I actually would like to take this occasion to praise and thank the TAs.

We've been teaching this course for about a dozen years and we've had some really excellent groups of TAs, but this year's crop is really off scale, really outstanding. And we're all very grateful.

[APPLAUSE] You know their names. I won't go through them all.

But the fact of the matter is these TAs teach this course because they're told to teach the course, and at the same time they're doing all their thesis research, so they end spending about 168 hours a week on various kinds of work. So it's not a natural thing for them to spend an enormous amount of time, as they have been this year, really just off scale extraordinarily good.

Here they are, Winston, Susan, Michelle, Sara, Divia, Jim, Sydney, Yasmine and Cha. So thank you all.

At the same time, I'd also like to thank Claudette Gardel who runs this thing. This is a large undertaking, believe it or not, with almost 350 students enrolled, but it's moved seamlessly and without any problems this year for which many of us are very grateful. So, thank you Claudette. I'm going to spend today trying to broadcast into the future, forecast into the future I should say, about where all of what we've talked about this semester is taking us.

Where is it going to get it us in terms of where we're going to be ten or twenty years from now and what you're going to be in the middle of ten or twenty years from now as you begin to move, as it will happen surely, as day follows night, into midlife.

Imagine that. When you're 35 or 40 this will happen.

And in order to do so I just want to go back 125 years or so to give you a feeling for what the history of biology has been like, some of it, since the end of the 19th century.

Just to give you a little flavor for what can happen to biology if things aren't done right. Charles Darwin had a cousin named Francis Galton. He was knighted by the Queen and called Sir Francis Galton. And he was an early pioneer in statistics. And he coined the term eugenics. And, as you may note, eugenics is simply the science of trying to use genetics to bread better livestock, better plants, and ultimately maybe to breed better human beings.

And we humans have been doing eugenics on plants and livestock for at least 10,000 years. That is to say we have continually been selecting out the best of the breed as the progenitors of the next generation of the breed. And in that way corn, which was originally this large when it was grown 5,000 years ago in Mexico, the cobs have now become this large and quite tasty.

And all of that is through selective breeding. But in the last half of the 19th century, inspired by Darwin and subsequently by Mendel's work on Mendelian genetics, a whole science of eugenics grew up in this country which included not only the improvement in the quality of livestock and plants but also improvements in the gene pool of humanity. There was a strong conviction that genes were directly responsible for all kinds of physical traits, as well as mental and psychological traits. There was a strong belief that some races were superior and other races were inferior because of genetic gifts or genetic deficits. And this included as well within races, however one defined them, different ethnic groups. There was a firm belief that science could ultimately solve a lot of social problems including urban violence, labor unrest, manic depression, schizophrenia and even mental retardation.

And the eugenicists, as they came to be known, came to believe that the problems of the world, alcoholism, poverty, prostitution, criminality, feeblemindedness, chess playing ability, tendency to commit industrial sabotage, that was big in the beginning of the 20th century when the unions were coming into power, they were all associated with one or another rather penetrant Mendelian allele.

A well known geneticist named Davenport, who subsequently was associated with an unnamed university up Mass Ave.

studied various ethnic groups and races and concluded that on the basis of genetics the Germans ranked highest in quality such as leadership, humor, generosity, sympathy and loyalty.

Italians and Irish ranked lowest in most of these traits, he was lucky he survived in this town since together Italians and Irish, I think encompass 70% of the population.

British were lowest in two of the traits. Irish were highest in suspiciousness. Jews were highest in obtrusiveness, whatever that is. And all of these things were said to be genetically templated. And so at the beginning of World War I IQ tests were first instituted in this country during the draft in order to determine who was genetically fit to serve and who was below standard.

And using IQ tests, which were implemented in great numbers and throughout the society in the 1920s, a well known geneticist named Goddard discovered that 80% of Jewish, Hungarian and Polish immigrants, as well as Italian and Russian immigrants were mentally defective or feebleminded, and that these traits, these mental defects in 80% of these groups were transmitted as regularly and as surely as the color of hair or eyes. I'm not making up fairy tales now.

I'm telling you what's happened in our history. In the 1920s there was a Eugenics Record Office in this country which existed for the next twenty years, an American Eugenics Society which has 1200 people, and J.H. Kellogg of Battle Creek, Michigan, you know how he made his money, don't you? Cornflakes. He founded a Race

Betterment Association whose intent was to better the gene pool of the American population through selective breeding. By 1928 there were 376 college courses taught across this country on the subject of eugenics, i.e., how to improve the human race by beginning to breed more fit individuals. And so when the Nazis came to power, as they did in 1933 in Germany, they had much to draw from.

In fact, most of their scientific rationale, to the extent they had any, didn't come from Germany, it came from eugenicists in the United States. And so they began to look amongst their society for people who were useless eaters, i.e., they consumed food but didn't produce, they lived lives not worth living, the elderly, the chronic poor, the crippled and the misfits. And they began involuntary sterilization. So, people who were regarded as genetically less fit were sterilized. By the time the Nazis finished their 12 years in power, 400,000 people had been sterilized in Germany because for one or another reason they were regarded as somehow defective. And as the Second World War made resources more tight, they just did something much simpler, they just euthanized people, they just killed them if they were regarded as in one way or another genetically defective.

In fact, my father had a first cousin who around 1936 or so was gassed because he had a bad stuttering defect.

So, this is all things that really happened to people.

As a consequence of all of this eugenics, by 1924 Immigration Act was passed which severely circumscribed the amount of people immigrating into this country because the immigrants were widely viewed as diluting and contaminating the American gene pool.

And this probably, well, this undoubtedly had a devastating affect on this country which we'll never really be able to know because the truth of the matter is that to the extent we have economic and scientific robustness in this country, it has come, for the last century, year after year, generation after generation from the immigrants who come to this country, not people who were here three, four, five generations.

It's the immigrants who brought in the new ideas, the energy, the power, and I venture to say that if I were to ask what fraction of you are first generation Americans the number would be pretty high, right? But in 1924 that was for a while stopped simply because people coming into the country were viewed as genetically less than acceptable.

By 1940 thirty states had compulsory sterilization laws in this country, i.e., people who were deemed to be genetically less gifted were sterilized against their will. 60,000 of those sterilizations were performed in this country. And the eugenics moment gained more and more adherence. What shut it off ultimately was what happened in World War II where six million Jews were killed, along with probably five or six million Slavs and other races who were deemed, and gypsies, there were probably half a million gypsies killed by the Nazis, different

groups of people who were deemed to be genetically less deserving of living and genetically less likely to be productive and useful human beings.

And were it not for World War II, it's quite plausible that the eugenics movement would have continued to grow and that today, when we talk about genetics, much of it would be referred to a belief that somehow we can determine people's phenotype and genotype and that we can predict how useful or useless they're going to be on the basis of our insights into genetics. And this ideology of genetic determinism, I say it had a great decline, this is the phrase we use, genetic determinism, i.e., to say that an individual's life course is strongly dictated by his or her genome.

These are her alleles. You heard a lot about the alleles last time from Eric. But genetic determinism is once again coming to the forefront. Why? Because now, for the first time, we actually have a science of human genetics.

When all of this other stuff was going on 50 and 100 years ago it was all pseudo-science, it was all made up. No one had the vaguest idea what genes were present in people's DNA.

They didn't even know about DNA. They didn't really know about most Mendelian traits being passed in human populations.

And they had no way of knowing, in the vast majority of cases, whether a certain person's phenotype was or was not dictated by genotype.

So is this notion of a strong genotype-phenotype connection totally nonsense? Well, I'll give you an example of where you might begin to think it isn't. And it comes from studies of identical twins who were separated at birth and brought up in different families. So these identical twins obviously have an identical genotype. So here's a famous story that I like to refer to. There was a chance meeting in 1979 between a steelworker named Jim Lewis and a clerical worker named Jim Springer. They both lived in Ohio. They were separated five weeks after birth and they were raised 80 miles apart in different towns in Ohio. And at the age of 39 they discovered themselves through some change meeting.

They discovered each other. Well, they both had dark hair, they both stool six feet tall and they both weighed 180 pounds.

That's not so surprising. They both spoke with the same inflections, which they clearly had not yet learned to speak with when they were five weeks old. They walked with the same gait.

They made the same gestures. They both loved stockcar racing.

They both hated baseball. They both married women named Linda.

They were both divorced and in their second marriages both of them married women named Betty. They both drove Chevrolets.

They drank Miller Lite. They both chain smoked Salems.

They vacationed on the same half-mile of beach in Florida.

They both had elevated blood pressure, severe migraines, both had undergone vasectomies, they both bit their nails, and their heart rates, their brainwaves and their IQs were so similar that you couldn't tell whether it was the same person or two separate people being studied. Now, what do you begin to think of all that? Well, that's an extreme case.

The fact is most identical twins raised apart do have a bit of divergence in their phenotype, in the way they grow up, but it begins to plant in your mind the notion that maybe many aspects of the way we think and act actually have a strong genetic template in them. And one can begin to study identical twins and ask things about, especially those who are separated at birth, and not use such extreme anecdotes like the one I just used. And one begins to find that there's an impressive list of attributes that can only be explained by their being a strong genetic determinant in them. And these traits include being alienated by people around one, extroverted, being a traditionalist, looking backwards in terms of one's customs, leadership, career choice, risk aversion, attention deficit disorder, religious conviction and vulnerability to stress.

Heritability it turns out, if you study identical twins, is about, I'm sorry, happiness, if you study identical twins, is about 80% heritable it turns out and depends little on one's wealth, achievement or marital status. But 80% of it, if you study identical twins, seems to have a genetic template. And you'll say, well, that's all very satisfying, but it begins to be a little unsettling because it begins to cause each of us to ask are we really who we think we are or are we just kind of cassette recorders who are playing out the program that was stuffed into us when the sperm hit the egg that lead to each of our appearing on the face of the planet? To what extent are we individuals or to what extent are we simply manifestations of genotype?

And to what extent do we have freewill? That's kind of an interesting question. Now, people like Eric, I'm not pointing an accusing finger, people like Eric have begun to refine the science of genetics so it really is a science.

And so, restriction fragment polymorphisms, SNPs, haplotype analysis are now uncovering a staggering array of human traits. I believe that the number of human traits that have now been localized, specific genes, most of these are diseased genes, exceeds 2,000 is my recollection.

And there are only 21,000, 22,000 genes in the human genome.

And the pace with which genes and genotype and phenotype will be linked to one another is going to increase if nothing else.

Many of the traits that one thinks about in terms of human beings are obviously polygenic. They're not single strong Mendelian alleles with strong penitence. They represent the confluence, the collaboration of multiple alleles that are conspiring to create one or another phenotype. And these polygenic traits or even polygenic diseases have traditionally resisted analysis because mathematically they are so complex to dissect out, to dissect out the contributing genes which together as a cohort create a genotype. But, as Eric told you last time, people like you who are great software developers will one day begin to figure out how one can take extraordinarily complex datasets and begin to associate specific chromosomal regions, and ultimately genes, with specific genetic sequences that contribute to a polygenic trait. I think at one time Eric spent, about three or four years ago, he worked with people at Cornell studying the polygenic trade of ripening in tomatoes.

It's a polygenic trait like probably chess playing ability in human beings. And was able to localize ripening rate of tomatoes to five or six distinct genetic regions in the chromosomes of the tomato plant. But that's only a harbinger of what could come.

So let's imagine now, again, I'm not blaming Eric for this, I'm just telling you he's the one, he more than anyone else almost on the planet is the person who is leading the charge to refine and strengthen these extraordinarily powerful tools that enable us to discern how our genome creates us the way we are.

But he's not going to be the one who applies these tools.

They'll be applied all over the planet.

There are geneticists everywhere who are interested in looking at how different aspects of human phenotype, including disease phenotype are governed by the alleles, by the SNPs, by the polymorphisms that we carry, and obviously by the genes and proteins that we make. So let's begin to imagine, let's put ourselves fast-forward ten years and begin to imagine where this is going to take us. We already know about a very substantial number of genes that determine the risk of different kinds of cancer, i.e., there's at least 15 different cancer syndromes that people have which have been associated with specific genetic loci. I talked briefly about retinal blastoma, which is a rare one, but even commonly occurring cancers will soon be connected with specific alleles in the genome.

And the risk of getting them in one's lifetime will be relatively accurately predictable. It might take another decade but it will happen. Manic depressiveness, some people have great swings in mood. 2% or 3% of the population doesn't wake up happy every morning. And this is also, I believe, going to yield two specific analyses and

association with certain genes.

There's already a suggestion that the D4 dopamine receptor, which is involved in receiving one of the neurotransmitters in the brain, may have a polymorphism that's connected with manic depressiveness. There will be probably alleles which are connected with, in some way, novelty or adventure seeking. There are going to be alleles that are associated with anxiety, probably maybe connected with the serotonin transporter in the brain. Cardiac disease susceptibility is already mapped out in a number of traits in the most extreme cases, but cardiac disease is very frequent in this population.

And there undoubtedly will be alleles that are discovered that determine whether one has a high risk or low risk of getting heart disease, of getting arthrosclerosis, and whether or not one can go to McDonald's every day and Big Macs with impunity.

Can one do that or not? Some people probably can.

Some people can eat as much salt as they want and it doesn't give them high blood pressure. Other people cannot.

We still don't really understand that. Schizophrenia is probably also very strongly genetically templated, not totally but very strongly. Susceptibility to rheumatoid arthritis probably also has a strong genetic component. Difficulty or ease with which you solve math problems probably also will one day be associated with a certain number of genetic loci. How many difficulties in learning languages? There's already a trait that was discovered in a family in the Netherlands, I believe, and they had a very specific grammatical defect in the way that they assembled the syntax of sentences associated with a certain allele of a certain gene.

Difficulty in just adding rows of numbers may also be associated with certain combinations of alleles. Now, you will say, well, it's impossible, it's inconceivable that these different aspects of cognitive function can be associated with a small number of genes.

But let me tell you something else. We talked a week ago about the evolution of humanity over the last couple hundred thousand years.

And the pace with which the human brain has evolved over the last half million years, and more recently the last 200, 00 years, has been so frighteningly rapid that the evolution of cognitive function and perception in different ways can only have happened through the actions of a small number of genes.

If one needed to have dozens of genes change in concert in order to acquire the penetrating minds that we now have in which our ancestors 500,000 years didn't have, the evolution could not have occurred so quickly. And, for

that reason alone, one begins to suspect that the genetic differences between people who lived 500, 00 years ago visa vie their cognitive function and ours are not so large. And, therefore, a rather small number of genes may have been responsible for conferring on us the powerful minds which we now, which most of us, I didn't say anything, which most of us now possess.

So where is this going to take us? What are the consequences of this?

Let's imagine ten or twenty years down the road when we can do some kind of SNP analysis on one of these chips that have been developed in California and here and in various places. And we can begin to imagine the allelic diversity in a newborn child's DNA or even prenatally if you want. So what are you going to do if you begin to find on a chip of a child's DNA that this kid is likely to be very good in language, probably is going to have poor math skills, will be a rather anxious and obsessive person, will have difficulty associating with his or her peers, and is likely to come down with heart disease at the age of 45?

How is that going to affect your relationship to that person, that child? And will you give that child a different kind of education than a newborn who has SNPs which indicate that without doubt they're going to get 1600s on their morning boards and their shoe-ins for admission to MIT? Are you going to treat those kids the same or are you going to treat them differently?

Do you give them the same kind of education and nurturing?

And how do you treat them throughout their elementary and high school? Are you going to segregate them into different groups or is everybody going to be given an equal chance?

Well, you might say it's our tradition in this country to give everybody equal footing, in part because of a reaction to what happened in World War II in no small part. But what if the time comes when people say we need to be more efficient economically in this country and we need to devote our resources, need to maximize the investment, the benefit we get from various investments, and so it's much more efficient to put kids in a certain genetic class in one school and kids who have another level of genetic giftedness in another school? Of course much of this will be foolhardy because all of these genetic tests, although they will give you probabilities of certain phenotypes, they'll never, at least for the foreseeable generation or two give you certainties. No one will be able to predict with absolute total certainty about the potentials of one or another young person on the basis of DNA tests, at least not in the near future.

Right now one can predict with total certainty that somebody who has a certain allele will come down with Huntington's disease at the age of 30 or 40 or 50. There the predictability, the penitence is 100%. But what if somebody has an allele that says with 60% likelihood they're not going to very good at math?

Is that already going to be enough to justify their segregation amongst a group of the mathematically less gifted?

Let's say that they've gone through elementary and secondary education and high school and they've made it through college and they start looking for employment. Actually, there are jobs out here to be had in this economy, you wouldn't know it, but there actually are people who can find jobs. And let's say one has now an employer who is evaluating a certain job candidate for employability.

Maybe they'd like to have a good medical checkup before they employ this person ostensively to see whether this person is healthy enough to last for ten or twenty or thirty years of employment.

And maybe they'd like to include among that medical exam that person's DNA just in case. And what if the DNA tells the employer that this individual is likely to get colon cancer in 18 years and has a slight susceptibility to mood instability and perhaps even manic depressiveness, that this person is not one of those who can go to McDonald's and eat Big Macs with impunity but has a tendency to arthrosclerosis?

You can think of whatever possibilities you will.

Will that be, therefore, a ground to reject that person as an employee? Well, you'll say they really have no right to do that. But keep in mind that with increasing frequency in this society medical benefits, medical insurance is paid by the employer. So does the employer want to have a whole workforce of people who are in various stages of terminal disease or would this employer like to be able to pay the lowest possible health benefits because the employer has taken care to employ only people who have a really terrific genotype, whatever that is defined as being arbitrarily admittedly? And what about marriagability?

As my sister always says to me, if you want to marry a man the first thing you should do is look into his genes. That's a double entendre. Anyhow.

See, somebody finally got it. [LAUGHTER] The fact is that maybe certain people will be deemed to be less desirable genetically.

Well, the fact is we've been doing that for the last million years.

If you're attracted to someone and you end up marrying them then they have phenotypes which you think are in one way or another valuable.

Consciously or unconsciously, you are practicing a form of eugenics. But obviously there could be a much more subtle form of eugenics where part of the marriage contract states that you want a sample of that person's buccal swab or some lymphocytes to check out what kind of DNA he or she has. Now you say, well, that could never

happen. But it happens today regularly.

There are villages in Greece where there are a substantial percentage of people who carry the trait sickle cell anemia which, as you may know, is not so serious phenotypically in heterozygous form, but in the homozygous form is actually devastating.

And the reason they have sickle cell anemia is that those areas of Greece historically had high rates of malaria. And, as you may know, sickle cell anemia actually protects, in the heterozygous state actually protects one from the ravages of the malarial parasite. So about 20 years ago it became possible to do a simple genetic test to determine whether an individual was heterozygous for sickle cell anemia. And what happened is that somehow what was supposed to be confidential medical genetic tests got out. They became public. And young individuals in the population became known as carrier, as heterozygotes for sickle cell trait, even though phenotypically they were reasonably normal because the heterozygote condition is not so devastating.

So those individuals were soon ostracized, to use an old Greek word.

They were soon put to the side. They were placed in the pool of the unmarriable because nobody wanted to marry them. And so they then, as a consequence, began to marry amongst themselves.

Remember what I told you about homozygosis with the sickle cell trait. But that's only one example of that.

Among Orthodox Jews, among Ashkenazi Jews between 2% and 3% of the population carries an allele for Tay-Sachs disease which is phenotypically silent in the heterozygous state but in the homozygous state is a devastating condition which leads to death in the first years of life. So now among the Orthodox Jews in New York before two young people will get married they will do a test to see whether they are heterozygous for the Ta Sacks allele.

And, in fact, it's not limited any longer to Orthodox Jews.

Because if they're both heterozygotes their marriage to one another, in spite of anything else they consider, is strongly discouraged. Among those who don't live in such a closely structured society such people might nonetheless decide to get married and then face the devastating possibility of one of their four offspring on average coming out as a homozygote and having an incurable genetic disease which is going to lead to their early death. But what about other traits?

And what time will this genetic discrimination, where will it begin and where will it end? What if you find an individual who has a trait of manic depressiveness among relatives?

And when will these genetic tests become public?

When will they be private knowledge? You say, well, they can all be kept private. But ultimately there are already insurance companies which are demanding to determine whether and individual can be insured by looking at whether they have genes for certain kinds of disease-causing alleles.

After all, why should they insure somebody, give somebody life insurance if they are likely to come down with Huntington's disease at the age between 35 and 40, which will surely and inevitably lead them to an early grave? You'll say, well, we cannot have genetic information like that become public or even become accessible.

Maybe that's a solution. The problem is we've been talking about these issues for 10 to 15 years in this society, and we've not yet converged any kind of solution. And the solutions to these problems should not be left in the hands of molecular biologists, because molecular biologists or biologically cognizant people by now, like you, are no more gifted and no more insightful to deal with these issues than anyone else is. They're intuitively obvious these issues. You don't need to know about SNPs to begin to understand the potentially devastating impacts that the misuse of genetics can have on our society. And what happens if one of these days people discover alleles for certain aspects of cognitive function? Chess playing ability. The ability to learn five different languages. The ability to remember strings of numbers.

The ability to speak extemporaneously in front of a class, for what it's worth, for 50 minutes several times a week.

Whatever ability you want, valued or not so valued, what if those alleles begin to come out?

And here's the worse part. What if somebody begins to look for the frequency of those alleles in different ethnic groups scattered across this planet? Now, you will say to me, well, God has made all his children equal. But the fact is if you look at the details of human evolution, some of which I discussed with you a week ago, last week, you'll come to realize that most populations in humanity are the modern descendents of very small founder groups. Remember about the story of the Fins.

70% of Finish men carry the same Y chromosome. All modern Fins, most modern Fins, all of them are likely to be the descendents of a small founder group that came into Finland 2,000 or 3, 00 years ago and carry with them the peculiar set of polymorphisms that founder group happens to have had. And arguments like that begin to persuade you that there'll be different allele frequencies in different populations of humanity. What if somebody begins to discover that Macedonians have an enormously high rate of the ability to play chess because of a certain allele? And here I'm talking very speculatively. I'm not literally meaning that.

And Tibetans have a very poor ability to construct software programs because of a genetic allele they carry? I hope nobody's Tibetan here. I tried to choose two. Are there any Macedonians? All right. I succeeded. All right.

Anyhow. So the fact is it's inescapable that different alleles are going to be present with different frequencies in different inbreeding populations of humanity or populations of humanity that traditionally have been genetically isolated from one another. It's not as if all the genes that we carry have been mixed with everybody else's genes freely over the last 100,000 years. Different groups have breed separately and have, for reasons that I've told you, founder affects and genetic drift acquired different sets and different constellations of alleles. So what's going to happen then, I ask you without wishing to hear an answer because nobody really knows?

Then for the first time there could be a racism which is based not on some kind of virulent ideology, not based on some kind of kooky versions of genetics, because the eugenicists in the beginning of the 20th century, as well as the Nazis hadn't had any idea about genetics, they were just using the word, even though they knew nothing about the science of genetics as we understand it today. But what happens if now for the first time we, i.e., you who begin to understand genetics, begin to perceive that there are, in fact, different populations of humanity that are endowed with different constellation of alleles that we imagine are more or less desirable?

What's going to happen then? I don't know. But some scientists say, well, the truth must come out and that everything that can be learned should be learned, and we will learn how to digest it and we will learn how to live with that. But I'm not so sure that's the right thing. And you all have to wrestle with that as well. And even more insidious is the following notion. Remember the story about the two Jims, the two guys from Ohio who met one another at the age of 39 after they'd been separated at five weeks of birth? That story begins to persuade you of something I said before, and that is that a lot of what you think you are isn't what you made of yourself, isn't what your parents made of yourself, isn't what your environment made of you and your experiences.

Maybe it's all just in your genes. And if that's so then maybe you can't take credit for any of the good things you've done.

And conversely maybe you're not responsible for all the bad things you've done. Maybe three years from now somebody will begin to plead that even though they were not criminally insane when they committed a string of serial murders, in fact it really wasn't their fault because they happen to have this particular genotype which is known to be correlated with a strong tendency to violent.

And, by the way, there is an allele which has a correlation, I forget which one it is, has a correlation with violent behavior. So what if one begins to write off everything we do as not a reflection of our own freewill, our own volition, but instead a consequence of the genes which our parents hoisted on us?

Of course, we can blame it on them. As a father of children, I can tell you that it's amazing how many different things can be blamed on the parents. [LAUGHTER] Of course, the parents have their own out. The parents can

blame it on their parents.

So now it goes back to the grandparents, back to the beginning of time. We laugh about these things and they are amusing, but they are taking us on a collision course with some very difficult problems. And you guys have to wrestle with them and you guys have to explain to the people who haven't taken 7.

12 where the world of biology is taking us.

And on that note, I want to tell you that Eric and I have enormously enjoyed being with you this semester.

We wish you much luck and success in your future lives.

We hope some of you have become interested in biology and that you found this course a little different from what you took in high school.

And have a wonderful winter vacation. See you. [APPLAUSE]