()) (10:00). That happen inside of single gene deletion. I will

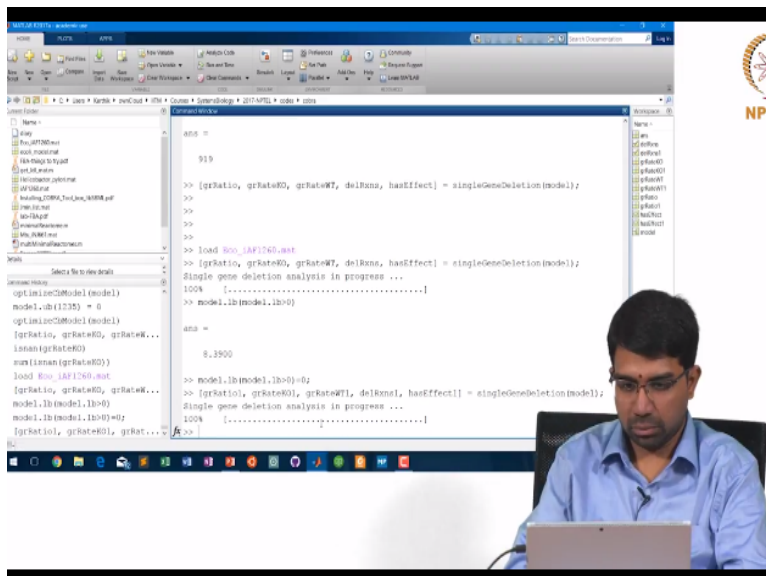
just do a simple analysis that should help. So let us now say, wait maybe, okay. I am just going to compare between setting ATP to 0 and keeping ATP as is and see how different are the results.

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What are the changes and any of them are infeasible? Okay so this (()) (11:18) difference will give you. This growth rate knockout difference I am going to check. How many of them are like nans? There are many not a numbers that are showing up. In the 8.39 only, well I do not know, I have not done the other one. So in the 8.391, yes, I do not know how many showed up because I had changed one more constraint as well, this, let me just check.

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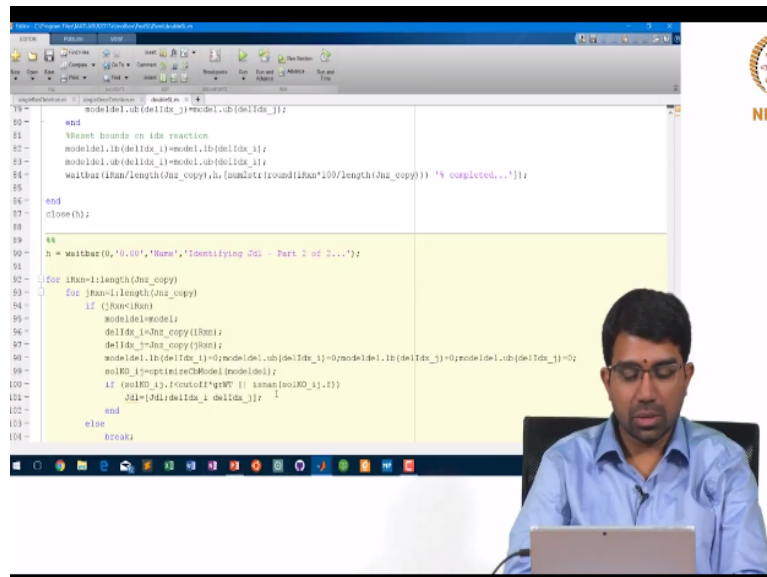


There was nothing, so I am going to how to find out deletions that break ATP. So there is no nan when ld are 0 when there is nan at ld is 8.39 is what that mean? No, no, no in both cases I



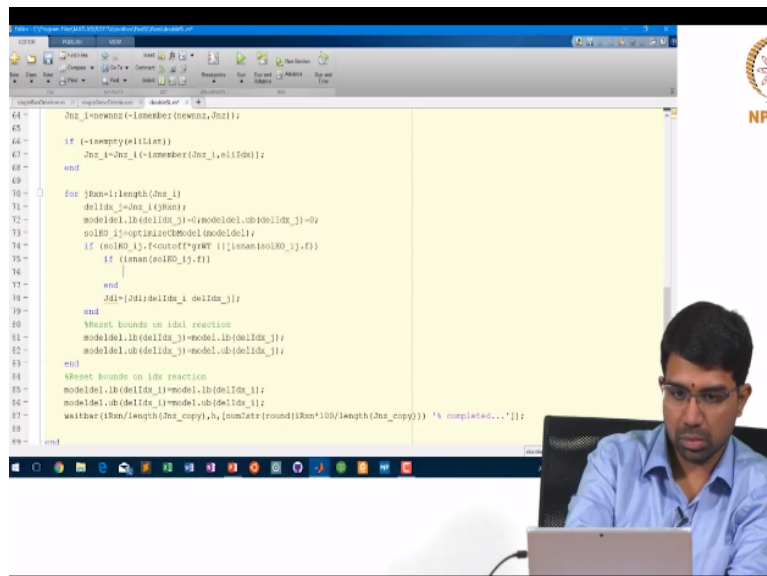
got no nans. Otherwise yes, otherwise there will be exactly what we want. It turns out that here, but if you look at this is faster cell code and you look at the criteria.

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So we are adding line 100, we are saying if this is solution of knockout dot f is less than cut off into growth rate of wild type which is like 0.05 or it is nan we are still adding it to JDL list of double gene deletions (()) (13:05) we talked about it.

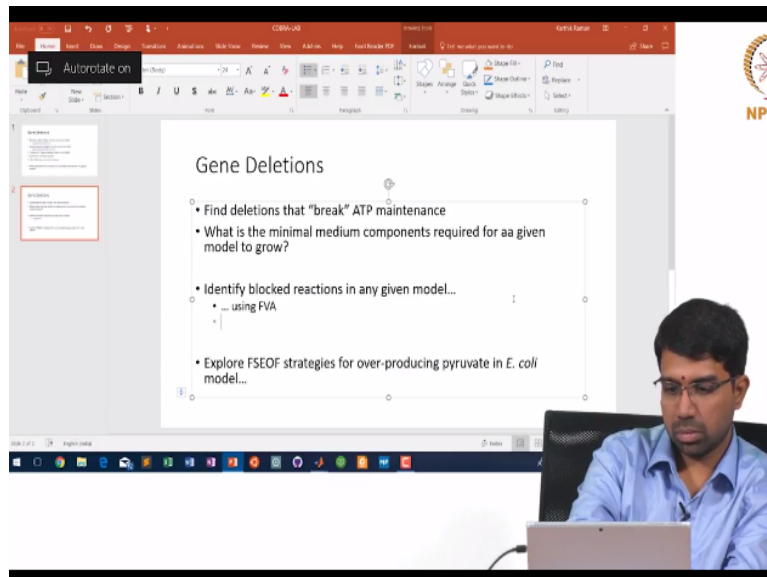
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Also try to identify blocked reactions.

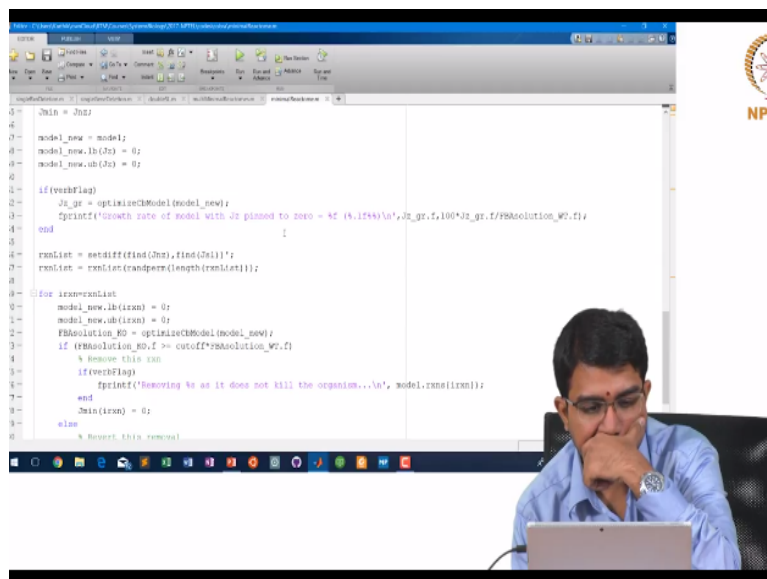
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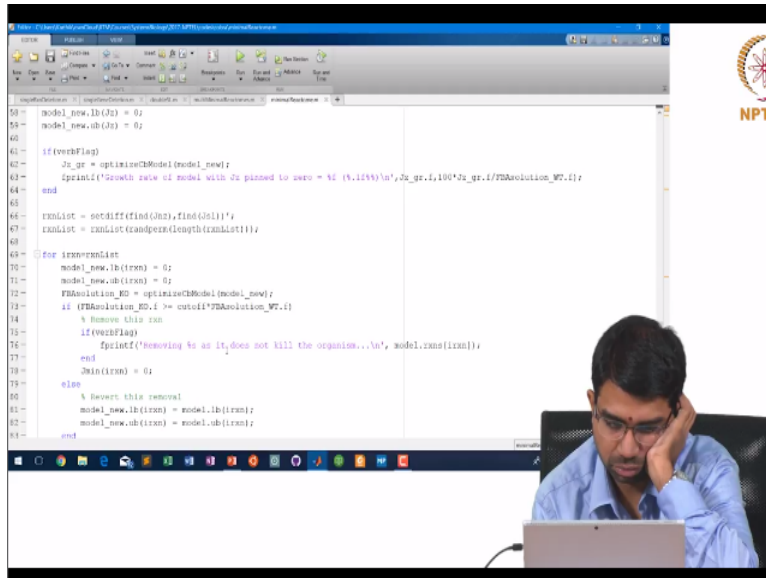


So far I have not found any example where there is nan. We have been doing double gene deletions. Nan means there is no flux or? No it is basically storing it as nan whenever the solver fails and that is exactly what we want.

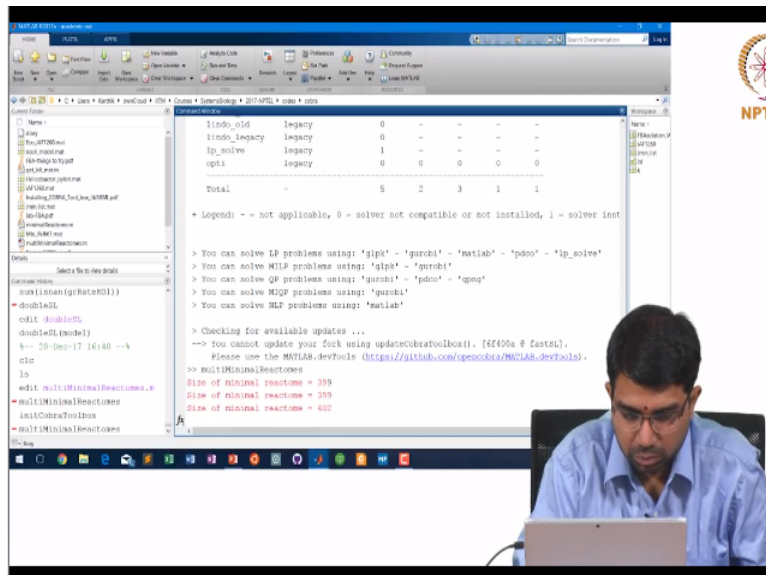
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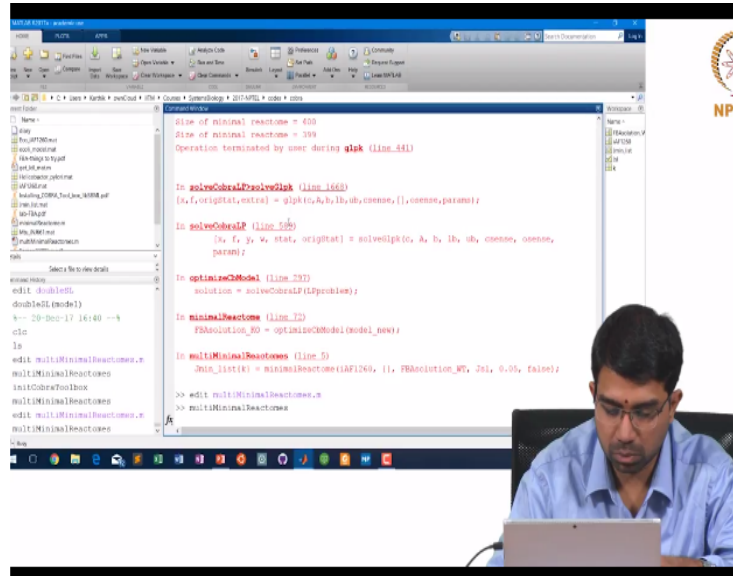
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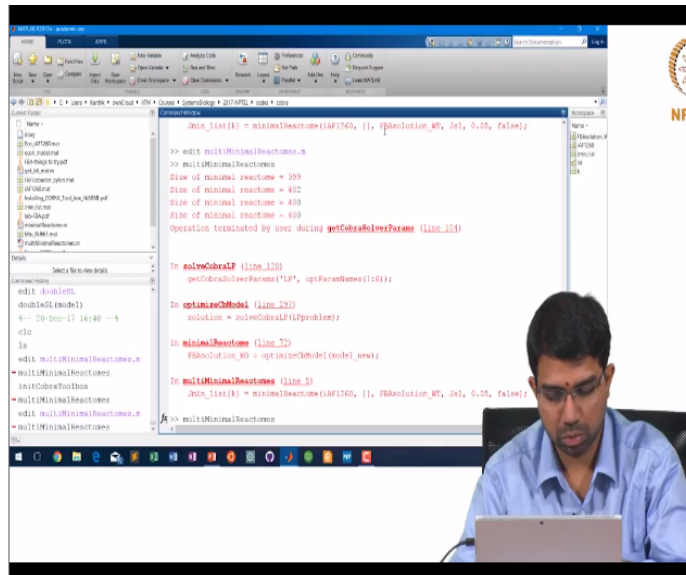
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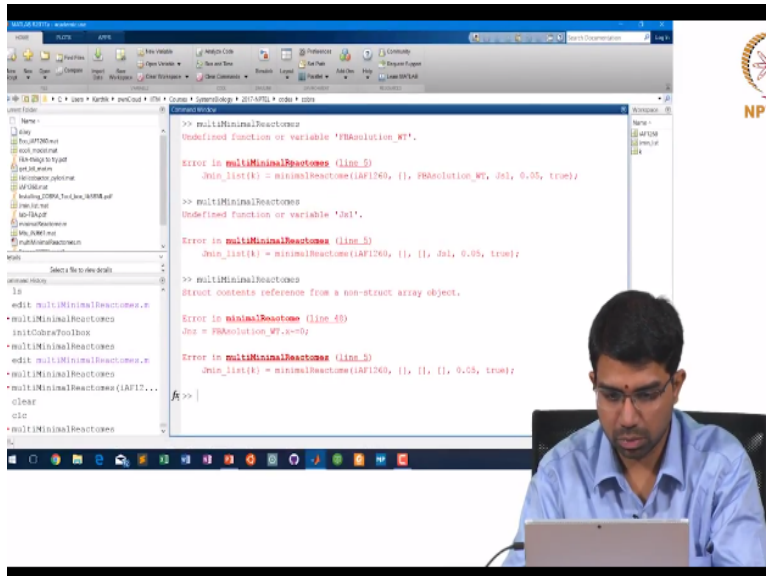


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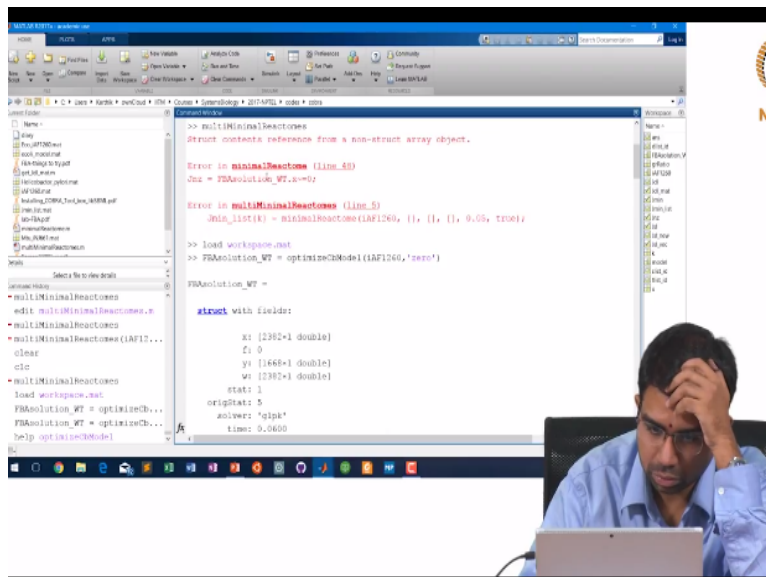


Sir delete model genes, should we give gene names as list or how? Gene names “Professor - student conversation ends”

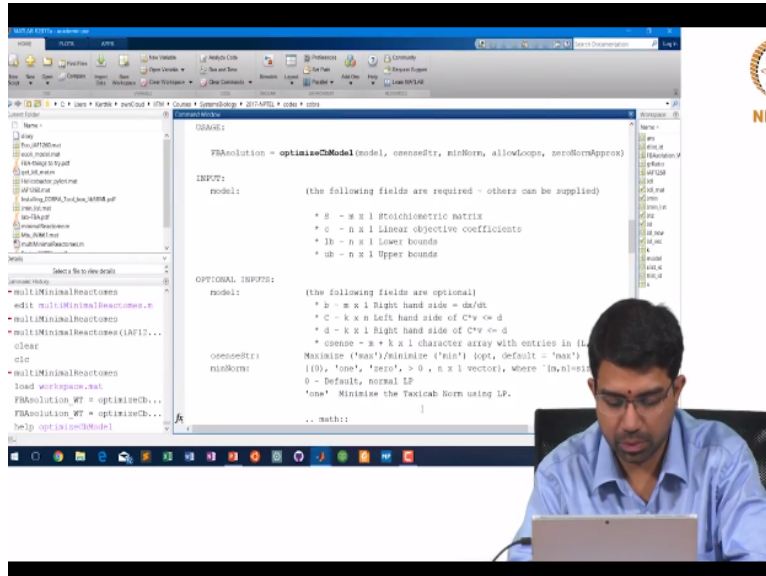
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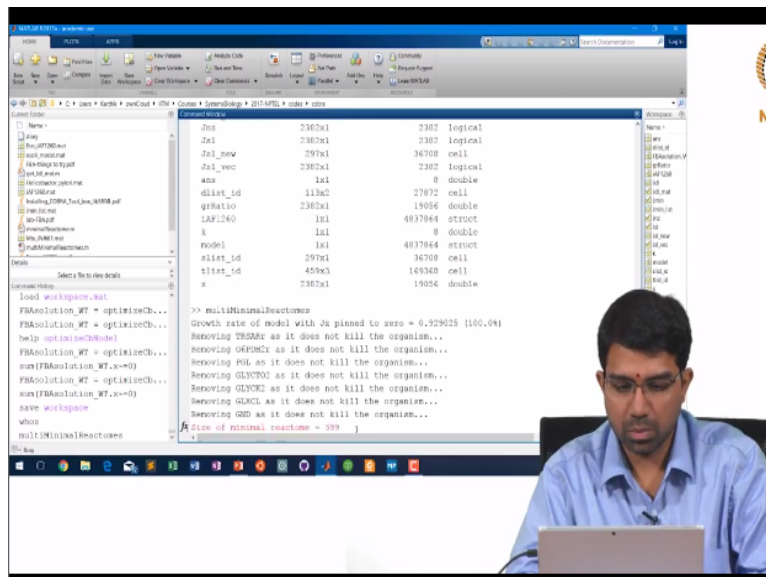
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## Recap

### Topics covered

- ▶ Single Reaction Deletion
- ▶ Minimal Reactome

### In the next video ...

- ▶ Stoichiometric Matrix
- ▶ Constraints
- ▶ Choice of Objective Function

So in today's lab session, we looked at single reaction deletion and how we can try to assemble the minimal reactome for an organism and in the next video, I will conclude constraint based modeling by recapping all the concepts we have covered so far beginning with the stoichiometric matrix, the kind of constraints that we impose and again the favourite topic which is the choice of objective function for flux balance analysis.