

The challenge

Imagine a segmented thread dyed in two colours. Your task is to remove the blue parts and to then reconnect the red parts. Use only one hand and hold the thread the whole time. This might sound difficult to do. Something similar happens inside your body.

Nature's equivalent

Instead of a hand there is a complex and very large molecular machinery named the spliceosome. It consists of hundreds of smaller parts, all working together. Instead of a thread it has to reassemble mRNA. This is a working copy of the DNA, the famous double-stranded helix that contains all the information necessary to construct and maintain our body.

This process happens in every cell of your body every second. However, it is more complex. Sometimes there are multiple possible red ends that could be used. Still, it is extremely accurate and a mistake happens seldom.

What if a mistake happens?

Despite control mechanisms to detect mistakes, some slip through. These can be disastrous. Use the wrong red end and an important part might be missing, leading to various malfunctions. It is closely connected to cancer and also plays a role in multiple diseases like spinal muscle atrophy, myotonic dystrophy or tauopathies.

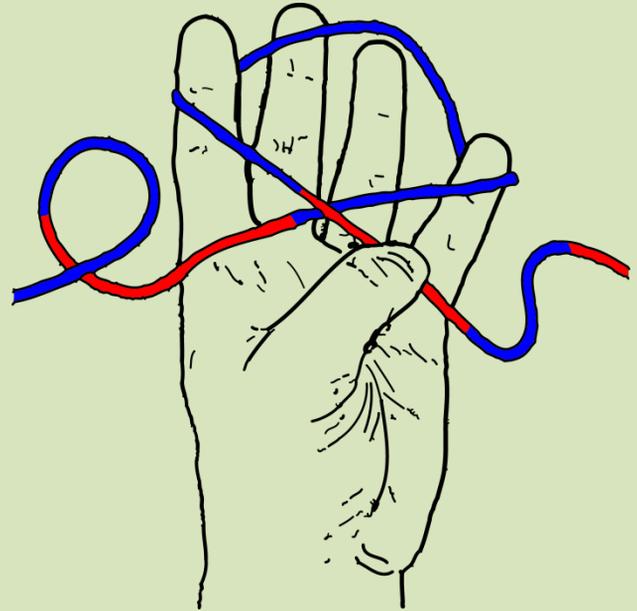
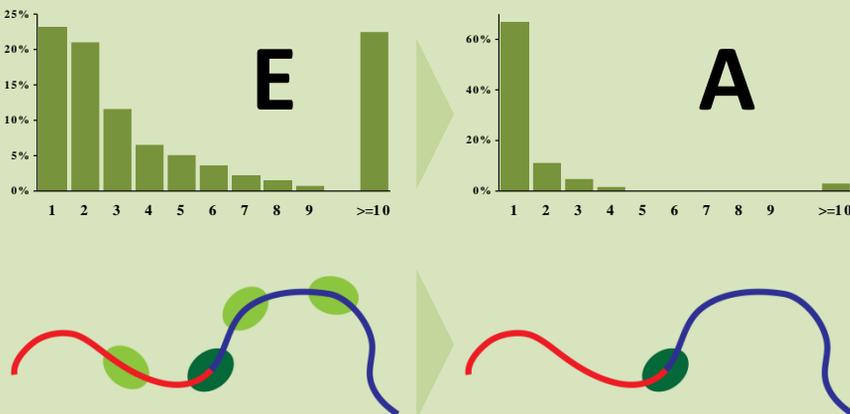


Figure 1. The blue parts have to be removed while not losing the red ones.

My research

I investigate how one protein, a large biological molecule named SRSF1, helps this machinery to find the correct end of the red parts, the splice site. This crucial step happens in the early stages. Here, two successive complexes form, named complex E and A. I used a microscope that collects light emitted from a modified version of this protein and counted how many of these proteins are bound to the mRNA in these complexes.



My results

There is a clear difference in the number of bound proteins. The first complex can have multiple proteins bound to the mRNA, sometimes even more than ten. The complex that forms next has notably less bound proteins, mostly only a single protein remains.

Explanation

Initially, multiple proteins bind to the RNA at different positions. Each indicates a possible place that could be a red end. All are removed and only the most stable one remains. This marks the correct position where the red end can be found.

Outlook

The correct processing of the RNA is a vital step and is not sufficiently understood. The selection of the splice sites is the first and a crucial part of it. Understanding the interactions that govern it is the first step towards a fuller understanding. This will lead to a better control over the involved processes and enable us to alter them in cases where the correct functioning is not given.