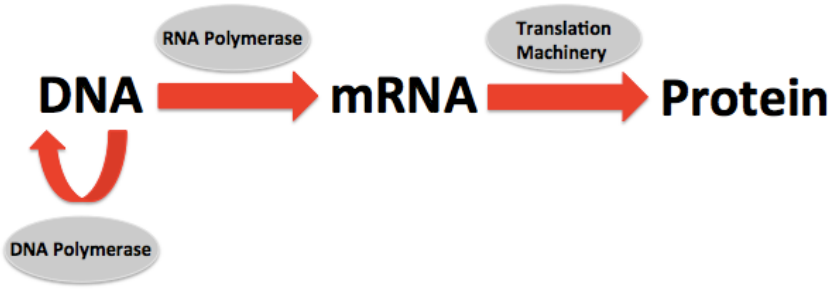
Viral Enzymes got you down?
Did the Baltimore system leave you hanging??

Welcome to Ashlee's almost stupidly simple guide to understanding what the heck kind of enzymes are needed for each virus's replication cycle!!!

First of all, we need a little re-cap on an important cell biology concept: "*The Central Dogma".* If you weren't asleep or daydreaming about Johnny Depp in your general cell biology class, you may remember that the "Central Dogma" refers to the one-way, universal flow of genetic information in an uninfected, everyday, garden-variety cell. To put it simply, the flow of genetic information in a cell is a one-way street and looks a little something like this:

DNA is used to make mRNA, which is used to make Protein. When it comes to the flow of genetic information, cells are a one-hit wonder. Cells can't make protein straight from DNA, and can't back-track with RNA to make DNA. They also can't make RNA from RNA; the only thing they can replicate is DNA. Both prokaryotic and eukaryotic cells are only capable of performing this one-way process and DNA replication, which is sufficient for their cellular processes. Consequently, since this is all they need to do; cells only contain enzymes that allow them to perform the central dogma and replicate DNA (shown below). (lets pretend the gray blobs = enzymes)



Take a good long look at the above diagram and try to imbed it into your retina…. Now, whenever we talk about a virus attempting to carry out it's replication cycle in a host cell, if it cannot go with the flow of the central dogma to eventually make viral protein using ONLY those three enzyme complexes, it MUST provide it's own enzyme, or it cannot get the job done… Analogous to bringing your own beverage in a restaurant without a liquor license (BYOB); the virus **MUST** bring it's own enzyme, or the party can't get started…and by "party", I mean infectious cycle.

This brings us to….

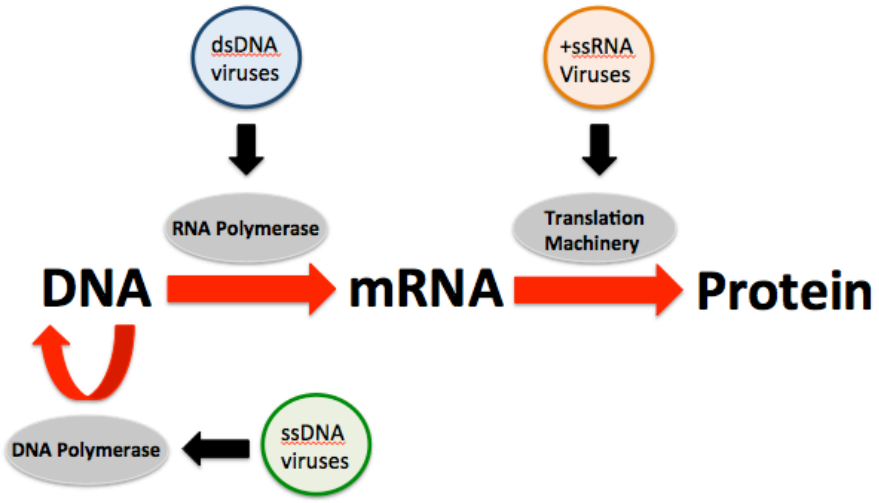
BYOE Viruses

Bring **Y**our **O**wn **E**nzyme viruses, are viruses that MUST bring their own enzymes when infecting a cell because no cell contains the [uniquely viral] enzymes necessary to deal with their genome. These viruses have replication cycles that do not fall in line with the Central Dogma, so they must come packing their own enzyme if they want the magic to happen.

NOT BYOE	BYOE Viruses		
	Must Provide -->	**RdRp**	**RT**
dsDNA	ss-RNA	yes	no
ssDNA	dsRNA	yes	no
ss + RNA	gapped dsDNA	no	yes
	ss+RNA w/dsDNA intermediate	no	yes

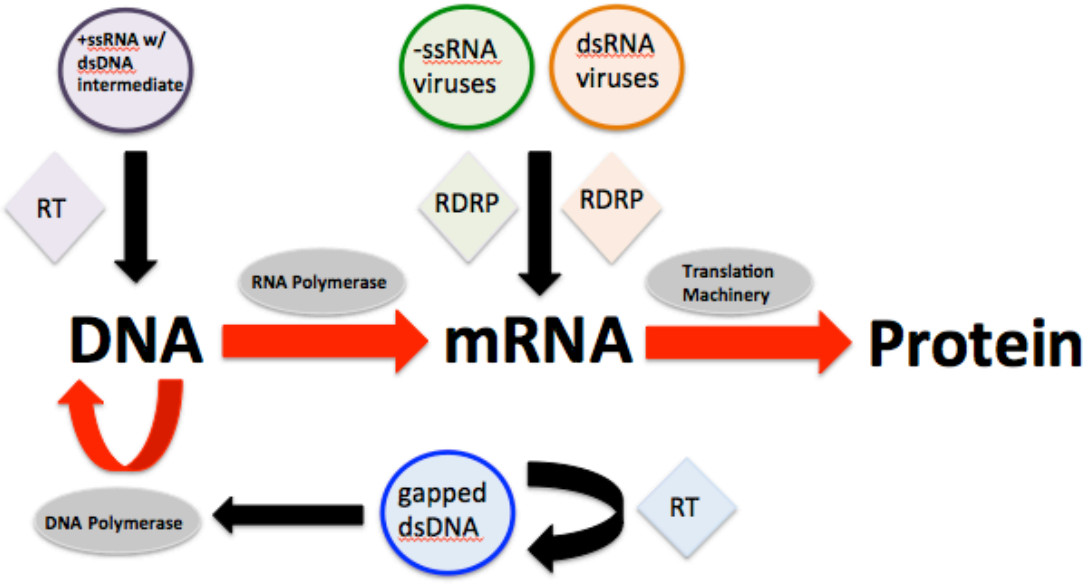
Now, at this point in time you have two options:
1) You could just push your internal "I Believe" button and memorize the above chart, or …
2) You could keep reading and convince yourself that I didn't just pull this chart out of my butt…

Let's start with the Non-BYOE viruses… The key to their non-BYOE status is their ability to fall in line with some part of the central dogma process as soon as they get in a host cell. More specifically, as soon as their genome is uncoated from the viral capsid, it can be recognized and processed by enzymes that the cell naturally has and uses to carry out the central dogma process of gene expression. Check out the diagram below: (lets pretend the colored circles = virus)



The arrow next to each virus type is pointing to the cellular enzyme machinery that can recognize that virus genome type and get the infectious cycle started. dsDNA viruses are recognized by the host cell RNA polymerase, just like the cell's own dsDNA. ssDNA viruses can be recognized by the host cell's DNA polyermase which will first make a double stranded version of the genome before the RNA polymerase takes over. +ssRNA viruses resemble mRNA, so they can be recognized by the translation machinery which use it to make viral proteins right away, including the RNA-dependent RNA-polymerase (RDRP) needed to synthesize more +ssRNA virus genomes.

So what about our BYOE viruses? All of the BYOE viruses share the common characteristic that they cannot simply jump on the central dogma train on its one-way track to protein town. None of the three main enzyme complexes above are able to process the viral genome, because the viral genome structure is not anything seen in a typical cell. (pretend the diamond shapes = viral enzymes)



Lets break these down one by one…

+ssRNA w/ dsDNA intermediate (aka the retroviruses)
The cell does not have the capability to make dsDNA from RNA since that's never part of the normal gene expression pathway in cells. Therefore, these viruses must use their own enzyme, Reverse Transcriptase (RT), which is brought with them in the viral capsid, to make dsDNA from +ssRNA. This dsDNA is then integrated into the host cell genome. Once this dsDNA copy of the viral genome is made, viral gene expression can commence following the central dogma pathway using cellular enzymes.

-ssRNA viruses
The host cell has no way of dealing with –ssRNA (cells only work with + sense mRNA), so this RNA must first be made into a complementary +ssRNA version of itself. Furthermore, the host cell has no enzymes capable way of making +ssRNA from –ssRNA, so the virus must provide an enzyme that can do so, and that enzyme is the RNA-dependent RNA polymerase (RDRP). Once RDRP makes +ssRNA that can be translated into protein like mRNA, the -ssRNA virus infectious cycle can get started using the host cell translation machinery.

dsRNA viruses
When it comes to RNA, the cell is a one-trick pony. Cells can only deal with +ssRNA that can act as mRNA. Even though dsRNA contains a strand of +ssRNA, the cell does not have the enzymes that can recognize and unwind the dsRNA +&- strand combo. Consequently, dsRNA viruses must bring along an RDRP enzyme that has the ability to unwind the dsRNA and make more +ssRNA copies that can be used as mRNA for viral protein synthesis.

gapped dsDNA viruses
Gapped dsDNA viruses are a special case. While the cellular central dogma enzymes can use their dsDNA genome for viral gene expression after the gaps are repaired, their zany-looking gapped dsDNA genome requires a RT (Reverse Transcriptase) enzyme to create more genomes for progeny virions (more on that to come in future lectures). Assuming that the RT necessary to make more viral genomes could be synthesized by the cell from the viral mRNA which encodes it; they may not theoretically need a RT brought with them in the viral capsid. However, the capsids of these viruses have been observed, experimentally, to contain a RT attached to the viral genome. While current research has produced divergent results as to the necessity of this RT in the viral capsid upon infection, for this course, you just need to know that a RT is needed and brought with the virus in the capsid.

Ok, so hopefully this little guide has made your life (or at least your studying) a bit easier and made you less likely to pull out your hair or punch a teddy bear in frustration. Just remember the seven viral genome types and how they can (or cannot) interact with the three enzyme complexes that follow the Central Dogma of the cell, what RT & RDRP do, and you should be good to go!