HOW TO READ AN MCAT SCIENCE PASSAGE

When the new MCAT was introduced in 2015, our company became a teaching workshop and development incubator. Our previous course, WikiPremed, had specialized in interdisciplinary methods for the old exam, so we were uniquely poised to help our students with the new one. We have become expert in the challenges of the new MCAT in the years since it was first introduced. All good MCAT courses are built from teaching, and we have done a *great deal of teaching* to build **The Integrated MCAT Course**.

Every MCAT course claims that it is both revolutionary and effective. However, no MCAT course has ever *substantively* demonstrated these things in its own introduction to the world, so we decided to do something different with this discussion. This will be a relatively long presentation, but it will be worth your time. As lead develop and instructor for our MCAT course, I will share perspectives and strategies for MCAT science with you. We will explore together how your scientific knowledge-base works *while you read an MCAT passage*. This will introduce the Integrated MCAT Course in a more useful way than a typical course introduction, because exploring the nature of MCAT science passages will benefit you *on its own,* while demonstrating the rationale for the structure of our learning program.

Who am I?

My name is John Wetzel. I have taught the MCAT for more than twenty years and served as lead designer for three MCAT courses - MCAT Academy, WikiPremed, and the Integrated MCAT Course. After graduating from Stanford University, I worked in healthcare and biotech, but my most significant work has been in the field of MCAT prep. I was proud when WikiPremed became a popular course for the old exam. I have been helping students prepare for the MCAT for many years. WikiPremed helped many thousands of students online. I believe there are many dimensions to becoming a good doctor. My job is to help future doctors improve their understanding of science. Many doctors across the country are my friends and former students.

Light the way with science

This discussion will help you gain a better understanding of how your scientific knowledge-base works to make an MCAT passage intelligible. Think of how reading an MCAT science passage is a subjective experience. Reading the same science passage is a different experience for every person. Science passages are not special in this way, because reading is always a subjective experience. For example, imagine reading a few sentences in a novel about a family walking along the seashore, laughing together, led in front by a boy pushing a red wheelbarrow. From reading this simple scene, you understand and see *something* in your mind's eye. What you see depends on what you made of the words. You are supplying the meaning that makes what you read *exist* in your imagination. This is a very important thing to understand about reading an MCAT science passage.

Insights from psychology and philosophy can make us aware of ourselves and our world in new and different ways, but they are not usually applied to understanding MCAT science passages. When I am trying to get across that reading an MCAT passage is a mental performance, I will sometimes say that from the very beginning of the passage, we work to *open a clearing* into the passage. Opening a clearing into the passage is like shining a light into a cave entrance and bringing a world into view. Everyone has their own intuitive understanding of how ideas take shape in their mind. A more explicit consideration of your own experience leads to a more self-aware approach when reading science passages. Let us investigate how these insights can benefit us within the flow of the test. There is a performance spectrum in the richness of the scientific ideas that take shape in your mind as

you make progress through an MCAT passage. High performance is like squeezing the meaning from the passage like you were squeezing an orange. Let me show you how to turn an MCAT science passage into a rich world of scientific ideas *as you are reading the passage.* In this presentation, we will also work to understand an MCAT passage as the product of the craft of the test-writer. A strong, scientific knowledge-base combined with a good understanding of the test-writer's intentions and repertoire will help you see many of the questions coming *while you are reading the passage.*

The author of the passage

There are many ways that a science passage is different than a CARS passage. We can see that while CARS passages are *selected*, science passages are *constructed* by AAMC for the exam. Unlike the CARS author, the author of a science passage is NOT actually doing their best to communicate with you. *Science passages are constructed by AAMC as a series of intelligibility puzzles. Every element of a science passage is intended this way.* When you encounter a passage element, you bring it to light in your conceptual imagination *as something.* You see a fact, a concept, a connection, something familiar. Maybe a surprise! We say *as something* to differentiate the moment of reflection from its stimulus and capture how a passage element becomes intelligible and reveals its nature to you. How do you prepare your knowledge-base to make MCAT passage elements form into rich scientific ideas as you read the passage?

Every MCAT passage is constructed to challenge your ability to make it intelligible. Does the signal transduction pathway, organic bench-top synthesis or hospital chromatography method for purifying radioactive nuclides exist in your mind the way it existed before in the passage author's mind at the time they constructed the passage? To envision the world of the passage brings the test-writer from behind the curtain. A successful approach to an MCAT science passage involves understanding that *the passage was communicated to you as something different than its scientific ideas*. The passage-writer is actively working to knock the light out of your hands. They will leave a black box in the passage that you can't open without something outside the scope of the exam. They turn things upside-down and flip them around. They are cryptic on purpose. They think to themselves, 'Yes! We do all those things!'

The MCAT can seem very daunting at first. The knowledge-base is large, and the test has a way of suddenly becoming sophisticated from any direction at any time. However, there are moments in study, like the moment when you first gain a bird's eye view on the knowledge-base, or maybe after a review cycle through biochemistry, when your skill with MCAT science passages suddenly leaps forward. I have spent years studying these various *shifts in gestalt* that occur along the way to a great performance. What has changed in the knowledge-base of the student? Through content review and practice we are making progress on two fronts. I believe there are two cardinal attributes of a knowledge-base that is prepared for MCAT science. These are *completeness* and *integrative complexity*.

A mental exercise

A mental exercise is coming, which I hope will be both interesting and useful for you. We will practice reading the very beginning of an MCAT passage as if it were the real thing. We will look at just the first three sentences and one figure of a passage. Just the beginning! Let us imagine we were at the Pearson Test Center this very day. It is test day! Let us imagine the beginning of an MCAT passage in the chem/phys section. I understand that you *might have just begun* this whole MCAT review process, so I warn you, we will be taking a deep dive into some biochemistry. This kind of thing may not feel exactly manageable until you have a bird's eye view on the knowledge-base, but getting to that point is not so hard! I am demonstrating in this discussion something that you can achieve. Do your best! We will look at this together. In this exercise, as you read the three sentences at the beginning of the passage and examine the figure, you will notice that you are calling ideas to mind from science knowledge *as you are reading* the passage elements. Slow down and take your time. Everyone always rushes too much at the start of an MCAT passage. Your general sciences knowledge-base will transform the passage elements into *scientific ideas* within your conceptual imagination.

Imagine an MCAT passage

So here we are in the chem-phys section, and it is test-day. Let's imagine that you just finished the 3rd passage in the section, and you close your eyes for a moment. *You always have permission to take the time you need at the beginning of any MCAT passage.* The time you invest in the beginning of an MCAT passage will return to you later in the passage because you will understand the rest of the passage much better. Take the time you need to look at the first paragraph as a whole.

Several inherited metabolic disorders (IMDs) affecting the malate aspartate shuttle (MAS) have been discovered in recent years. Enzymes of the MAS include cytosolic and mitochondrial isoforms of malate dehydrogenase (MDH1 and MDH2), as well as cytosolic and mitochondrial aspartate aminotransferase (GOT1 and GOT2). MDH exists as a homodimeric protein with subunits between 30 and 35 kDa held together through extensive noncovalent forces and hydrophobic interactions.

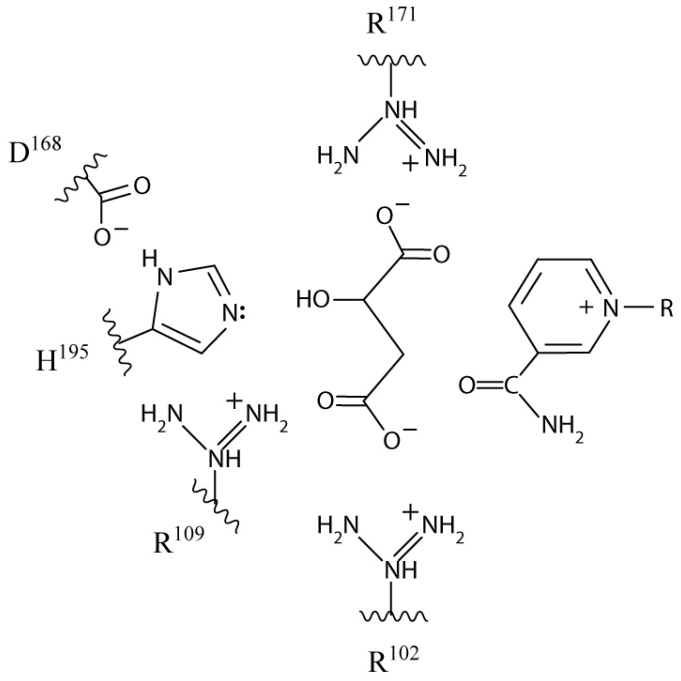


Figure 1 Active site of mitochondrial malate dehydrogenase.

How is it you see this figure as more than just symbols? How do we see the symbols as ideas in our conceptual imagination? We all know *intuitively* how ideas form. Let us look at what is going on in our minds *explicitly*. Imagine you had come across this figure a few years ago. Think of how opaque and mysterious it would have looked to you then. Something complex has happened to you in the interim years. Now you see Figure 1 *as something rich*.

Reading an MCAT passage is a subjective experience that becomes richer through MCAT preparation. Your ability to project the world of an MCAT science passage as ideas in your conceptual imagination is the central figure of merit of the science portion of the exam. Let us

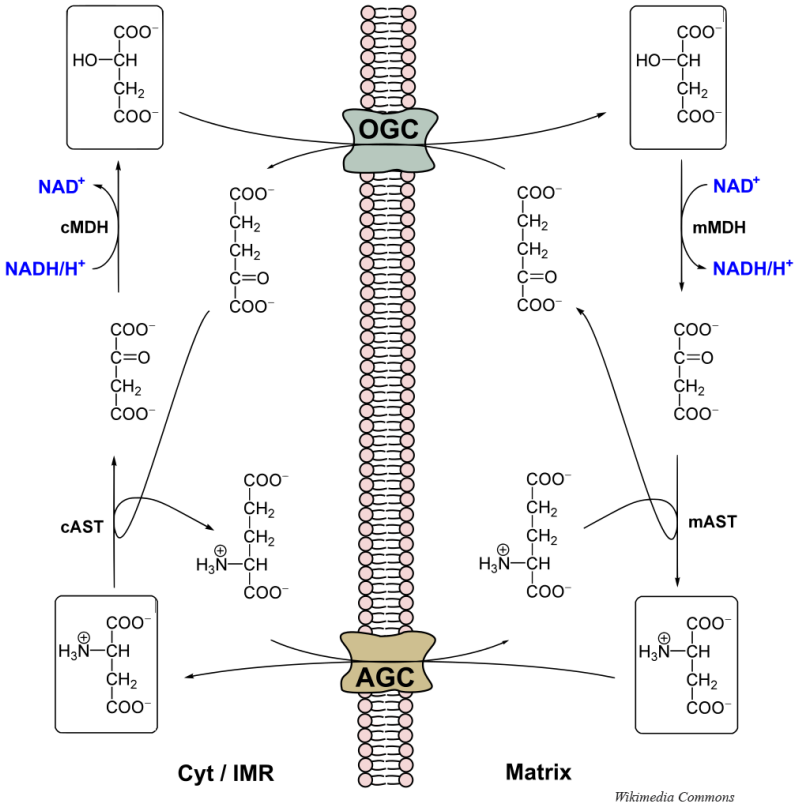
examine how MCAT science passage elements are constructed and how they work to create a spectrum in performance. Let's take a close look at the text.

> Several inherited metabolic disorders (IMDs) affecting the malate aspartate shuttle (MAS) have been discovered in recent years. Enzymes of the MAS include cytosolic and mitochondrial isoforms of malate dehydrogenase (MDH1 and MDH2), as well as cytosolic and mitochondrial aspartate aminotransferase (GOT1 and GOT2). MDH exists as a homodimeric protein with subunits between 30 and 35 kDa held together through extensive noncovalent forces and hydrophobic interactions.

The beginning of an MCAT passage is like entering a cave. Shine a light and allow the shapes to take form before you enter. *Make yourself call to mind the immediate thing you are reading. What does it call to mind?* You have the job to make everything in an MCAT passage articulate itself to you *as you are reading* and reveal its nature to you. “Malate aspartate shuttle” wants to fall away into the stream of language as an empty signifier. It wants to float away like an empty boat.

The malate-aspartate shuttle IS within the scope of the basic knowledge for this test. It is likely familiar, *but being familiar does not mean you have called it to mind*. Exert a positive will. Bring what you know about it to mind. *It takes positive acts of reflection to make scientific language take on its meaning.* What do you remember about the malate-aspartate shuttle? Can you come up with two sentences? How much stronger you will be in this science passage if you can make yourself do this right now! Make the malate aspartate shuttle run harder in the cells of your brain *right now*. What are you saving it for? It takes energy, focus and discipline to make an MCAT passage unfold. The malate aspartate shuttle carries electrons produced in the cytosol from the G3P dehydrogenase step in glycolysis to the electron transport chain in the mitochondrion for oxidative phosphorylation. A portion of the malate aspartate shuttle overlaps with the Krebs cycle, and another portion overlaps with a particular mode of gluconeogenesis. Make your memory productive while you are reading. Nobody gets stuck in an MCAT passage by taking a little extra time to understand everything at the beginning. This is how you keep yourself from getting stuck later in the experimental section of the passage.

Don't look for the passage to supply its meaning to you. You supply the meaning to the passage. Read actively, not passively. Make entry into the world of the passage. Give yourself a little extra time at the beginning to study and understand. *Later on in the experimental section of the passage, you will be required to manipulate and interpret changes in this world within your imagination*. Starting with the very next sentence, you are better off if you have called *something rich* from memory.



Let us make a study of perfect performance like Brahms studied Beethoven. We will strain to exceed ourselves. There is a spectrum all the way to perfect performance whereupon reading "the malate aspartate shuttle" at the start of an MCAT passage triggers a practiced approach that *brings it to mind* within the flow of the test, which means bringing it so richly into your working memory that it looks something like the figure above in your imagination. Struggle for perfect performance and get yourself to the other side of that line where you can demonstrate you are qualified to enter medical school. Never make the perfect the enemy of the good. Never let the idea of perfect performance harm your self-efficacy. Struggle towards it!

Puzzles

What if we could see the question-writer setting up questions to pitch while we are reading the passage? *What are isoforms, for example*? Notice that you are being told about the genetic relationship of MDH1 and MDH2. By reading *reflectively*, you collect MCAT riches like a bear collecting honey from a hive, so you have noted that MDH1 and MDH2 proteins are expressed by the same gene or closely related genes within a family. With practice and learning to trust yourself, you won't allow the stress of the exam to push you forward too quickly, especially at the beginning of a passage. *Everything in a science passage is intended as a puzzle*. In our virtuoso's performance, we make all the puzzles reveal themselves and see the questions coming.

Why did the passage-writer use the name “aspartate aminotransferase” for an enzyme practically everybody knows by the name of “aspartate transaminase”? The test-writer knows that “transaminase” is the name in the textbooks. It's a staple of 1st semester biochemistry. They chose the more obscure name instead, however, because their intention is to hide transaminase away from you. They are being cryptic while pretending to have a good conscience. Always respond to the invitation. Uncover what is being concealed from you. As it relates to cognitive psychology, *spreading activation* describes how the brain iterates through a network of associated ideas. The passage-writer knows that “aminotransferase” will not nucleate spreading activation within your memory unless you first recognize it as the enzyme you originally learned as “transaminase”, so the puzzle creates a spectrum of performance. Recognizing transaminase, you are now more likely to remember that the oxaloacetate produced through oxidation of malate must be changed into aspartate by transaminase before it can cross back to the cytosol. When you sense the passage-writer is being cryptic, you have likely discovered them setting up a question.

So the author has given you a puzzle. *You must always reach an accommodation with any passage element.* You can puzzle the meaning of “aminotransferase” from its word parts, or you can puzzle it from your recollection of the malate-aspartate shuttle. Reach an accomodation, even if the element doesn't completely clear or resolve in your understanding.

There is one kind of passage element you may encounter, often in the experimental section, which will seem very specialized or advanced for the scope of the exam. Turning this type of

knowledge item into your best guess is the proper strategy. *It could be that your best guess is the figure of merit*. Fence it in, and manage it as an open question. What do you think it is? Fencing in the uncertainties of an MCAT passage is a high art. Maybe you didn't recognize a chemical substance or an experimental technique. Take a deep breath and manage it as your best guess. Keep track of the related contingencies. It is an open question.

The passage may seem to strongly imply you should be familiar with a specialized or very advanced knowledge item. This is difficult to accept, but never take this implication as actual evidence you are supposed to be familiar. When your knowledge-base has completeness, trust yourself. *Was I supposed to study yeast-three-hybrid assay? I do not know that assay, but I can see it uses a reporter gene to operationalize how strongly that ligand is binding with the various potential binding partners in the experiment.* Maybe they want to see that you can hold your footing, using the context of the passage to make sense of something from beyond the frontier of the expected knowledge-base.

AAMC expects you to have mastery of the general sciences fundamentals with enough conceptual depth in biochemistry and molecular cell biology to know your way around journal level scientific language. What is their rationale for going beyond the scope of the AAMC topic outline with a passage element? They want to see you go down the rabbit hole. They want to see you handle yourself *somewhere unfamiliar*, so keep your footing. When people hit a passage element they can't resolve, there is a tendency to lose site of everything built up to that point in the passage. Let us return to the analogy of the cave. Keep your light on all the way through, even if the light doesn't reach into every nook and side tunnel. *The quality of your best guess or open question is sometimes the intentional figure of merit*. You are doing the MCAT right.

An MCAT passage element is an invitation to a kind of mental play. Malate dehydrogenase was described as a “homodimeric protein with subunits between 30 and 35 kDa held together through extensive noncovalent forces and hydrophobic interactions”. Even though they themselves are not covalent, hydrophobic interactions are distinguished from “non-covalent forces” by the passage-writer. This is because the thermodynamic impetus with hydrophobic interactions is the behavior of water driving the hydrophobic groups together, not the direct weak forces between the specific groups. The distinction between “non-covalent” forces and

“hydrophobic interactions” has a complicated warrant. This invites a moment of thought, a momentary meditation. Something happens as fast as the speed of neural activity and it comes to light in your mind there are no disulfide bridges between the subunits of this enzyme. Something like that. Unfolding the passage through mental play allows ideas to rise up. Trust yourself. Often it's not the knowledge *per se* that is missing but a willingness to create a space through play for ideas to rise up through reflection. A strong read in the first half of the passage will make things much easier for you in the second half. Our rich ideas about what we are reading have primed us for the questions.

> *How would the bands compare on a gel in reducing vs. nonreducing SDS-PAGE for this protein?*
>
> *How many amino acid residues would you expect there to be present in the complete enzyme?*

Pretend you have landed an internship at AAMC in the Department of Question Writing. You work in the Question Brainstorming Section. What a great internship! Very competitive! The Department of Passage Writing sends its passages to you. They send them through a pneumatic tube. A new passage arrives at your desk every five minutes. Your job is to read the passages and think up questions. That's your job. After doing it a few months, you can see all the questions of any MCAT passage *as you read the passage. M*aybe they will promote you to Passage Writing after you take your MCAT!

One important type of question you can see ahead of time is no different than a stand-alone question. Every science passage on the MCAT is followed by a few questions which are no different than simple stand-alone questions. The only real difference between these and stand-alone questions is that the given information is presented in the passage instead of in the question stem itself. Every science passage serves as a storehouse of given information for questions like these, questions which will not depend on the passage as a whole. Always keep this in the back of your mind. Carry it like a chalice through the valley of fear. *Even within the hardest passage of the exam, the easy half of the test is still there*. No matter how much trouble you have gotten yourself into, you can always get 3 of the 5 questions right in any passage. You will see these questions coming beforehand. If they give you the

wavelength of the laser, ask yourself is it UV or visible? Picture deriving the photon energy. If they give you the volumes and concentrations of laboratory solutions, mentally practice a few calculations right there while you are reading. Acclimate and prepare yourself. There is no happiness like the question you saw coming beforehand. You have primed yourself to answer it correctly, and this particular type of question is easy to see coming.

Approaching the figure

AAMC knows how to be cryptic in their descriptions with a good conscience, and they will design a figure that looks like a plate of spaghetti. They congratulate each other on their skill in making bad figures look well-intentioned. Take my advice and never stare straight into one of AAMC's big, complicated figures the first moment you come upon it. *Read the caption first*. Then find some element in the figure, down in the corner, something you recognize. Find a game to play. Identifying the amino acids in Figure 1 would be a good start, because it's an obvious thing you need to do anyway, so it will give you something productive to do while you *acclimate* to the figure. Never expect to understand a big, complicated figure when you first look at it. Find a game to play and let the disorientation dissipate. You know you will acclimate to the figure. You will shine the light of science, and it will reveal itself. Play with it. Think of it as shining a powerful light exploring the parts of a forest, bringing everything *into a clearing.* First this part, and then that part, and then the whole forest reveals itself.

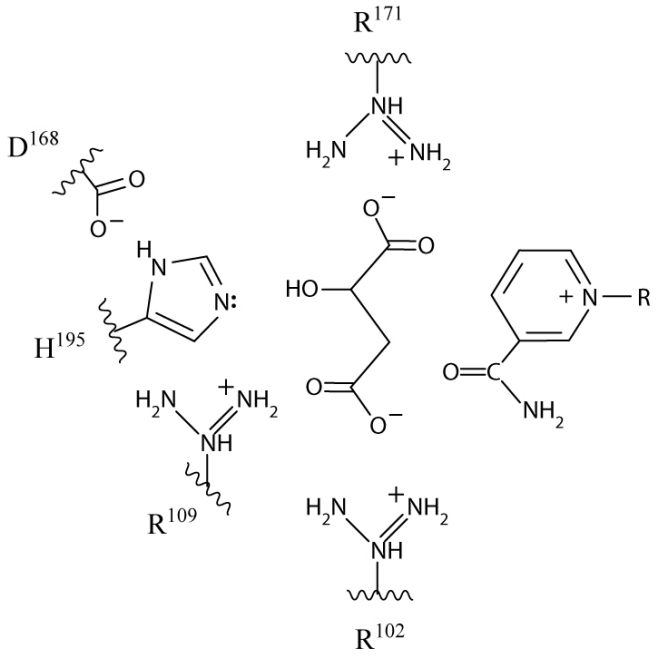


Figure 1 Active site of mitochondrial malate dehydrogenase.

When you examined Figure 1 earlier, did you manage to recognize the NAD^+ in this figure, or did it manage to slip past you? It is actually my job to ask my students these kinds of questions. My students and I are always honest with each other about things like this. We learn from them. Always approach a figure in an MCAT science passage as if it were a game between you and the test designer. *Sometimes they are hiding things. You are bringing them to the light, and the more you bring to light, the more other things will unfold*. The structure of NAD^+ is intentionally drawn by the test designer to make its recognition unlikely. You will miss it, if you move too fast with the figure. In the psychology of perception, we learn that a *visual percept* is a mental construct developed as a consequence of visual stimulus followed by processing in the occipital lobe. The gestalt principles of similarity and grouping have been used by the designer in this instance to give the nicotinamide ring of NAD^+ the gestalt of an amino acid side-chain in the figure. The illusion is only possible because the R group is being made to stand in for much more than it should. Look again at Figure 1 above, and you can see NAD^+ hiding itself as an amino acid in the figure.

Puzzles like these are constructed by the passage-designer to create a spectrum of performance in a game where you are responsible for supplying the meaning. At least in CARS, you can count on the author trying their best to communicate, but MCAT science passages always have a bad conscience about everything. You could say they have a bad conscience for good reasons, so they must have a good conscience about their bad conscience! *Do not imagine you are getting clear communication of scientific ideas from their figures.* You have to fill in the meaning yourself. Nevertheless, because the nicotinamide ring is so consequential in biochemistry, you certainly ought to recognize it, especially in the context of a dehydrogenase in core metabolism. Nicotinamide adenosine dinucleotide is a good friend at the intersection of many important ideas.

Depth of processing, alongside interest and scientific curiosity, will greatly strengthen your memory for biochemistry! The oxidized form of nicotinamide is an aromatic cation. This structure is the key to its personality and the key to recognizing NAD^+ tacitly. It gives you a deeper level of processing that connects NAD^+ to other ideas. The aromaticity of NAD^+ will be lost when NAD^+ takes on the two electrons through the addition of the hydride from malate. This is what happens when NAD^+ becomes NADH. At the start of the mechanism, the ring electrons had been completely delocalized in aromaticity, spread out in the extended π

system of the ring in NAD^+. As reduction of NAD^+ moves forward, however, these electrons will have no choice but to find themselves pushed together into conventional orbitals on the other side of the nicotinamide group in NADH after the addition of the hydride. Forcing negative charges, ie. the ring electrons, into smaller spatial volume is an uphill battle in terms of its classical work-energy physics, an increase in electrostatic potential energy. This is such an important coenzyme! Pushing two new electrons onto NAD^+ is an uphill battle because they are pushing the other six into conventional orbitals on the other side of the nicotinamide ring. It is an uphill battle on the bench-top from a standard hydrogen electrode, so in general chemistry, we say $NAD^{+\cdot}$ possesses a negative standard reduction potential. The reduced form of the coenzyme, NADH, is like a waiter holding two glasses of champagne high on a tray with another six crowded behind pushing those two off. After NADH can give its electron pair as a hydride to FMN in complex I, the six electrons can spread out and relax again in the aromatic ring of NAD^+.

Completeness

For the purposes of MCAT preparation, your knowledge-base is complete when you have comprehensive, fundamental level mastery of the AAMC topic list. In AAMC's presentation in the Official Guide, the topic list is organized in an interdisciplinary manner to reflect the systems levels integration they are devoted to communicating to you. In other words, topics are not sorted into physics, general chemistry, organic chemistry, biochemistry, molecular cell biology and physiology in the Official Guide. However, each discipline does have a traditional outline, the traditional structure with which you are familiar from college, and you can see this from the bird's eye view. You can see the city of science laid out on the map. There are the suburbs of the city - Physics, Chemistry, Biochemistry, Molecular Cell Biology, and Physiology. Each of these suburbs, *the scientific disciplines*, have neighborhoods within them. For example, above the suburb of Physics, you could take a bird's eye view and see the individual neighborhoods of Physics, which are Mechanics, Waves, Thermodynamics, Electricity & Magnetism, Light & Optics, Modern Physics and Nuclear Physics. If you flew down low to the street level in the neighborhood of Mechanics, for example, you could drop in on the neighborhood and land on a wire on Fluid Mechanics Boulevard and see the Density of Water, Pressure, Pascal's law, Pressure with Depth, Archimedes' Principle, Continuity Equation, Bernoulli's Law, Venturi Effect, Viscosity, Turbulence, and Poiseuille's Law. Maybe a passage within the context of the circulatory system has prompted you to visit Fluid

Mechanics Boulevard, and you are interpreting an embolism presented in the passage with scientific ideas from fluid mechanics. With good structure, you can drop into any neighborhood of your knowledge-base like this. You understand the scope of the exam, and you know what the frontiers look like at the edge of the knowledge-base. Because your knowledge base is complete and well-structured, you are able to find the ideas *as you are reading* to make the elements within an MCAT passage reveal their nature to you.

With completeness you are always at home in the passage. You are always a local and never a tourist. You can find your footing within any figure, *even the figure you did not expect within an MCAT passage that is nothing at all like the full-lengths*. A complete knowledge-base gives you an approach for even the unfamiliar elements of the *unexpected MCAT*. You are patient to let any figure unfold *as something rich* in your understanding. Begin with the caption of the figure. Then find a game to play within it. This will keep you from staring straight into it, which will hypnotize you. Don't try to take it all in at once. Find a game to play and gain an entry point. Identifying the amino acids seemed to be a good choice for Figure 1, as a place to begin, but maybe looking for malate, the substrate, would have served just as well. Begin with something familiar and you will nucleate a process of recognition and relation within any figure. You patiently crystalize an unfolding synthesis that brings interrelated scientific ideas to mind. You enrich your perception of the figure with understanding.

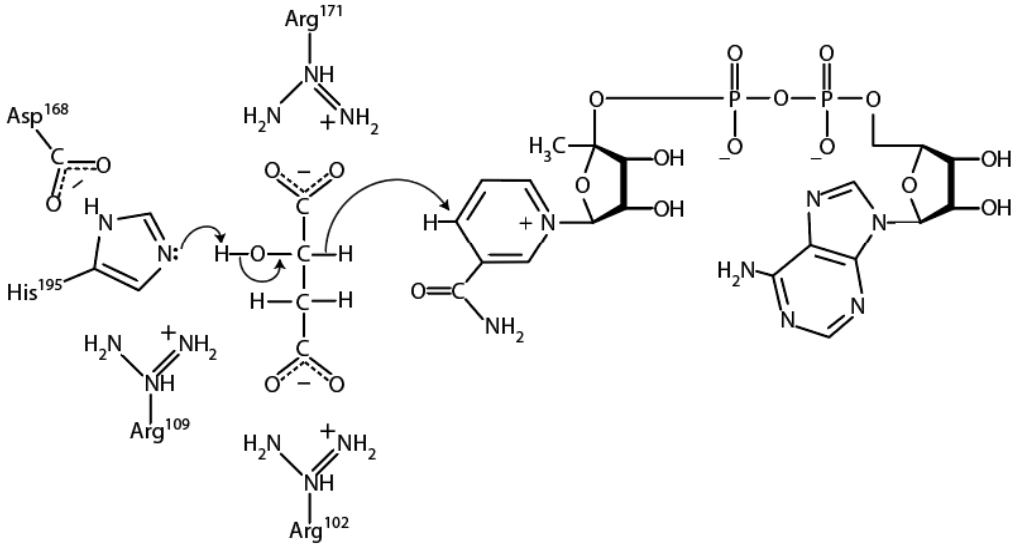


Figure 2 Figure 1 after its projection in the imagination as scientific ideas.

The understanding you build from the beginning of the passage is the lantern you carry forward. Keep this light on all the way to the end of the passage, and you will emerge into a pleasant meadow after exiting the cave where you are answering questions about your passage through the cave with ease. By taking a few seconds to study and understand the text and figure at the beginning of a passage, you have made the beginning into a rich world in your conceptual imagination. You have put yourself into a good position for this passage. There will be more challenges ahead. Soon the passage will take the turn to "*Researchers were interested in* . . ." and the experimental section will begin. Your disciplined approach may have represented an extra twenty seconds from the start compared no approach at all, but your understanding has become so rich that the remaining challenges the passage will bring, including the experimental section, will unfold much more easily. The easy questions of the MCAT were always going to be easy questions, but now you are making real progress towards the harder two or three questions of this passage. *You can win almost any MCAT passage by taking your time at the beginning of the passage*.

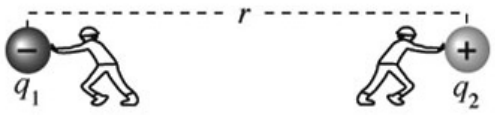
> *Suppose you carried out respective enzyme assays with prepared MDH2 phenotypic variants D168A and R102A. Which trial would you expect to show significantly decreased V_{max} compared to wild type? Which variant would you expect to demonstrate increased K_M compared to wild type?*

We have shown the enzymatic mechanism in Figure 2 complete with the movements of the electrons. Would AAMC actually expect you to demonstrate knowledge of the mechanism after examining Figure 1 at test pace? Is that realistic? How can we predict the MDH2 mechanism from Figure 1 without ever having seen the mechanism before? What are the tools to interpret the underlying plot in biochemical mechanisms, even in mechanisms we have never seen before?

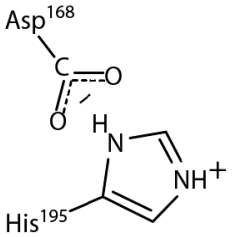
Integrative complexity

Here is a positively charged particle, by itself in the middle of empty space. It used to be located near a negative charge, but now it is all alone.

The positive charge used to be near to the negative charge. Let's go back to the time when they were near to each other in space. To move them apart against the attractive, electrostatic force between them, there was an investment of mechanical work. This moved the positive and negative charges so far away from each other that the electrostatic force between them became tiny. Now they don't feel anything significant from each other anymore. No more work would be required to move them even further apart. They are completely separated and the force between them now is infinitesimal.



We invested the mechanical work to move the positive and negative charges apart. Therefore, we know that if the two charges were to fall back together again, this would represent a *decrease* in the electrostatic potential energy of our system.



The conjugate acid of histidine has found itself in near proximity to a negatively charged aspartate residue within the active site of MDH2 after initiation of the enzymatic mechanism. As soon as histidine takes on the proton in the malate dehydrogenase mechanism, it will fall down into a well of electrostatic potential energy with the nearby aspartate. In other words, the presence of aspartate will lower the electrostatic potential energy of the conjugate acid of histidine.

Begin at particle level electrostatic potential energy changes, and then you take a road from there. This road will cross several conceptual bridges. You must cross these bridges many times and make this conceptual progression into a habit. Make this conceptual journey a form of tacit understanding. Make this throught process a *way of seeing* chemical change. The road begins with your common sense idea of the particle level electrostatic potential energy changes involved in the particular transformation, whether at the chemical bonding level or

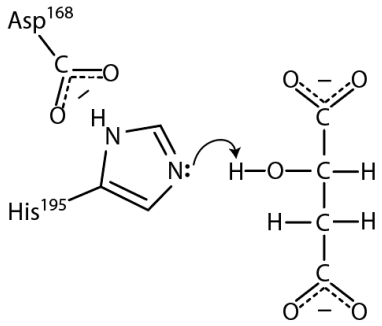
the intermolecular level, whether an oxidation-reduction reaction, solution or acid-base process. Then you cross a bridge into thermodynamics, where you now see the change occuring within a very large ensemble, such as a mole. After you cross into thermodynamics, you can see the particle level electrostatic potential energy changes in terms of the thermodynamic idea of the internal energy change of a chemical system within its surroundings. But we're only half-way there! The road continues onward from internal energy change, and you cross another conceptual bridge. This is the 1st law of thermodynamics, which let's you translate the internal energy change of the system you have conceptualized into the heat flow between the system and its surroundings through the reaction or process. After predicting the heat flow, you cross the last bridge, the 2nd law of thermodymanics. Gibbs free energy will act as as your guide to cross this last bridge into the honeysuckle world where you know the direction of spontaneity and the position of equilibrium. There are many paths connecting the physical and biological sciences. The road I am describing is the royal road of chemical thermodynamics.

Protonated histidine alongside aspartate has lower free energy compared to protonated histidine by itself in aqueous solution. Aspartate has raised the pK_a of histidine. You may have seen aspartate and histidine do this together before in chymotrypsin mechanism. Within the mechanism of a serine protease such as chymotrypsin, aspartate provides histidine with the power as a base catalyst to pull a proton from an active site enzyme serine. This makes serine a good nucleophile to attack the peptide bond in the mechanism. We have seen the same thing happening within the tight structure of hemoglobin where it underlies the Bohr effect. As O_2 departs from hemoglobin, the resulting conformational change in the direction of the tight structure brings a beta chain histidine and aspartate into near proximity. As hemoglobin assumes the tight structure, the two amino acid side-chains fall together into a well of electrostatic potential energy as histidine takes on a proton from surrounding water, forming a salt bridge with aspartate and stabilizing the tight structure. Protons load onto hemoglobin as oxygen unloads. There is an important general concept here that the pK_a of a side chain may depend on its electrostatic microenvironment within a folded protein.

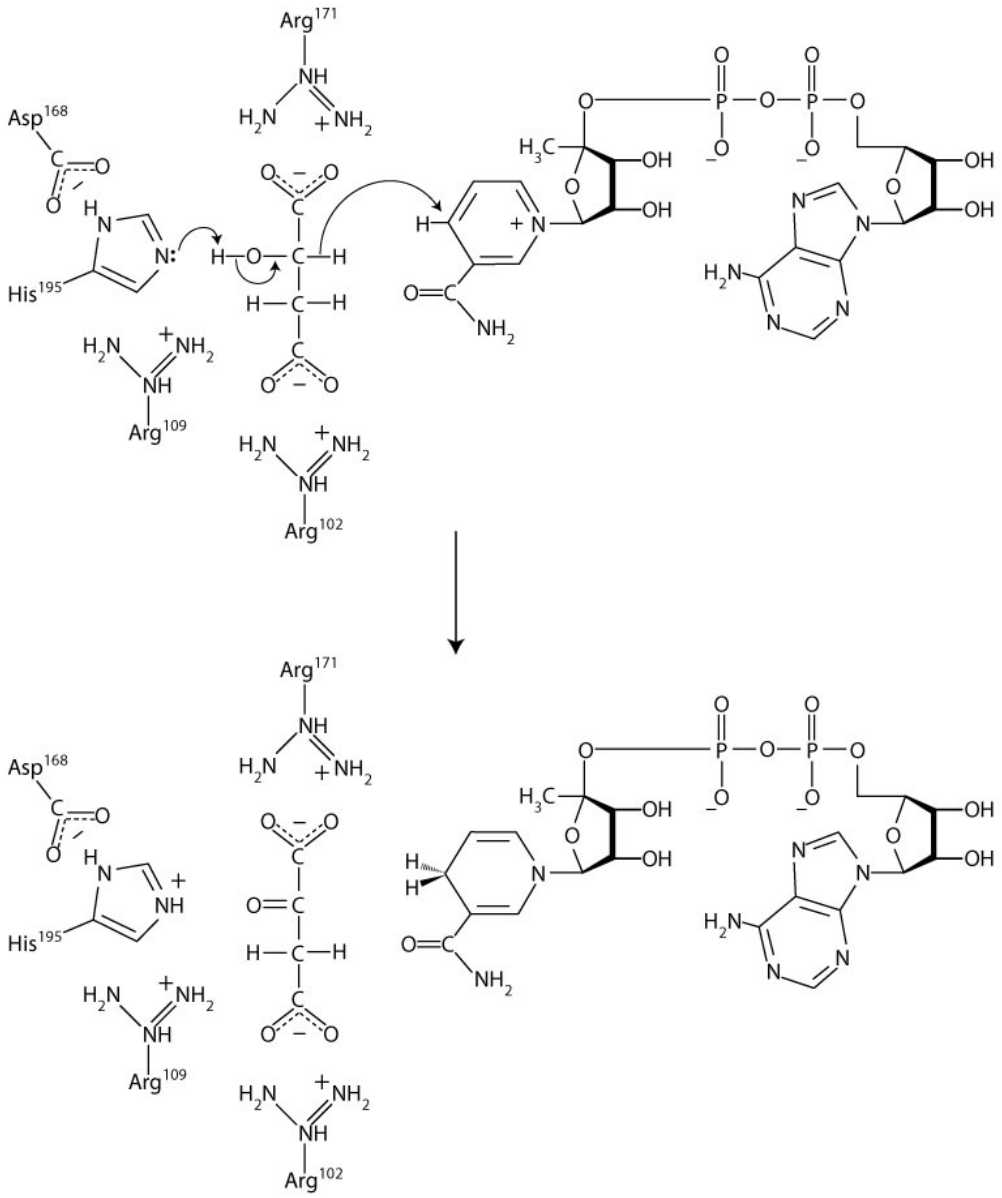
AAMC has a collection of figures of merit like this, that allow them to see if you have fought for sophistication through a history of 'aha! moments' It's amazing to think that something similar is likely the mechanism for pumping the protons through complexes I and IV, pK_a's of

ionizable groups phasing with conformational changes associated with redox cycling of iron-sulfur clusters like two bucket brigades in opposite directions, electrons moving downhill in free energy, powering conformational changes in complex subunits that shift pK_a's of ionizable groups to move protons uphill.

According to E.M. Forster in *Aspects of the Novel*, a story is a “narrative of events arranged in their time-sequence,” whereas a plot organizes the events according to a “sense of causality.” In the proximity of aspartate and histidine, you can see the *plot* of the story beginning to take shape. Aspartate has raised the pK_a of histidine after induced fit has brought them together, giving histidine the power as a base catalyst to pull the proton from C2 hydroxyl of malate. AAMC might definitely expect you to see this happening from Figure 1. You see aspartate is making histidine a stronger base catalyst. You could recognize the interaction of aspartate and histidine from the chymotrypsin mechanism, a teaching classic they expect you to know about, or from the Bohr effect in hemoglobin. If physics and chemistry ideas were present at the time you learned the chymotrypsin mechanism, a *deeper level of processing* was built into your knowledge of it. Deeper processing at the time of learning is what gives ideas complexity, connection and retention. We can see the plot begin through the interaction of aspartate and histidine. They will get the mechanism going, and the rest will follow logically.



The electron pair left behind by deprotonation of the C2 hydroxyl group isn't going to sit around on an alkoxide anion, especially with the negative charge already present on both ends of malate. What happens in terms of oxidation-reduction is a two electron transfer from malate to NAD^+, which transforms malate and NAD^+ into oxaloacetate and NADH.



Integrative complexity without content

In the field of psychology, integrative complexity is a psychometric used to measure the structure of a subject's thoughts. The measure of integrative complexity has two components: differentiation and integration. Differentiation is the perception of different dimensions when considering something. Integration refers to the recognition of connections among differentiated dimensions. Insofar as it may be a natural aptitude, in my experience, most premedical students are very strong in integrative complexity, but this aptitude will not operate within a scientific knowledge-base where the connections have not been formed through

learning. This is why biochemistry is likely to become a thousand acts of brute memorization for many premedical and medical students. It has been taught in the university setting without a foundation primed to form complex ideas about it. To develop the ability to think and reason about biochemistry in a rich way requires a thousand aha! moments, or it can be facilitated by the presence of organic chemistry, general chemistry and physics concepts at the time of learning.

Every amino acid has a personality. Some, like histidine, have a big personality in enzymatic mechanisms. Others, such as alanine, have a big personality in metabolism or on the benchtop. Like the amino acids, all of the important coenzymes have personalities too. NAD^+ has a complicated and multi-faceted personality. There is a rich intersection of ideas within every important coenzyme. Energy metabolism and its core pathways comprise one of the most important themes of the entire premedical curriculum. On test-day, you will need to have built your understanding from the ground up in this subject area. It is central dogma for AAMC. They are bent on it. Electrons which were originally the property of carbon in glucose are now shuttling onto NAD^+ with near Carnot cycle efficiency in the mitochondrial malate dehydrogenase step. The malate dehydrogenase reaction operates near equilibrium in the mitochondrion, pulled forward by product removal of oxaloacetate by citrate synthase one step ahead. Citrate synthase is the engine moving things forward in the Krebs cycle, and malate dehydrogenase gets pulled along reversibly a step behind. It is better for MDH2 to be operating reversibly because those two electrons were once the property of glucose, and their free energy is precious.

In MCAT review, you are being asked to accomplish what might take a laboratory scientist a decade or more, depending on particular specialization, happenstance and curiosity. You cannot rely on a career of laboratory problem solving to develop an integrated understanding of science, because you are not in a PhD program. AAMC is bent on you becoming sophisticated right now in your understanding of biochemistry and molecular biology before medical school. You don't need to memorize every rabbit hole. AAMC wants you to gain a rich, fundamental understanding through coursework and MCAT review, so that your preclinical years in medical school will be more productive and engaging. Why is Gibbs free energy the most frequently mentioned topic on the AAMC outline? This is because you need to understand Gibbs free energy to understand the plot in biochemistry.

The MCAT in the age of scientific revolution

We are in the age of biochemistry revolution. The molecular biology revolution. The world has changed. A paradigm shift in scientific understanding has occurred over the last fifty years, and there is a profound systems levels unity now between the physical and biological sciences at the granular level. This was not the world of medical doctors even two generations ago. When AAMC envisions MCAT preparation, they see a process that instills interdisciplinary understanding as a kind of everyday common sense. When AAMC redesigned the MCAT in 2015, they made interdisciplinary understanding the key to mastery of the science sections because they want to give you interdisciplinary understanding as a fully formed superpower for your career in medicine. The scientific understanding of a doctor cannot be fenced away from itself by disciplinarity because there is only one world in the patient. *The unified approach is the common sense approach to scientific ideas*. The scientific disciplines are not commensurable in their traditions, instrumentation, and verifiability criteria for meaningfulness. Even though chemistry seems to be more fundamental than biology, you cannot go analytically from chemistry facts to derive biology facts. Scientific facts refer to aspects of the world which are identifiable as particular delimited questions or issues. There is another kind of fact which may refer to structures inherent in any possible world. The underlying unity of the scientific disciplines is an existential fact which grounds scientific facts as the intelligible descriptions of a world revealing its nature.

I will share whatever perspectives I can discover that help me be a more effective coach for my students. I hope perspectives from psychology and philosophy in this post have given you some insights as well as some helpful strategies for mastering MCAT science. There is no path to masterful performance that does not involve hard work. My goal is to help you develop self-efficacy towards MCAT review by helping you understand the knowledge-base you are building. The exam is a call for you to fluorish. In my experience, students do not have a clear idea regarding their own potential for this exam

Why is content review trickier for the new exam than the old one?

There was not much lead time for the developers of MCAT prep materials before AAMC released the new exam in 2015. AAMC had an enormous challenge to bring the ship in, and they weren't thinking too much about the world of MCAT prep. The new MCAT is a wonderful achievement, in my opinion, but the transition to the new exam was difficult for the MCAT

prep courses. The big companies adjusted to the new exam by addition and subtraction, *as if AAMC had not fundamentally changed the MCAT.* Some companies took down their shingle forever or went back to the incubator. Some have struggled in the in-between, still excellent but now complicated in how their materials fit in. One big problem is that you can't create an MCAT course from just an idea. Good MCAT courses start in teaching. For our part, we went back to the incubator to teach. WikiPremed was a good course for the old MCAT. We knew that our new MCAT course would be built through teaching the same way. We carried out a great deal of teaching, nearly one hundred course cycles in one-on-one or small-group teaching, to build the Integrated MCAT Course, and now it exists in a form accessible for everyone.

A big disconnect seems to exist between how content review is practiced these days and the value it has for the new exam. The typical MCAT bookset can help you in many ways, but it cannot convey understanding sophisticated enough for the demanding side of the new MCAT. It will help you see the city-scape of science, the bird's eye view. Explanations are always concise and to the point. The traditional concise approach, perfect for the old MCAT, is still extremely useful for the new one! However, after the collective experience of thousands of shipwrecks, students have learned not to ask too much from content review from any bookset. The general advice these days seems to be to use the bookset for the basics and rely on extensive question-bank and full-length practice. A thousand “aha! moments” can build integrative complexity because you are naturally wired for it. This is not a bad strategy! However, none of those things is an MCAT course. The Integrated MCAT Course is the first proper content review for the new MCAT. It will make everything else you do in MCAT preparation more effective.

Why we teach electricity in the first module

Below is the content review sequence for the first eight modules of the Integrated MCAT Course. There are twenty modules in the course. Content review is completed by module 15, so below is the first half of the topic sequence. Physics topics are shown in blue; general chemistry is magenta, and so forth. You may notice that we do not complete physics before beginning chemistry in our course. We begin chemistry after only a few topics in physics.

1. Kinematics
   Newton's Laws
   Work & Energy
   Electricity

2. Atomic Theory
   Periodic Trends
   Chemical Bonding
   Organic Structure & Stereochemistry
   Intermolecular Force

3. Temperature & Heat Flow
   The Ideal Gas
   1st Law of Thermodynamics
   Stoichiometry
   Thermochemistry

4. 2nd Law of Thermodynamics
   Chemical Thermodynamics
   Solutions
   Acids & Bases

5. Fluid Mechanics
   Harmonic Motion
   Waves

6. Substitution vs. Elimination
   Aldehydes & Ketones
   Alcohols
   Carboxylic Acid Derivatives

7. Amino Acids & Protein Structure
   Protein Laboratory
   Coordination Chemistry
   Hemoglobin

8. Chemical Kinetics
   Enzyme Activity
   Enzyme Kinetics

Why is electricity being covered in the first module? Electric charge, electrostatic force and voltage are not ideas typically covered until the second semester of physics. As far as we know, we're unique in beginning our MCAT course with electricity. Instead of looking exclusively at the mechanics of frictionless surfaces, contact forces and free-fall scenarios, we also examine mechanics between capacitor plates or within simple systems of charged particles. We cover the mechanics topics *in themselves* in the traditional way, but we are also priming ourselves for chemistry, which is coming next. Chemistry begins in the very next module, so we are priming it with physics ideas. Mechanics and electrostatics will show us atomic theory and chemical bonding in a rich, common-sense way. Physics is required for chemistry. Let me put it this way. Basic physics ideas, not advanced physics, are *substantively* prerequisite for a good understanding of chemistry.

In modules 3 and 4, we are visiting neighborhoods in physics where the system is an ideal gas in a piston, and we are taking those ideas to neighborhoods in chemistry to understand enthalpy change and Gibbs free energy. In addition to physics and chemistry, the discussion at the start of our course also tracks the interface between physical science and biological science. We are working towards *big ideas* in metabolism from the beginning of this course. It became our mission to help our students understand energy flow in living systems, and this is the overriding theme of the first six modules. When you master a topic *in itself,* you are building *completeness.* When you master a topic *for the rest,* you are building *integrative*

complexity. We look at the mitochondrial membrane to understand the electric field or 1,3-bisphosphoglycerate to understand how a molecule can be like a compressed spring. In module 6, we study the organic chemistry mechanisms *in the context of biochemistry,* and our organic practice items are in the biochemical context as well. These are biochemistry lessons as much as physics, general chemistry, and organic chemistry lessons. The Integrated MCAT Course gives you a step-by-step method to prepare a scientific knowledge-base with integrative complexity already built into it.

The Integrated MCAT Course

There are 20 modules in this MCAT course. Completing the assignments in each module takes a student on average about 25 hours. There are assignments for content review in each module as well as conceptual integration, psychology, and CARS. Many hours were invested in editing the course videos to give the videos a good pace as well as a lively sense of engagement. They were carefully edited to give you the sense you are participating in the one-on-one tutorial sessions yourself.

The Integrated MCAT Course brings MCAT content review into harmony with the nature of the new MCAT. This learning program was created through years of teaching, and it has helped many students. Now it is available in a more accessible format for everyone. Along with an extensive collection of practice items, flashcards, CARS lessons, diagnostic quizzes, and other learning tools, the Integrated MCAT Course provides a complete, spiraling review of MCAT science topics in video format. The complete course video library is available through $14.95 monthly subscription. All other site resources are open access.

Visit the Integrated MCAT Course!