LORNA GIBSON: What I thought I would do today is two things. I wanted to give this talk about osteochondral scaffolds, and this is just slides. I'm not going to write anything down. So there aren't going to be any notes. And I'll put the slides on the Stellar site, I don't know, this afternoon or tonight or something.

And this isn't going to take the whole time we have today, so the other thing I thought I'd do is I wanted to walk you through this little booklet that I handed out about how to write a paper.

So this is by Mike Ashby, who you know, I've written books with. He was my PhD advisor and we wrote the books on cellular solids together. He has written many books. I looked him up on Amazon this morning, and even though I know he'd written many books, I was shocked how many books. They had 58 listings for just books with him as a co-author and some are second editions and third editions.

He's written a lot of books. He's written a lot of materials, papers. And he's, in the materials community, he's seen as a very clear and lucid writer. So he's written this thing for his students and I thought we could just walk through it and I can talk to you a little bit about writing. Because I know you're not quite there with your projects, but later on in the term you're going to want to write up your project, and it's not too early to start thinking about writing.

And there's some really good advice and it's short and it's to the point. It's really helpful, that little brochure. So we won't read every single thing, but I wanted to kind of walk through some of the main points in it, and that pretty much should take the hour.

So last time we talked about tissue engineering scaffolds, and today, I wanted to do a case study, and this was a project we had here at MIT and in collaboration with some people in the materials department at Cambridge University.

And we made what we called an osteochondral scaffold. So osteo means there was a part for regenerating bone and chondral means there was a part for regenerating cartilage. And really the point of the scaffold was to try to repair small defects in cartilage. And I'll explain why we

did the bone thing as well.

So this is just a little outline. I'm going to talk a little bit about what the structure of cartilage is. We have a little schematic of that. Then talk about how small defects in cartilage are currently treated. So these are things that, say you're an athlete, you might tear some cartilage, that kind of thing, not like you have osteoarthritis and you need a new knee. It's not going to do that.

So I'll talk a little bit about cartilage and the current treatments. I'll talk about some of the things we thought about in making an osteochondral scaffold, like what parameters were important. And we based it on that collagen-GAG scaffold that I talked about last time. So the collagen glycoseaminoglycan scaffold that we talked about last time.

And what we did was we had a layer that was a collagen based scaffold for the cartilage and we had another layer that was a mineralized version of that. And one of the main things we did in this project was figure out how to mineralize that scaffold. And then we made this two-layer osteochondral scaffold. So I'll talk about that, OK? So are we good?

So this is a schematic of articular cartilage. Articular just means it's in a joint, so between like, say, two of your long bones, and there's several regions. So this shows both the cartilage and the bone underneath it.

And so this top layer is called the superficial layer, and then there's a transition zone, and then there's this deep cartilage here. And the little white lines represent how the collagen is oriented in the cartilage. So the collagen is oriented, more or less, vertically here and then it becomes more kind of woven and horizontal towards the top. And so those three different zones, the collagen is oriented differently.

Then there's a region down here called the tidemark. Everything above here is just cartilage and everything below is calcified to some extent. So this next layer down here it's more cartilage-like, but it's got some calcification in it as well.

And then here's the compact bone. They call it subchondral bone. It's the bone below the cartilage. So chondral is cartilage. And then here's the trabecular bone. We talked about trabecular bone a couple of weeks ago, OK?

So one of the things is there's different types of collagen and the different types may have

slightly different fiber structures or slightly different compositions. They're all related, but they're slightly different types. And bone has what's called type I collagen and cartilage has type II collagen. So when we made the scaffold, we wanted the bony layer to be made with type I and the cartilage layer to be made with type II.

So I think with the 3032 people have probably seen it. I think I did a version of this for you guys, didn't I at the end of term, something? Yeah, but there's other people, so it's really for them.

So if you think of articular cartilage, it has difficulty repairing itself and one of the reasons that it's difficult for the cartilage to repair itself is that there's no blood supply in it and another reason is that there's not very many cells.

So chondrocytes are the cells in cartilage and if there's a low volume fraction of the cells, then it's not so easy for that small number of cells to actually produce the extracellular matrix, which is kind of what you think of as the cartilage.

And it can be damaged, either as I said, from sports injuries, typically that's what young people get, they tear their cartilage in some sporting injury accident, or from osteoarthritis. So these scaffolds we're talking about, they're not really meant to repair large amounts of cartilage that are damaged. And as I said, the cartilage has a poor capacity for self-repair.

So there's several treatments, there's three treatments that are given currently and the most common one is called marrow stimulation. And some of these orthopedic treatments are fairly crude when you look at it. So this marrow stimulation, what's involved is they take a drill. So here's the drill. And they basically drill through the cartilage. So this would be the cartilage layer here. And they drill down into the bone and they want to get down into the trabecular bone. So they want to go below the cortical or the subchondral bone and they want to go down into the trabecular bone.

And the reason they want to do that is the trabecular bone has bone marrow in it and the bone marrow has mesenchymal stem cells, and they want those mesenchymal stem cells to move up into the cartilage layer. So that's what this red glob is here.

The idea is that you've made a hole and now that hole is going to fill up with a blood clot, which will have these mesenchymal stem cells, and that those will form cartilage. So it does work to some extent, but it's not really a great result. There's something like 75,000 of these

done a year. As I said, this is the most common kind of repair.

The next most sophisticated type of repair, what they do is they take plugs of bone and cartilage from another place. So say this is where the defect is and they want to repair that. They take bone and cartilage from this spot up here. So they sort of drill out little cylindrical cores and then they plug them into this bit here. And that's called an osteochondral autograft. Sometimes it's called mosaicplasty because they build up a little mosaic from all those little pieces. And then they just leave these donor sites, where they took the plugs from, they just leave those empty.

So they try to take the bone and cartilage from regions where the loads are lower, but they end up leaving holes, which is not so desirable. And again, those holes may fill a little bit by the previous mechanism.

Then the most fancy method that they use now is called autologous chondrocyte implantation. So what they do is they harvest cartilage cells from the patient. They then take them to a lab and they culture them for two or three weeks and they get them to multiply and proliferate and grow and then they re-implant the cells.

So this works fairly well, but the difficulty is it involves two surgeries, so one to get the cells out and one to put them back in, and there's the cost of the cell culture. So this is a much more expensive procedure because of the two surgeries and the cost of doing the cell culture, but I think it's the method that works the best.

And when I talked about this in 3032, I mentioned Dara Torres. Dara Torres is an Olympic swimmer. She's 47. She began swimming in the Olympics in 1984, more than 30 years ago. And she has swum in the Olympics, not every one, but up until 2008. And even 2008, she won three silvers that year. She was, I think, the oldest person who's ever won a medal in the Olympics.

And she had this surgery done at the Brigham a few years ago. And it used to be, they've stopped running these commercials but the Brigham for a time was running these commercials, that featured Dara Torres and saying basically that she had this surgery done there. I'm assuming she was happy with it.

OK, so that's what they do currently and what we were thinking of and what other groups have thought about is could you repair damage in the cartilage by using a tissue engineering

scaffold?

So what we were thinking about when we tried to do this project was we wanted to use a healthy articular cartilage joint as a model for our scaffold. We wanted to have a layer that would go down into the bone so that you would have access to those mesenchymal stem cells. And that's why we wanted an osteochondral scaffold, so that we would have a layer for the cartilage but also a layer that would go down into the bone.

We wanted to be able to control scaffold parameters, things like the mineral content and the pore size. Remember, I said these tissue engineering scaffolds, the pore size is one of the parameters, that you want to have the pore size in a certain range.

And we wanted to use materials that would be appropriate for approval from things like the FDA. So typically, when people make tissue engineering scaffolds, they don't start with some material that's never been approved before. They start with something that already has approval for something else and that's what we wanted to do too.

So this was our idea of what we wanted the scaffold to look like. We wanted an unmineralized type II collagen scaffold up here that would be for the cartilage. We wanted a mineralized type I collagen scaffold down there for the bone. And we wanted some region that had some gradient in mineralization because it would be like that layer of cartilage that was slightly mineralized. So we wanted to duplicate that whole structure.

So that was our picture of what we wanted to do and we had a pretty good idea of how we were going to make this. We were just going to use that same process that [INAUDIBLE] developed for the skin scaffolds. He was involved with this project but just used type II collagen instead of type I.

The challenge was really figuring out how to make the mineralized collagen scaffold and then how to get this gradient in the mineralization between the two layers.

So this, I think, I showed you last time. So this is just the method we used to make the collagen-GAG scaffold. So we take type II collagen. We put it in acetic acid. Remember, that destroys the periodic banding of the collagen and it improves the immunological response.

We add the chondroitin 6-sulfate, the GAG, to crosslink it. We then just make a slurry out of that. So we mix that all together. We keep it as a slurry. And then the second stage is you put the slurry or the suspension into a pan, and then you do the freeze drying process.

So you go through this process where you start at this room temperature and atmospheric pressure. You cool it down to freeze it, and then you sublimate it, and you're left with a very porous collagen-GAG scaffold.

So these are pictures. I think this was with a type I collagen, but it looks the same with the type II collagen. So that's what the structure looks like.

I think I showed you this last time. We can control the pore size by controlling the freezing temperature. So the way the freeze dryer works is there is shelves that you put these pans on, and these cooling elements go through the shelves, and you can set the temperature of those shelves.

So we would set the temperature of those shelves to different values and we got different pore sizes. So the colder the shelf temperature was, the faster the freezing, and the smaller the size of the ice grains, and then the smaller the size of the pores.

And this is just the mechanical response again. So we did mechanical tests on it. These are some of the numbers for the properties. So we tested it dry and wet, and we measured a modulus and a buckling collapse stress for it. So those are just some values there.

And then it came to making the mineralized collagen-GAG scaffold, and one of the students in Cambridge, England was really the main person who did this, Andrew Lynn. And he worked with Brendan Harley, who was our student here, and after they graduated, I had another student, Biraja Kanungo, who worked on this too. So Andrew Lynn really developed this technique.

And this involved taking the collagen and the GAG, so the same as for the other scaffold, but this time, if we want to make a mineralized scaffold, we somehow have to get calcium phosphate into it. So it's got to have sort of a hydroxyapatite-ish type of component to it.

So this time we used phosphoric acid instead of the acetic acid and we put some calcium salts into the mixture as well. And Andrew was really the one who figured out how to do this and what salts to use.

And then the process was very similar. So we have this slurry. We mix the slurry up. We did a freeze drying process, and then we crosslinked it with a chemical crosslinker called EDAC. So it's just a chemical that you put into this and it crosslinks it all. So that was how we made the

mineralized scaffold.

The mineral we got was something called brushite, which is a calcium phosphate, but it's not exactly the same as hydroxyapatite. And we could control the amount of brushite by different weight fractions or volume fractions by controlling how much of the calcium salts we put in and what the molarity of the phosphoric acid was.

If you take brushite and you put it in water, it then converts to octacalcium phosphate and then to apatite by a hydrolytic conversion. So the apatite is related to the hydroxyapatite in bone.

And this was the structure of the mineralized scaffold that we got. So you can see it looks a little different from the collagen-GAG scaffold. It's much denser. Typically, the densities were like 5% or 10% dense. And remember, the collagen scaffold was 0.5% dense. So it's a lot denser.

But if you notice, there's a few things to notice here. So one is the pore size, that's a 500 micron bar. And we could make pores between about 50 and 1,000 microns, depending on the freezing conditions. And the range of pore sizes we were shooting for was somewhere between 100 and 500, so we could get in the right ballpark with that. And you can see, just looking at that picture, if that's 500 microns, those pores are somewhere of that order.

Another thing to look at is this image here, and this just shows, the white little dots are the calcium phosphate mineral, and it just shows that the mineral is uniformly distributed throughout the thickness of the scaffold.

So some people had tried to make scaffolds for regenerating bone where they take, say, one of those polymers for resorbable sutures or they take collagen and they coat it with hydroxyapatite, but the shortcoming of that is that the scaffold is going to resorb over time. The cells are going to secrete enzymes, which are going to eat away at the scaffold.

And if the scaffold resorbs, you're eating away at the hydroxyapatite first and then you're left with whatever polymer is underneath that. Whereas this gives you a more uniform composition throughout the thickness of the scaffold, and you've got calcium phosphate everywhere throughout the thickness of the struts in the scaffold. So that's the structure of that.

We wanted to make sure that the mineral was uniformly distributed throughout the scaffold, and we did some micro-CT imaging, some micro computer tomography. And this is our

sample here, and this red line just says that is the plane at which this image was taken, and the black is the mineral. And then here's a lower plane and here's another image. And you can see the calcium phosphate's pretty uniformly distributed throughout that specimen there.

And this was just another way of looking at the same thing using EDX in an SEM to look at where the calcium was and where the phosphate was. So again, this is uniform distribution of the mineral.

We did mechanical tests on these scaffold as well. So we measured moduli and collapse stresses. We get the same kind of stress strain curve as all these other cellular solids. This was done by- Biraja Kanungo was the student who did this bit.

One of the things we found was that with these mineralized scaffolds you could manually compress them. If you pushed them down and you hydrated them, they would recover all the deformation, but we were increased in improving the mechanical properties of the mineralized scaffold for improved handling during surgery. And there's another reason that I'll get to as well.

So the second reason is that, if you look at how bone itself forms, it forms from a collagen precursor, so bone in your body. And there's something called osteoid, which is this collagen-based precursor to bone, and it has a modulus of about 25 to 40 kilopascals and Angler showed that if you have mesenchymal stem cells and you put them on substrates of different stiffnesses, they differentiate into different kinds of cells, depending on the stiffness of the substrate. So the substrate stiffness can affect what kind of cells you get.

And the idea here was we thought, well, if we could get a stiffness that was close to this osteoid, what the natural bone formation has, then that might help the mesenchymal stem cells differentiate into the bony cells that we want them to. So we wanted to try to reach a stiffness of this in the wet state.

And if I back up here, you can see the stiffness we had was around four in the wet state, four kilopascals and we want to get to 30 or 40, something like that.

So these are our equations for the modeling of the mineralized scaffold, the open celled foam models for the modulus and for the collapse strength. So we could change different things. We could change the solid properties or we could change the relative density. The geometry of the thing is probably not going to help us too much.

So basically, that's what we did. We first started off trying to increase the mineral content. We thought if there was more mineral content that would make it stiffer. So Biraja made these more highly mineralized scaffolds and these are just some SEM images of those.

But the thing he found was that the properties actually got worse when he had the more highly mineralized scaffold. The modulus went down and the strength went down, so that wasn't very helpful.

And when he looked into it more detail, he found that he had more voids in the cell walls and he had more disconnected walls. This shows some of the micrographs, so this isn't really very quantitative, but you can see there's holes here. There's a few holes here, but there tended to be a bigger volume fraction of holes in the more highly mineralized scaffolds and more walls that were disconnected. So we realized increasing the mineral content wasn't going to work very well.

And then the second thing he tried was increasing the relative density. So we started off at this density of 4 1/2% dense and he developed a method of increasing the relative density up to about almost 20% here.

He did this by, first of all, he tried to just mix more of the constituents into the slurry, that's kind of the most obvious thing. But as you add more constituents, it gets harder and harder to mix the thing up and have it homogeneously distributed. So in the end, that's not how he made these things.

He started with the starting mixture and then he had a vacuum system for sucking water out of it. So he would reduce the amount of water, which essentially increased the amount of solids that was in there.

And you can see in this last one here, the most dense scaffold, he was sucking the water in one direction, and he sucked it so much that he was starting to get the cells collapsing. So this one here, these cells that have this sort of elongated orientation, that's because the cells are starting to collapse because of the vacuum that he was applying.

But he could get a pretty good difference. This was almost 5%. That's almost 20%, so roughly a factor of four. There are, yeah, four difference between them.

So then he did mechanical tests too, and he measured the relative density. Here's the moduli

wet and then the strength dry and the strength wet.

So you can see here, if you look at the dry moduli, for instance, when you go from this relative density to that relative density, from about 14% to 19%, the modulus actually drops down. And if you look at the structure, I think, it's because you've got this flattened structure here. You've collapsed the cells a bit already.

So there's a maximum density that you might want to go to, probably somewhere around 14% or 15%. But the wet modulus we've got here is around 35 kilopascals, so that's close to the target that we had. It's close to what we wanted to have.

So one way you could get the right or the appropriate modulus is by increasing the density to that value. Another way is by playing around with the crosslinking. So those values were for non-crosslinked scaffolds.

So here, this is the 14% dense scaffold wet, non-crosslinked it was around 35 kilopascals. This is a dehydrothermal treatment, just basically heating it up. It gives you a higher modulus. And then this is a chemical crosslinking technique that increases the modulus again.

So if you put all of this together, you can show these results for the modulus on one table. So these are all the wet modulus. So it's pretty clear by playing around with the relative density and the crosslinking, that you can get a scaffold in that range. And the idea is that that would help get the mesenchymal stem cells to differentiate into these osteoblast-like cells.

So then we wanted to also see if our models for the cellular solids could be applied to this scaffold, and we needed the solid properties. So Kristyn Van Vliet helped us with this, and we isolated a single strut, bonded it to a glass slide, and, I think, I mentioned this last time, we used an AFM tip to then do a little bending test. So I think the one I mentioned last time was for the collagen-GAG scaffold. Then we also did the same thing for the mineralized scaffold.

And here we measured a modulus of about seven gigapascals, so that's a dry modulus. And just for comparison, the modulus of the solid and trabecular bone is something around 18. So it's lower, but it's in the same ballpark.

And by nanoindentation, we measured a strength of about 200, and that's similar to what you would get in trabecular bone. So the solid in the struts themselves is not exactly like trabecular bone in mechanical properties, but not too far off.

And then here's a plot of the scaffold modulus divided by the solid modulus against the relative density. And this line here, the curve, is a squared relationship. So that's what we'd expect for the foam models.

And this is the strength. These things fail by a plastic or a brittle failure, and this curve is a three halves power with relative density. And again, that's what you'd expect from the cellular solids model. So that gives you a reasonable description of the behavior of the mineralized scaffold.

So again, these were the considerations in trying to make the osteochondral scaffold. So now we have a collagen scaffold and we have a mineralized scaffolding, and we want to put the two of them together. So we wanted to use the joint as a model, and we wanted to have some intermediate layer that had some gradation in the mineralization. So that was the next step.

And the way we did that was we used what we fancily called liquid-phase co-synthesis. This just meant that we took the mineralized collagen-GAG slurry, we poured that into a mold, and then we poured the non-mineralized slurry into the same mold. And then we just allowed the two slurries to interdiffuse for some time period. And then we did the freeze drying step.

So the idea was, that if you poured the one on top of the other, the mineralized one is denser and then you put the less dense one on top, but over some period of time, there will be some diffusion between the two. And then we just did the freeze drying step.

So this is the scaffold we ended up with. This is a micro computer tomography image. So here's the collagen-GAG scaffold for the cartilage on top, and here's the mineralized collagen-GAG calcium phosphate scaffold on the bottom for the bone. And that just kind of shows what it looked like.

The porosities and the pore sizes we got, the collagen-GAG was about 98% porous and had a pore size of around 650 microns. The mineralized scaffold was 95.5% porous and had a pore size of 400, roughly, microns.

And then this is what the structure looked like in the EDX. You can see, this is the collagen-GAG layer, this is the mineralized layer, and there's some zone in between that's a little bit mineralized, not as much as the bony layer but more than the cartilage layer, and the same with the phosphorus. So we have this collagen-GAG slightly mineralized layer, and then a more mineralized layer

And then finally, there was a student, Scott Vickers, who worked with Myron Spector at the Brigham. And oops, oops. No, I don't want the weekly updates, thank you. Sorry. Well, let me just get rid of this. Oop, where's my little mousy mouse? There we go.

OK, so Scott Vickers worked with Myron Spector, and Myron had a surgeon who could do animal studies. So we did some animal studies on goats. I think there were six goats at the Brigham. And they took a plug out of the knee of the goats, and they put our scaffold in.

So this is one of the surgeries as they're about to poke the scaffold in. And then, Scott waited, I think it was four months, and then sacrificed the goats, and then did the histology.

And this is one of the images from his PhD. So this staining shows that you've got tissue growing in. The scaffold was where these little black dotted lines are. So you had bony tissue in here, and there was a cartilage-like tissue formed at the top. It wasn't perfect articular cartilage, but it was something similar to that.

And really was as far as we took the project with the funding that we had. We had a-- I don't know if you remember that-- well, it's beyond before your time. But Cambridge and MIT had a big research collaboration and the student exchange was part of that. And this was done through that research collaboration between Cambridge and MIT.

So this was as far as we took it with that research funding. Andrew Lynn, who was the student in Cambridge, who developed the mineralized scaffold, he then started up a company called Orthomimetics, and he had longer term animal studies done, and he took it a little further.

In Europe, there's something called CE Mark approval, and CE Mark approval means you can start doing clinical trials. So he never got FDA approval for it, but he got approval to have clinical trials in Europe.

And the first clinical use was in February of 2009. And they started off using it for the donor sites for the mosaicplasties. Remember the second method I talked about? They take plugs out of one region and put them into the region with the damage.

So what they were doing was using our scaffold to fill up these donor sites here and they found that worked quite well. And then eventually, they started using it for the primary sites as well. And as of about April a few years ago, April 2012, they had treated about 200 people with this.

AUDIENCE: Wait, so why not just directly start putting it in the-- why start with the--

LORNA GIBSON: I think because these were supposed to be sites that were less loaded, weren't as highly stressed, and they thought that was a more, not as critical a place to put them in. Yeah?

AUDIENCE: So what is different about this scaffold? Is it the lack of the dense bone that allows all of the marrow cells to migrate up to the cartilage?

LORNA GIBSON: Well, I think, there's not that many people that have made osteochondral scaffolds, so it's good that we've got these two layers. And the idea that you try to get the stem cells up into the cartilage. The stem cells will differentiate into the bone or the cartilage, I think, partly depending on the stiffness of the surrounding tissue.

AUDIENCE: But they don't do that in normal bone because of the dense layer?

LORNA GIBSON: No, I think they would. But the thing is, I mean, in some ways, that very first technique where you just drill holes in, I mean, in some ways, that's what it's counting on, right, is that the marrow mesenchymal stem cells are going to differentiate either into the bone or into the cartilage. But it's just got a hole to differentiate into. So this gives the cell something to attach to and I think, gives a better result. Yeah?

AUDIENCE: So is part of the scaffold and this bone, are they removing the original bone?

LORNA GIBSON: Yeah, they remove-- yeah. Let me back up a step. So when they do this thing here, so this is in a goat, but they would do the same thing in a person. So when they drill the hole to put that in, they go through the cartilage, they go through the compact bone, the dense bone, and they go into the trabecular bone, because you don't really get into the marrow until you're in the pores of the trabecular bone. OK? Are we good?

AUDIENCE: How do they attach it?

LORNA GIBSON: How do they attach it?

AUDIENCE: Yes.

LORNA GIBSON: I think it's just a press fit. I think they just drill a hole and stick it in. And these are all in joints, right? So there's always another bone pressing against it. I mean, in the surgery, they kind of peel things apart so they can do the surgery but there's another bone pressing down on it. So I don't think there was any glue or anything. So there's that.

So this is just a summary. So we were able to make this two-layer scaffold with a gradient interface, and we tried to make it so that it mimicked the osteochondral tissues. And this freeze drawing process allowed us to control things like the mineral content, the porosity, the pore sizes. And then we used materials that had already been approved for medical devices.

And this was funded by a number of places. So the Cambridge MIT Institute was that collaboration I mentioned. I have a chair and I used some money for that. Brendan Harley was one of the students involved and he got a fellowship from MIT. And Andrew Lynn got a fellowship through the Cambridge Commonwealth Trust and through St. John's College in Cambridge, that's his college there. So he had had funding through that.

So I think that's the end of that talk. So are we good with scaffolds? Yeah, you're good?

So obviously, this probably whole course is on tissue engineering. This is just scratching the surface and giving you an introduction to it, but I wanted to show you how a lot of these scaffolds look a lot like the foamy materials that I work on, and that you can use the same models for trying to understand the mechanical properties of the scaffold. And even though the scaffolds are acting in a biological way, there's actually a connection between the mechanical behavior of the scaffolds and the biological response.

So I'm going to talk on Monday about cell/scaffold interactions, so how the environment biological cells are in can affect how they behave. So we're going to talk about things like cell adhesion and cell migration and cell contraction, contractile behavior. So I've got another talk a little bit like this and that means I'll have a few notes I'll put on the board on Monday about how the environment that the cells are in affects how they behave, OK? So this is leading up to that. It's sort of a similar thing.

So I thought for the rest of the time today, because I knew this was going to end early, I thought what I would do is just switch gears and talk about writing. So normally when I give a class, I don't talk about writing all that much. I talk about the technical stuff.

But it turns out writing is actually a huge part of what scientists do and engineers do and whether or not you end up with an academic job or a job in industry or working for government, no matter where you are, you are going to have to write things. And the better you write, the better off you're going to be.

So I made copies of this brochure and I have a few little slides. And you're going to have to write up your project report for me, and I thought it might be helpful to just go through this little brochure.

So I'm not going to write stuff on the board. Everything is pretty much in this brochure, but I thought I'd just walk you through some of the main parts of it.

Oh, did you get one? Here, have one.

So you might want to think about this when you're writing up your project report for this class, but this really is, it's general. It's really for any time you have to write something. This is helpful.

So Mike Ashby put this together. And as I mentioned, he's done a lot of scientific writing and especially in material science and engineering. He also makes paintings. This is one of Mike's little paintings of him writing a paper. And what I was going to do is just walk through it. So there's just a few figures, and mostly it's text, but let me go through some of the figures.

So I'm going to just turn to what's page three, OK? So one of the things that he says to start, and I think this makes a lot of sense, is that you can think of writing a paper the same way you can think about designing something in engineering.

So when you think about design, there's different stages of design, right? There's a conceptual design, where you just decide roughly what the thing's going to be. There's embodiment, where you work out a lot of the more details. You design one version of it. And then there's the detailed design, where you do all the fine-tuning. You do all the final design things.

And before you really start your design, if you were going to design an engineering thing, you would first of all think about what's the market. And if you're writing, the market is your readers. And so when you think about what you're going to write, you have to think about who's going to read it.

And it's the same thing when I give a talk. When I give a talk, before I make a single PowerPoint slide, the first thing I think about is who am I talking to and what do they already know? What's the audience? What are they looking to get out of the talk? What am I trying to convey in the talk? And the writing is the same thing. You have to think about your audience.

So for instance, I have technical talks. Obviously, I go give technical talks at meetings, but I do

other sorts of talks too. I've got the woodpecker talk. I go give the woodpecker talk at the Mass Audubon. And people come to listen to that talk who are interested in birds but they're not engineers. So when I do that talk, I have to make it so somebody could understand it who's intelligent but they're not necessarily an engineer. So I give a different kind of talk when I do that than when I give an engineering talk.

And I got invited to a student dinner. I'm going out to somewhere with some students on Friday. I'm going to give that how I became a professor talk, and when I do the how I became a professor talk, it's more general, and so it's a different audience that I'm thinking about.

And in some ways, when I do these talks, it can be the same group of people, but depending on what I'm talking about, the way they look at it is different, OK? So the market thing is something to think about.

So if you're writing a thesis, your market is your PhD committee, who's going to read the thesis and examine you on the thesis. If you're writing a paper, you've got to think about the market as being other people in your research field, some of who are going to be the reviewers, who are going to be reading it and criticizing it.

If you're writing a general popular science book, it's a different kind of audience. If you're writing a research proposal, the audience is going to be the funding agency. Are they interested in what you're talking about, but also reviewers, who are going to be deciding whether or not to give you the money and what the criticisms are. So you have to think about who the market is. So that's one thing.

And one thing that think about in doing the writing-- you know Mike and I have written several books together, and when I tell my neighbors I've written books, they somehow think-- their first idea is that we start on page one and we start writing the book from page one and then we work our way through to page 500. And that's not how we do it at all and that's not how I write papers. That's not how most people write papers.

You've got to think about the big picture and think about, roughly, what goes where. And then maybe think about a draft that gets the scientific facts right. You put the information down, and then you try to figure out about how do you make the style really nice? How to make it read well? How do you make it easy to understand? How does one paragraph lead into the next paragraph?

So it's an iterative thing. It's not like you start at page one or line one and you just start writing. So it's an iterative process, the same as engineering design is an iterative process.

If you were going to design, I don't know, a skateboard or something, you wouldn't just think you were going to make one and that would be it. That's how writing is, and often, students don't see it as this iterative thing. OK, so that's that page there.

Let's see, I already talked about market. I think I have another little slide about-- here's another slide here about markets. So this is what I just said. Who are the readers? How are they going to use it? So you've got to think about who you're writing for or if you're giving a talk, who's going to look at that.

OK, now the next phase is to make what Mike calls a concept sheet. I would just think of this as an outline. And I always make some sort of outline before I try to write anything.

And there's different ways you can do that. The thing that Mike's got here and there's a nice little figure on page six, which is what I've got up here, is he takes a big piece of paper. In Europe, it would be known as the A3. Here it would be known as the eight and a half by 17. You take a big piece of paper. This stationery company actually makes paper with big blank space in the middle and little note space on the outside or you could just use the back of it.

So you take a big piece of paper and you may think this is douffy, but it actually helps. So you take your big piece of paper, and you just make boxes about each topic. You're going to have an introduction, you're going to have methods and materials, you're going to have a result section. And you think about what should go into each of those boxes.

And what you're trying to do here is think about the whole paper and how it all fits together and what goes where and what are you going to include and what are you not going to include.

So people think about writing as sitting at the keyboard and typing, but that's just the-- how when you get a problem on a problem set, you turn and crank, that's the turning and cranking part.

The thoughtful part is figuring out what to put in, what to leave out, what figures you want, how you organize the whole thing, how you put it all together, and this helps you do that.

And you can make this-- it's just for you. It doesn't have to look great. You can make this messy if you want. It doesn't really matter. But it's good to have some sort of an overview of

how you want to put the thing together, and that's what this stage helps you do.

So Mike's put other little things here. So see papers by so-and-so and so-and-so. So you've got an introduction. You want to talk about something. You know there should be some references go here. Maybe you think there's some extra references you haven't got. Maybe something in the method, there's some analogy you can use here.

Maybe you need a figure, needs a good figure. You don't have to actually have the figure. You just say I need a figure and you have a vague idea what the figure looks like.

Here there's some discussion point. Discuss this with collaborators, Ed, all this stuff. So you just put down roughly what needs to go where and you think about the whole thing and how it's all going to fit together.

And then as you work through it, it looks more like this. So this would be on page seven. And this is filled in, and if fact, this particular one, what he's written down here is the overview he made for making this booklet, OK? So the things refer to this book.

So here's the introduction. Here's the little chart we went through and through, the concept design, embodiment, and detail, blah, blah, blah. Here's the need, the market need. We just talked about that. Here's the concept thing that we we're just talking about now. Then we're going to talk about each of these different phases.

And his initials are MFA, Michael F. Ashby. Think out, that means think about this more. I haven't figured this out yet. I need an example here, all these kinds of things. So this is the way he does it.

There's a couple of other ways you can do it. One way is to just make a bullet outline, that's typically what I do. You know you're going to have an introduction, these different headings. And you might put in the bullet outline these same sorts of things, like I need this figure or we need to get one more set of data or I need to look up this reference. So it doesn't have to be finished, but it's a thing that tells you what have you got, what do you need to do to make it all come together. So that's one way to do it.

Another way to do it is by thinking about what figures you want in the paper. So some people, before they write any words, they say, well, I know I want to have these figures, and then they build the words around the figures. And they can even sketch out what the figures are. Some people even start before they start the project, they say what kind of figures do I want at the

end of the project? And they don't know if the data is going to do this or that. They don't know which way the data is going to go, but they say I want to have a plot of one thing versus another thing.

Oh, you're looking like this is not OK?

AUDIENCE: No.

LORNA GIBSON: No? OK, yeah, some people do this. So even when you're ready to write, you could say to yourself, well, in the methods, do I need a figure that's a schematic of some apparatus? In the results, how am I going to present the results in the discussion? Do we need some other kind of figure? So if you have a set of figures, you can work the text around those figures. So that's another way to do this.

So those are just three options, but all of them have in common that you think about the whole paper and how it all fits together and what goes where and what do you have already and what else do you need to get, OK? So that's that.

And then what I was going to do-- I think that's probably the last figure that's-- yeah, OK. So there's just this little thing here.

So what I was going to do is just talk about some of the other things in this little booklet that work through each of these stages of the writing. So that's the concept, and then the next phase would be what's called the embodiment, if you think of the design language, and that would be the first draft.

And I think most people find the most difficult thing is to write the first draft. I mean, I find that the hardest. Once you've got something, editing it is relatively straightforward. You go, oh, this piece should go over there or there's something missing. But getting the first draft down is the hardest thing.

And one of the things-- it's like when I talked about writing the book, you don't write the draft sequentially either. I typically tell students to start with the materials and methods because that's the most straightforward and it's the easiest to write. There's not a whole lot of mystery to how you actually did something you've already done.

So I tell people don't write the introduction first. That's a bad idea because it's actually often not so easy to write the introduction. So I tell people to write the materials and methods first.

Write the result section because you've got your results and you know what the results are going to be. So those are the two easiest things.

And often, I think, what people find is if they find it hard to write it's because they don't know what they want to write or they haven't thought things through. They haven't got their thoughts together. And if you've got your thoughts, if you know what you want to say, then the writing becomes easier.

So one of the pieces of advice Mike gave me, and it's in this booklet too, is in the first draft what you should try to do is just get the facts down. Just get the information down and don't worry about if it doesn't sound quite right or if this sentence doesn't lead into that sentence. Don't worry about the style of it at all. Just try to get the facts down. Just try to get the information down.

And once you've got the information and you've got some kind of framework-- I'm not saying that you don't want to make the style good, you do, but you don't need to do that the first thing. The first thing is just to get the facts down, and then you can edit it later on. It's more of this iterative process.

OK, so the first draft, the most important thing is just to get the facts down. Then, I'm not going to read all of these things because you can just read them yourself, but I'll just comment on a few things.

So one thing he's got-- I'm on page eight now, is the abstract. So the abstract should be concise. It should be fairly short and you want to tell people why you're doing what you're doing, what you did, what the key result is, and what the conclusions are. So it can be pretty short.

There's a section on the introduction. You can just read that. Let's see here. Yeah, I think, you can read yourself these other things. I don't want to go through the whole thing. All right, so that's that.

OK, so you get to the end of the first draft, there's a little section on figures here. Let me just make some comments on that. People who are busy and may not want to read every word that you've written will look at the figures, and they'll look at the figures to make some judgment about does this look useful? Does this look like you've got something I want to spend more time on? So it's important to make the figures easily understandable and to be fairly self-

contained.

So you want to make the figures clear. You don't want to have too much information on it so that people can't follow what's going on, and you want them to illustrate the points that you're trying to make. So the figures are very important.

And then when you've got the first draft finished, the next step, which I find tremendously useful and students often don't get that this is a step. The next step is you put it somewhere and you don't do anything with it for a while. And this is why it's important not to write it up at the last second. Because there's something about, you work on something, you put it to one side, you don't do it. You just leave it and you go do something else. And then when you come back to it, all of a sudden, you see things that you didn't see the first time through.

So the next step is you just put it to one side for a couple days. But you can only do that step for a class if you started before the night before it's due, OK? So that's why you have to start earlier. That's why I'm telling you this now, OK? So you put it aside and then you go have a cup of coffee. You see there's several cups of coffee that Mike has happily drawn for us here.

OK, then the next part of this is all about grammar and sentence structure. I'm not going to go over that. You can read all that yourself.

But there is one amusing thing I want to tell you because there's a cute story. I'm on page 16 now. There's a thing about spelling. Mike is a terrible speller. When I was his student, he used to-- there were no word processors. And we used to write things and he would write things and I would say, I can't read your writing. And he says, ah, well, I make up for my bad spelling with my bad writing. So I couldn't tell if he had spelled something right.

The other thing we found was that, we wrote the cellular solid book, the first edition was in the 1980s. And I grew up in Canada, then I lived in England, then I moved here. He grew up in Australia, then he moved to England, then he moved to the States then he moved back to England. And words that end, that we spell I-Z-E, like normalized, like normalized variables. They're I-Z-E here. In England, they're all I-S-E.

OK, and then some of the words, it turns out, Canadians spell with an I-Z-E and some with I-S-E. So anyway, we wrote the entire fricking book. We were almost ready to send it off, and we have all those graphs where the axes are normalized, and we must have used the word normalized like 100 times, and we realized half the time we had spelled it I-S-E and half the

time we had spelled it I-Z-E. And then we had to go back and find them all and fix it all. So anyway, that's just our little story about spelling.

OK, there's a thing about punctuation. You can read that. That's kind of boring.

I wanted to move on to the bit about style, because style is important too. And people remember papers that are well written. Obviously, papers that have valuable scientific information are memorable too, but if it's well-written, it's more memorable, and the style really is important.

And it's the same with giving a talk. You can convey the same information, but if you don't have it presented in a clear way, people aren't going to remember it.

So the first rule-- so I'm on page 20. The first rule, now, is to be clear. And being clear, it doesn't mean having long-winded sentences with lots of jargon. It really just means make it short, make it concise, make it clear what you want to say.

So Mike has several examples here of headlines from the newspapers, which were not clear. So I'll just read these out because I find them amusing. "Red Tape Holds Up New Bridge." So, OK, maybe the red tape temporally held it up, but not spatially held it up.

OK, and then here's another one. "Something Went Wrong in Jet Crash, Expert Says." In fact, you hear this all the time on the news now. Obviously, something went wrong. You don't have to be an engineer to figure out something went wrong in a jet crash.

Then, "Chef Throws Heart In To Help Feed the Hungry." OK, well, maybe that's a little too much.

This is my favorite one, "Prostitutes Appeal to Pope." OK, there's different ways you can appeal. You don't have to appeal to the Pope in that way.

And then, "Panda Mating Fails, Vet Takes Over." I don't think the vet really took over with the mating, but you know what they mean.

OK, so one thing is clarity. Another point is don't waffle. You want things to be concise and get to the point. So he's got this example here from what he cites as a well-known but anonymous materials text.

"The selection of the proper material is a key step in the design process, because it is the

crucial decision that links computer calculations and the lines on an engineering drawing with a real or working design." But what does it say? It says material selection is important. So don't say something in some long-winded way that you could say in a short way.

OK, let's see. So let me move on to the next page. The next step that I-- let me emphasize one more time, is 8.5, revise and rewrite. So writing really is iterative. Those books that you've seen that Mike and I have written, I cannot tell you how many drafts of each chapter we went through over and over and over again. So to make it good, you have to do it over and over again. OK, there's that.

Let me see. Is there anything else I have here? Ah, here's a couple things that are not so obvious.

So one is, for each paragraph you should have a good first sentence. You should tell the reader something they don't already know. So there's some examples here, and you can read through them. But it is really helpful for each paragraph to have a good opening sentence.

Another thing is at the end of the paragraph it's good if there's a sentence that links it to the next one. So it hints at what the next paragraph's going to be about, so it leads the reader through it, and it is a logical progression. So an opening sentence for the paragraph and the final sentence, you might want to look at in a bit more gory detail.

OK, and then there are some references at the very back, at page 25. And I brought a couple of books in that I have found helpful. So you may have seen these. One is called *The Elements of Style* and this is by Strunk and White, so William Strunk, Jr. and EB White. You guys know EB White, *Charlotte's Web*, same guy. He's written this small, small, not too long to have a look at book about style.

So there's some rules of usage, which is grammar stuff, but there's principles of composition and there's a chapter called "An Approach to Style."

And so here's some of the headings. Place yourself in the background. Write in a way that comes naturally. Work from a suitable design. These people are not engineers, but they're saying work from a suitable design. It's like that concept thing.

Revise and rewrite, did I mention that, revise and rewrite? Do not overwrite. Don't make it too complicated. Avoid the use of qualifiers. If you say something's very stiff, what does that mean? You can just say it's stiff. You don't have to say it's very stiff. Very compared to what?

Let's see. Use orthodox spelling, blah, blah, blah, blah, blah. Avoid fancy words. OK, be clear, all this kind of stuff. So Strunk and White is old but good.

And then, there's this book here by Bill Bryson. *Bryson's Dictionary of Troublesome Words.* So this is, it is like a dictionary. It goes by letter and has different words, but it talks about how people sometimes use a word thinking it means one thing when it doesn't, it actually means something else. And so it's just words that people use commonly that they sometimes confuse with what they really mean. So it's a very handy thing too.

Do you know Bill Bryson? Very funny travel writer. If you ever go somewhere that Bill Bryson has been you should get the book he's written about it because he's very funny.

OK, so I think that's it. Oh, and then, I think, the very end of this booklet has some examples of good writing and bad writing. So you can have a look at that too.

All right, so are we good on how to write a paper? Do you have questions on how to write? Writing is important.

So I have one more writing story. So when I first got this job at MIT, I was living in Arlington, and my mom comes to visit me from Toronto. And I'm work, work, work, work, working, working, and my mom says to me, she says, my, you spend a lot of your life writing. I'm like, Mom, that's what I get paid to do. I get paid to write.

Like she always thought I was should be spending maybe 30 hours a week lecturing or something like that. Like she, well, you're a teacher. You only teach three hours a week, what is this? I'm like, I write, Mom. That's what I do.

So anyways, so writing is important and giving presentations is important. And no matter what you end up doing, you're going to end up having to do those two things. And if you do it well, it's going to make your life better, and if you do it badly, you're not going to be so good. So that's my message.

So I'm going to stop there because I haven't got the next lecture ready, and I can start that on Monday. So Monday we'll do the cell mechanic stuff.

And then let me just-- because we're getting ridiculously close to the end of term. Like four weeks from today is the last test. I know, it's shocking.

So there's one lecture on cell mechanics, and then there's some more engineering applications of foam. I'm going to talk about energy absorption in foams and foams in sandwich panels, that kind of stuff. And then, we're going to talk about some natural materials again.

We're going to talk about natural structures, so like natural sandwich panels and natural cylindrical shells with foamy cores. So I've got lots of nature things at the last part of the course, and you know how I like those nature things. So there you have it. Bob's your uncle, as my mother would say. You know what Bob's your uncle is? Bob's your uncle is an English expression. It just means there you have it. There you have it.