

Neural Science for Engineers
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Lecture - 37
COMSOL Multiphysics for Medical Devices

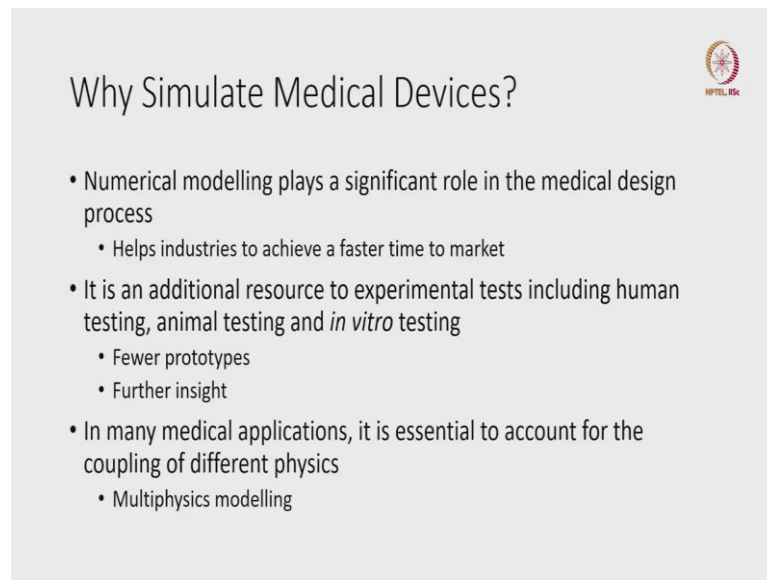
Welcome everyone. On this continuation of the course of Neural Science for Engineers, today we are going to talk about how the numerical tools can be used for various neural science applications.

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In addition to the neuroscience, we will talk broadly on of what all other biomedical applications can be solved with the numerical tool such as COMSOL Multiphysics.

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The slide is titled "Why Simulate Medical Devices?" and features the NPTEL logo in the top right corner. The content is organized into a bulleted list:

- Numerical modelling plays a significant role in the medical design process
 - Helps industries to achieve a faster time to market
- It is an additional resource to experimental tests including human testing, animal testing and *in vitro* testing
 - Fewer prototypes
 - Further insight
- In many medical applications, it is essential to account for the coupling of different physics
 - Multiphysics modelling

So, the first thing comes into the mind that what is the need actually to simulate a medical device. So, why do not we actually go ahead and make multiple prototypes of any medical device and see how it is working.

So, some of the reasons are as follows, simulating the device, help the industry to achieve a faster time to market especially, when you have different phases of trials rather than doing the trials on human or animal testing, it is always good that you first do a trial of a simulation in an animal model or simulation model first or a human model simulation.

And once you get the intuitive results out of it, how the currents are propagating through a tissue, how much is the flow of a chemical reagent through a tissue so, once you get an intuitive understanding of those physical phenomena, then you can go ahead and start to perform the test on animal models or let it be on human trials.

So, the outcome of performing simulation of medical devices would be you will have fewer prototypes that you will be building and further insights. What is actually happening, physically what is actually happening within the tissues? Also, why do we use a multiphysics tool, because any of the medical applications that you see in and around your world, what you see is that those have multiple physics that are coupled together. So, how do you couple multiple physics seamlessly is what we are going to see today.

For example, you can couple this flow of current within the tissue. The tissue itself is a conducting material. Because of this rise, because of the flow of the current in the tissue, there would be a rise in the temperature of the tissue. Now, whether this rise in temperature within the tissue is going to be a damage which could lead to a damage of a tissue is what you can kind of do pre-analysis before you try to implement your prototype in an animal model or a human trial.

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Medical Devices and Multiphysics

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- Structural mechanics
 - Cardiovascular applications
 - Orthopedic applications (contact and wear analysis in implants)
 - ✓ Contact lenses, eye surgery
 - Mechanical behaviour of tissues, blood vessels, skin, bones, plastics and polymers
- Fluid dynamics
 - Cardiovascular applications
 - Blood filtering devices
 - Blood modelling (single-phase flows, two-phase flows, particle tracing)
 - ✓ Biosensors
 - Lab-on-chip and microfluidics

Visualisation of total displacement and ray trajectories in a 3D parametric full-eye numerical simulation. Check out the [user story](#).

So, let us talk about what are the Multiphysics analysis that could be performed. So, we start with structural mechanics so, you have cardiovascular applications, orthopedic applications for example, contact and wear analysis.

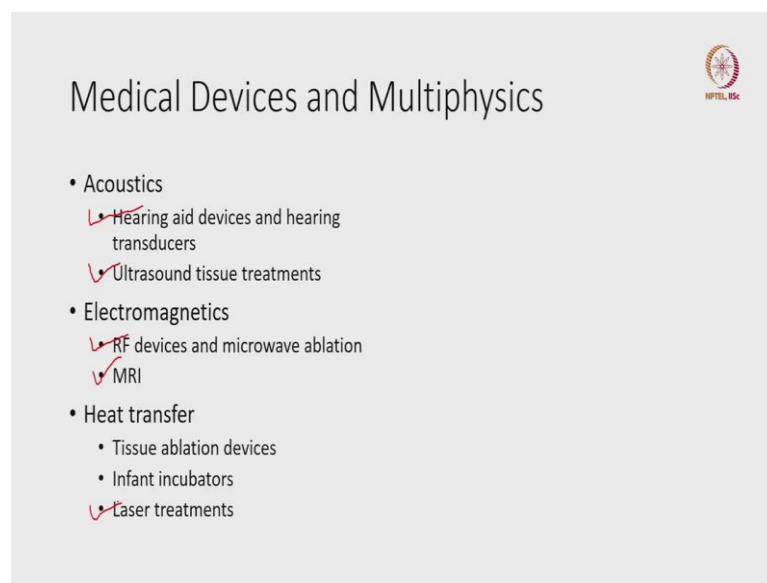
You have contact lenses analysis for example, what you see on the right side is a complete model of an eye within a COMSOL Multiphysics. And you can see the lens structure that you see over here, and this gets deformed in a particular manner so that the light; these are the rays that are propagating from this direction it focuses at the retina of the eye.

So, this complete analysis which includes the deformation of the lens material, you have the rays which are propagating through the lens or the deformed lens interacting with the retina. So, all of this could be modeled in a single interface and that is what is the beauty of this tool.

You can also model fluid dynamics applications. For example, what we are going to see in sometime, it is a blood flow modeling. So, you can see how complicated the flow of blood is and especially the different constituents that are available in the blood, and you want to model all those constituents of blood which are having different electrical as well as magnetic properties.

Biosensors is also one of the applications that we are going to talk about and some of the biosensors that we are going to talk about are going to be glucose sensors for example.

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Acoustics is also another application where simulation can help. One can actually use hearing aid device simulations to see what the effectiveness is or how accurate or how efficient the hearing aids and the transducers are. So, how sensitive those transducers are. So, those are the things that we could actually quantify.

Then, it comes about ultrasound tissues for example, you have very high frequencies of acoustic wave that are propagating within the tissue. So, you want to see what those effects are. Are they increasing the temperature of the tissues and to what extent are they increasing the temperature of the tissues? So, those things could also be studied.

In electromagnetic applications, there are huge applications, you have RF devices and microwave ablation devices. Specifically, if you want to damage localized region which is representing a cancer for example so, you want to kill a very localized region which is

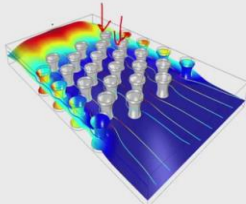
termed as a tumor at those places, so that it does not propagate or mitigate to other domains or the other places within the body. MRI coils are also one of the ways that you can use.

And then finally, we have the heat transfer. So, you can study tissue ablation for example, you want to see how much the damage in a certain region of a brain is. For example, you can see how much the rise in temperature is, if it is going more than the threshold, what are the changes we need to do in the devices so that the damage is limited to a certain region in the brain. Laser treatments on the skin as well as on a surface of any bone could also be studied.

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Medical Devices and Multiphysics

- Species transport
 - Drug delivery devices
 - Drug release systems
 - Biosensors
- Particle tracing
 - Biosensors
 - Drug release applications
- Apps
 - Make simulations accessible to everyone

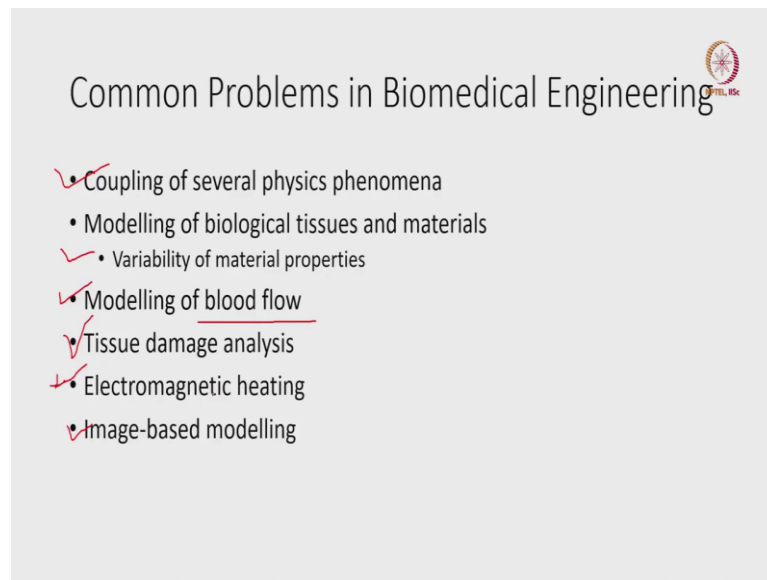


Simulation of a flow cell containing micropillars coated with an active material to support analyte adsorption. Check out the example [here](#).

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Finally, we have the drug delivery analysis. So, how effective the drug delivery is for example. How effective is the biosensor? So, here we have multiple micro pillars that you will see over here, so we see the micro pillar. So, they are arranged in a certain array and which arrangement is the best, which optimizes the device is what you can actually perform. So, here we flow an analyte and this analyte gets adsorbed on the surface of the micro pillars to see if there are any antibodies in the analyte.

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Common Problems in Biomedical Engineering

- ✓ Coupling of several physics phenomena
 - Modelling of biological tissues and materials
- ✓ Variability of material properties
- ✓ Modelling of blood flow
- ✓ Tissue damage analysis
- ✓ Electromagnetic heating
- ✓ Image-based modelling

So, what are the common problems that comes up in biomedical engineering? The first challenge that comes is the coupling of several physical phenomena. So, that is what we are also going to see in the demo that we are going to do.

We are going to do electrical stimulation within the brain and in that, we will see that there is not just the flow of the currents, but because of the flow of the currents, there could be a rise in the temperature and that could lead to the damage in those regions that we do not want.

So, we can see like how much are we going to affect the tissues before we actually implement it into any animal model, they prototype into animal model or a human trial.

Another is the variability of materials. So, whenever you are doing a simulation, the tissue properties are heterogeneous. So, there is always a challenge as to how to overcome such kind of issue of heterogeneity and few of the approximations could be to use a homogenized approach and some of the tissue properties have their own mathematical model. So, sometimes, you need to use those mathematical models to represent a certain tissue type.

When we talk about electrical stimulation within the brain, it is not just the tissue that we are going to model, but there is also an extensive flow of blood within the arteries and capillaries of the tissues in the neural regions. So, how do we take account of the blood

flow? So, those are also a kind of challenge while you model an electrical stimulation or magnetic stimulation per se within the brain.

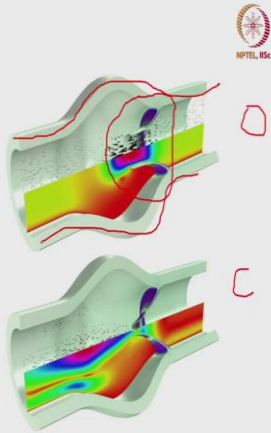
Tissue damage analysis means how much is the extent of the damage of the tissue's if any. Electromagnetic heating, this is what also we are going to talk about and then finally, Image-based modelling. So, what I will do in the first session is I will just try to give an overview of different examples that could be modeled and then in the end, in the next session, I will try to take a demo on electrical stimulation within the brain.

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Multiphysics Coupling

Medical device modelling requires coupling different physics and analysis types.

- Bidirectional or monodirectional couplings in problems involving more than one physics
 - Fluid-structure interaction, Joule heating, conjugate heat transfer, acoustic-structure interaction
- Multiphysics problems involving physics with a different time scale
 - Stationary electromagnetics and time-dependent heat transfer
 - Frequency-domain acoustics and time-dependent thermal study




FSI model of a heart valve opening (top) and closing (bottom). Check out our [blog post](#).

So, one example that comes over here is how do we actually understand the flow of blood within the heart valves. As you can see over here, this is a heart valve over here and this is the valve over here and it has two states, the first one is open, and another is closed. So, this on the top is an open condition and the one on the bottom is the closed condition.

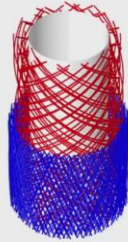
So, here you can try to see and visualize the flow of the blood once it is open and once it is closed and there are different kind of states that comes within the open and closed. And there could be any disease within this valve of the tissue that could lead to the turbulent flow being generated once the blood flows through this valve. So, we should always try to minimize this turbulent flow and from this, we can also understand what is the kind of disease that the valve is actually having.

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Modelling of Biological Tissues



- Biological materials can exhibit complex stress-strain characteristics
 - ✓ Large deformations
 - Viscous behaviour
 - Temperature dependency
 - ✓ Anisotropy
 - ✓ Creep
 - ✓ Prestress
- COMSOL Multiphysics® offers several material models to account for the complexity of biological tissues
 - ✓ Hyperelasticity, elastoplasticity, viscoelasticity, viscoplasticity, etc.



Anisotropic hyperelastic artery.
Check out the example model [here](#).

Biological tissues as I said earlier, has heterogeneous properties. So, this could be modeled into various different aspects. For example, there could be anisotropy within the tissue. So, such things could be introduced. You have the creep, or it is already prestressed the tissues. For example, the ligaments, it could undergo large deformations. So, they are very complex, the biological tissues.

So, you might need to also take into consideration different material models. For example, some of them would be hyper-elastic or it could be elastoplastic, or it could be viscoelastic or it could be viscoplastic, all of them have different properties.

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Smart Materials

- Shape memory alloys (SMA) are able, when deformed, to revert to their original shape after reheating
 - Souza-Auricchio, Laugodas models
 - Significant hysteresis
 - Cardiac stents, orthopaedics, glasses frames, etc.
- ✓ Piezoelectric materials can convert electric energy to mechanical energy and vice versa
 - Direct piezoelectric effect (electric polarisation upon deformation)
 - Inverse effect
 - Optics, transducers, pressure sensors, etc.

Von Mises stress in a SMA stent after crimping. Check out the example model [here](#).

Piezoresistive pressure sensor. Check out the example model [here](#).

$I = \frac{1}{P}$

There are now lot of applications regarding smart materials and one of them is shape memory alloys that you see over here. In the case of shape memory alloy, what you see over here is shape memory alloy stents is one of the examples and the stent which are introduced in the arteries of the sinoatrial capillaries which are covering the heart.

It has a certain property that it is able to get back to its original shape once it is relaxed. So, this particular stent that you see over here is actually constricted to a lower radius and then, it is introduced within the artery so, if this is the artery and once it is introduced within the artery, it then expands and then, it becomes like a big kind of thing.

So, if there are any blockages within the arteries, it could actually suppress those blockages. So, ideally, if this is the artery, you have certain kind of blockage like this, perhaps because of the deposition of cholesterol and after the placement of the stent would look something like this so, it will kind of get minimized over here and the positioning of the stent will come somewhere over here.

So, I am just trying to do a side view cross section over here. So, this is the stent over here which will actually help in increasing the blood flow in the center. So, here you can see that the blockage actually is impeding the flow of the blood. So, it is not allowing the blood to flow that easily, but in this case, after the placement of the stent that you see over here, the flow is now comparatively better.

There could be also various kind of materials that you would be interested to model and placement of those materials within the tissues. For example, it could be the piezoelectric materials which converts the structural deformation into electrical signals and vice versa.

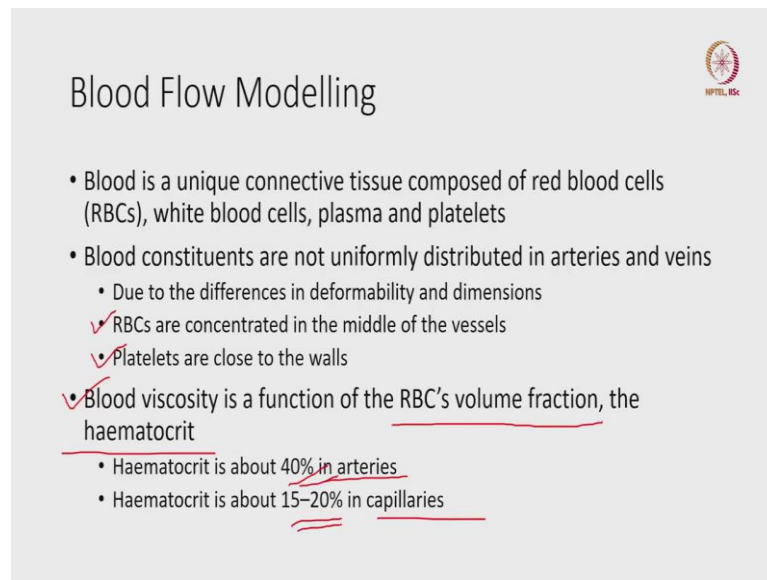
There are different physics that you can couple with this piezoelectric material, it could be optics, or it could be ultrasound transducers or pressure sensors. So, these different kinds of sensors could be built using such piezoelectric materials. In addition to piezoelectric materials, you could also be interested to use piezoresistive materials so such sensors could be used in neuroscience applications.

For example, if you have the brain tissue over here and you want to apply a probe over here. So, you want to see how much the probe is causing the pressure so, you want to quantify the pressure for example, so, how do you do that? So, one of the ways is to use a diaphragm that you see over here. This diaphragm could be a part of the probe and this diaphragm is going to give the force on this probe tip.

So, the probe tip if I just zoom in over here, so a probe tip would be something like this for example, it could be minimizing to like a small point over here which will be giving a focus on the or it would be in placed on the top of the tissue and this probe; this diaphragm has certain property that once you apply the force over here, the current that is flowing over here is going to change based upon the pressure. So, the current over here is a function of the pressure that we apply.

So, with this, we can calibrate the pressure with the current and we can understand the pressure that could be applied on a neural tissue.

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Blood Flow Modelling

- Blood is a unique connective tissue composed of red blood cells (RBCs), white blood cells, plasma and platelets
- Blood constituents are not uniformly distributed in arteries and veins
 - Due to the differences in deformability and dimensions
 - ✓ RBCs are concentrated in the middle of the vessels
 - ✓ Platelets are close to the walls
- ✓ Blood viscosity is a function of the RBC's volume fraction, the haematocrit
 - Haematocrit is about 40% in arteries
 - Haematocrit is about 15-20% in capillaries

Blood flow is also a challenge to be modelled specifically in the case of neural tissues because there are numerous blood capillaries that are flowing in the neural tissues. The challenge that we face is there are lot of constituents for example, there are RBC's, there are platelets, there are white blood cells, there are plasmas. In addition to it, they have their own properties.

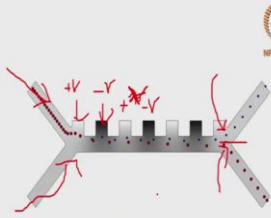
For example, the RBC's that is red blood cells are constituted in the middle of the vessels. Platelets are concentrated to the walls of the arteries or the vessels. So, they have their own properties. So, once you model those properties or those as particles within COMSOL or in numerical tool, then you would be able to better understand the flow of the blood within the arteries and veins.

Also, the blood viscosity is also one of the major analysis or a way to perform the analysis, this is one of the main properties of the blood and it is also a function of the RBC's volume fraction. And that particular volume fraction is dependent on haematocrit and that haematocrit is again different in arteries as well as capillaries. So, it is 40 percent in the arteries, but it is around 15 to 20 percent in the capillaries. So, such variations are a challenge when you actually try to model the blood flow.

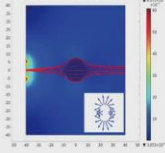
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Blood Flow Modelling

- In blood separation devices, blood flow can be modelled with a basis flow
- The relative motion of the blood constituents (e.g., RBCs) is modelled with particle tracing techniques
- It is not always efficient to model blood constituents as particles



Dielectrophoresis (DEP) Model studies the application of DEP to separate red blood cells from platelets in a microfluidic device. Check out the model [here](#).



Patterning cells with the flip of a switch for bioengineering applications. Check out the [user story](#).

In COMSOL you can actually couple the flow of the fluid. For example, it could be the flow of a kind of the plasma and in addition to the flow of the plasma, you have particles that you see over here and if you see over here, there are two particles one is red in color, another is blue in color. So, both of these red and blue particles are two different particles. So, one is the red color is the red blood cells and the blue color is the platelets.

So, here we try to understand, what we do is over here, we have plus 5 volts for example, then we have minus 5 volts similarly, again plus 5 volts, minus 5 volts and all. So, what we try to see is that because of this plus and minus 5 volts or plus or minus volts, there is a particular electrical field pattern, and that electrical field pattern segregates the platelets with the RBC's.

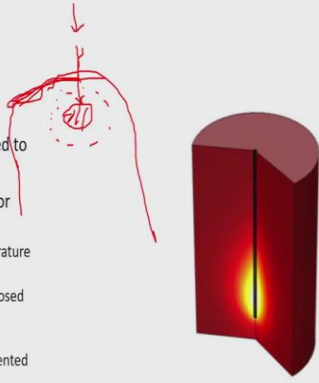
So, here you can see this actually works as a segregation filter and based upon the field and the property is known as dielectrophoretic property of these platelets and the red blood cell and that is related to the permittivity of the RBC's and the platelets which differ. So, based upon that, you can see there is more deflection of particles in the platelets in the top region towards the top directions while the RBC's actually a deflect toward the bottom wall.

So, this is how you can couple two or more physics, and this is true even when you talk about a neuroscience. You have lot of capillaries and veins, and you want to see how effective a particular drug is through a micro channel, you can see how that works.


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Thermal Damage

- There are several forms of damage related to biological tissues and medical devices
- Tissue damage due to excessive heating or cooling in tissue ablation
 - Instantaneous tissue damage when temperature exceeds a given upper/lower limit
 - Cumulative damage when the tissue is exposed to high/low temperatures for an extended period of time
 - Both forms of damage are already implemented in COMSOL Multiphysics®
 - Customised damage models can be easily implemented



Microwave heating of a liver cancer tumor.
Check out the example model [here](#)




Finally, we have thermal damage. One of the examples is there is a brain tumor that you want to kind of destroy. So, for example, you have the brain tissue over here and this is the region which is actually having the tumor. So, what as you can see over here is we introduce a probe over here and what happens over here is that we introduce an RF power so, we have around 20-30 megahertz of electromagnetic energies introduced at significantly higher power, and it tries to increase the temperature within this region.

Now, important part is that the damage, because of the rise in temperature in this localized region, should be limited to a certain region, but it should not go pass through to the nearby healthy tissues.


So, simulation could actually help to understand what the fraction of damage is, what are the volumes of the localized region of damage before it is actually implemented into a rat model, or it could be on animal model or a human trial right. So, this is an excellent way to understand or visualize the damage before it is actually implemented.

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Electromagnetic Heating in Human Tissue



- Specific absorption rate (SAR) is used by scientists to determine the amount of radiation that human tissue absorbs
- Three forms of electromagnetic heating available in COMSOL Multiphysics
 - Resistive losses
 - Dielectric losses
 - Magnetic losses
- The volumetric heat source is coupled to the thermal problem, which has a different time scale



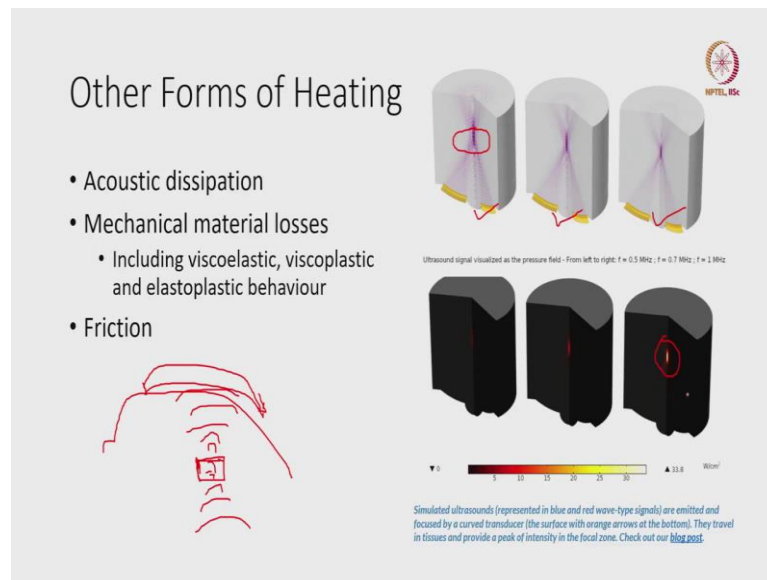
Specific absorption rate in the human brain. Check out the example [here](#).

One more in the case of neural science is a hot discussion that is happening nowadays, is how are the mobile phones affecting the tissues of the brain and that is known as specific absorption rate that is because of the radiation, people working using 4G and now 5G, the power of the radiation are significantly increasing as you go on improving the technologies.

So, those power which is getting coupled with the tissues of the brain which introduces the rise in temperature, there could be different reasons to that, it could be either resistive losses, it could be dielectric losses or magnetic losses, but those losses could lead into the rise in temperature within the brain tissue.

So, what is the fraction of the rise in temperature? Whether it is 1 degree Celsius, 2 degrees Celsius, 3 degrees Celsius and for how much time it is there? This what could be studied in some of the examples and this one example is a tutorial model so, if you are interested you can just go through those and just to see if it is under the safety level which is required.

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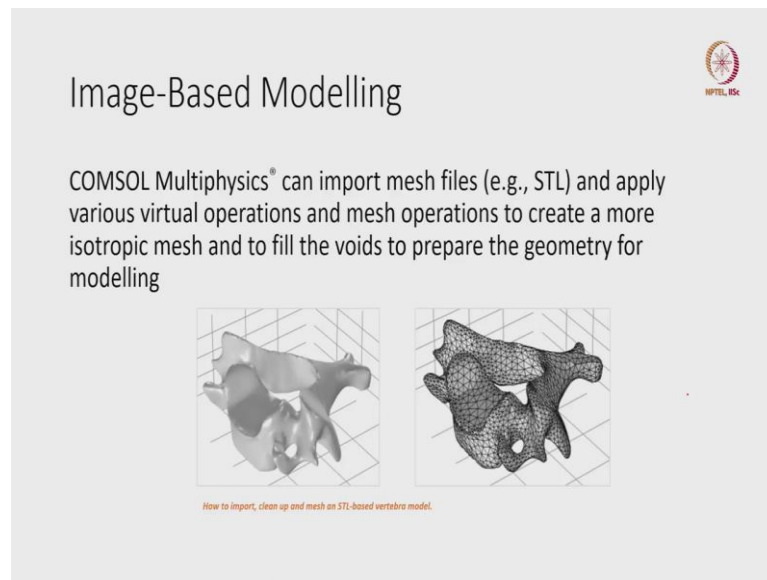


Other forms of heating could also be used for example, you have ultrasound transducer, and you want to image the brain, you want to do a localized brain imaging using the ultrasound transducer or you want to again to introduce, if this is the brain tissue and you want to you have an ultrasound transducer like this and you want to damage or you want to inhibit to this particular localized region of the tissue which is actually a cancer. So, you can launch this ultrasound radiation which is actually getting focused somewhere over here.

And then because of the focus, somewhere over here, you can see this is the focus area. The rise in temperature is going to be significant as you go on increasing the frequency. So, you can see this is 0.5 megahertz, this is 0.7 megahertz, this is 1 megahertz.

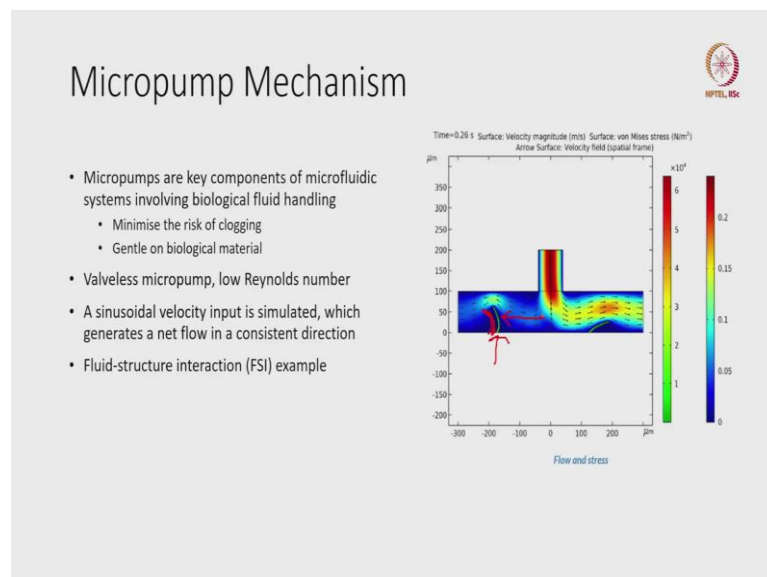
And you can see the thermal profile on the bottom images and you can see for 1 megahertz, the rise in temperature is significant, this is around 30 degrees, 30 watt per centimeter square is the losses volumetric losses that are occurring over here. This is what you can also see and understand.

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You can also import the images, STL images within the tool and mesh those geometry and try to see how much stress is being generated on this vertebrae for example.

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The final thing is micro pump mechanism. So, you can couple structural mechanics. So, you can see over here, these are the kind of extrusions on the micro pump, and this is under the exertion of the flow of the fluid which is making it to bend as you can see over here, and this bending is changing the flow of the blood. So, this requires the coupling between fluid dynamics and structural mechanics.

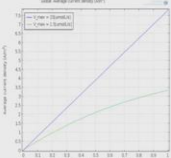
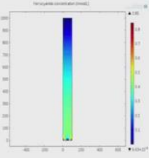
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Glucose sensor

- Electrochemical glucose sensors use amperometric methods to measure the concentration of glucose in a sample.
- This example models the diffusion of glucose and ferri/ferrocyanide redox mediators in a unit cell of electrolyte above an interdigitated electrode.
- The sensor gives a linear response over a suitable range of concentrations.
- The Electroanalysis interface is used to couple the chemical species transport to the electrolysis at the working and counter electrodes, and the glucose is oxidized by the glucose oxidase enzyme in solution according to Michaelis-Menten kinetics.



Glucose monitoring system
(Source: Wikipedia)



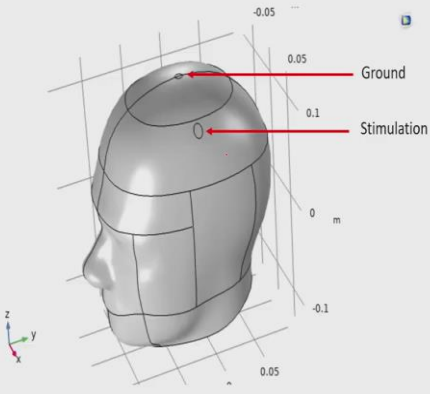
Current density versus glucose concentration

<https://www.comsol.co.in/model/glucose-sensor-16269>

And then, we have glucose sensor so, people who are from chemistry background, such kind of electrochemical glucose sensors could also be performed, this is the electro analytical simulations that you need to perform over here. It is not just limited to the glucose sensor in the finger, but you can also perform a similar kind of analysis in the brain on similar line.

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Brain electric stimulation demo



Ground

Stimulation

So, that ends the first session of the numerical analysis for Neural Science for Engineers. In the next session, we are going to talk about how you can perform electrical stimulation within the brain.

Thank you.