

Clash of the Titans

What Happens When the DNA and RNA Polymerases Collide

Sanjeev Galande

Soon after the discovery of the structure of DNA, it was suggested that the flow of genetic information is unidirectional and that DNA serves as a template for making RNA molecules, which are subsequently used as templates for assembling proteins. This pathway for the flow of genetic information was referred to as the 'central dogma' of molecular biology. Barring a few exceptions where this flow of information is reversed, the central dogma has retained its validity. Its most important feature is that each of these molecules requires a template for its synthesis. Thus, DNA acts as its own template and therefore self replicates, and all RNA molecules are synthesized on DNA templates. Both these processes take advantage of base complementarity; a feature that is central to the structure of DNA and RNA. All proteins are determined by RNA templates by employing a universal code called the genetic code. For survival of a species it is essential that the genetic information is utilised in an accurate manner and therefore nature has evolved distinct machineries for the faithful copying of all these templates into their corresponding products.

The process of copying DNA is called DNA replication, and is carried out by an enzyme called DNA polymerase. The process of copying DNA into RNA is referred to as transcrip-

tion, and is mediated by a multi-subunit enzyme called RNA polymerase. The DNA and RNA polymerases together with a battery of accessory proteins, constitute the respective copying machinery. The fact that both the replication and transcription machineries utilise the same DNA template poses some mechanistic problems for the cell.

During the process of replication and transcription, the polymerases bind to DNA and start assembling the appropriate building blocks while sliding across the template molecule. The diameter of the polymerase enzymes and their accessory proteins is several times larger than that of double-stranded DNA. Since the process of synthesis of new RNA or DNA molecules involves tracking of such gigantic molecular complexes ('titans'), the management of their intracellular traffic is an important issue for the cell. During this sliding act both the polymerases may use the same DNA single strand as a template, a process referred to as co-directional replication and transcription, or, they may use alternate strands and move in opposite directions. In *Escherichia coli* for example, the rate of replication is known to be 10-15 times faster than the rate of transcription. Thus, irrespective of whether the two polymerases move in the same or opposite directions, collisions between them are inevitable.

Bruce Alberts and his research team at the University of California, Berkeley have been studying co-directional collisions and have demonstrated that the replication machinery can overtake the transcribing RNA polymerase



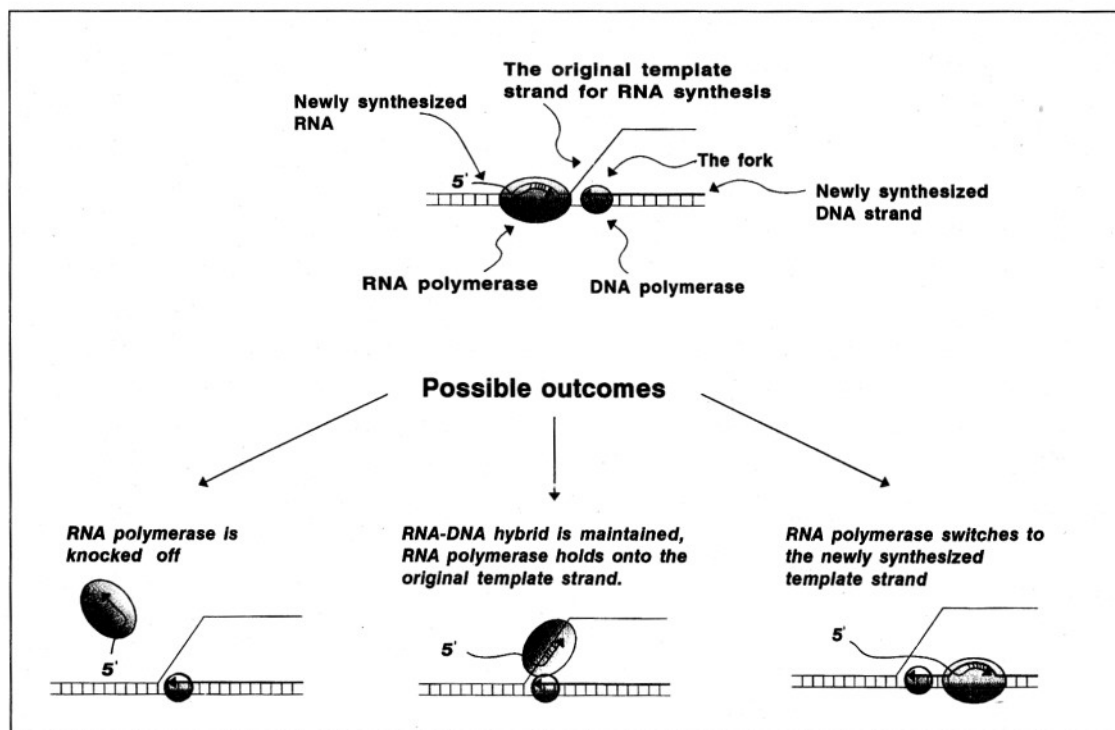


Figure 1 The possible outcomes following a head-on collision between DNA polymerase and RNA polymerase.

studying co-directional collisions and have demonstrated that the replication machinery can overtake the transcribing RNA polymerase without displacing it. They mimicked the situation inside the cell by mixing, in a test tube, purified components of the replication and transcription machinery of the bacteriophage T4, a virus that infects *E.coli*.

In a recent article which appeared in *Science* (Vol. 267, 1131-1137, 1995), Bin Liu and Bruce Alberts examined the consequences of a head-on collision between RNA and DNA polymerases trafficking on the same strand of DNA in opposite orientations (see Figure 1). The authors found that the movement of the

replication machinery is impeded for a long time when DNA helicase, an enzyme that separates the two strands of DNA, is absent. However, addition of DNA helicase (which is a normal component of the replication apparatus of the cell) allowed the replication machinery to bypass the transcription machinery after a brief pause. As a consequence of such a bypass, the transcription machinery switched its template DNA strand and began to utilize the newly synthesized DNA strand. To get a better idea one may imagine a situation where one passenger train is compelled to change over to another track in order to avoid collision with a superfast express train approaching from the opposite direction (some-

spent by the cell. It therefore appears that a head on collision is more expensive for the cell than a co-directional collision.

Hence, the cells appear to have evolved a strategy by which these highly efficient copying machineries have some degree of flexibility in switching template strands. Since a co-directional collision between RNA and DNA polymerases is more energy efficient than a head-on collision, the genetic material of several prokaryotes such as bacteria and viruses is organised in a manner which ensures that most of the frequently transcribed genes are oriented in the direction of the replication fork movement. The clash between the "Titans" being inevitable, cells have to choose the least harmful way to deal with it. The genetic material of eukary-

otes is quite complex and its sheer size makes the understanding of such processes a daunting task. At this moment one can simply hypothesize that since the eukaryotic replication and transcription machineries share common structural organisations with their prokaryotic counterparts, what is good for *E.coli* may also hold good for an elephant!

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Discovery of the Top Quark

Missing Member of the Family Traced

R Ramachandran

All matter in the universe is believed to be made up of quarks (which are subconstituents of protons, neutrons, mesons, etc.) and leptons (such as electrons and neutrinos). The dynamics of these quarks and leptons which lead to electromagnetic, weak radioactive and strong nuclear forces are governed by laws which are a generalized form of Maxwell's laws of electromagnetism.

Most matter exists as molecules and atoms.

Atoms consist of compact nuclei containing protons and neutrons held together by nuclear forces, and negatively charged electrons which are bound electrically to these nuclei. High-energy scattering experiments enable us to see

Our universe consists mostly of the 'up' and 'down' quarks and the electron and electron neutrino.

if protons and neutrons have a substructure. Indeed experiments involving high-energy inelastic scattering of electrons (or muons) reveal that nucleons (protons and neutrons) are bound states of two species of quarks, generally referred

