TopoICE-R Example.

We will model Xer recombination. Our analysis follows from Colloms SD, Bath J, Sherratt DJ. *Topological selectivity in Xer site-specific recombination.* Cell. 1997 88(6):855-64.

Xer recombinase acting on supercoiled unknotted DNA produces the four crossing right-handed torus link.

Hence the substrate is unknotted circular DNA = N(1/1) = 

Use either load zoo or rollers to enter this as the first knot, N(A/B):

The product is the four crossing right-handed torus link = N(4/1) = 

Use either load zoo or rollers to enter this as the second knot N(Z/V):

In many cases protein-complexes bind supercoiled DNA trapping k consecutive supercoils. A protein complex binding k consecutive DNA supercoils can be modeled by the 1/k tangle. Hence we set f1 = 1 and g1 = k for some choice of k. We will choose g1 = k = -3, i.e. we assume Xer traps 3 negative supercoils (as per Colloms et al).

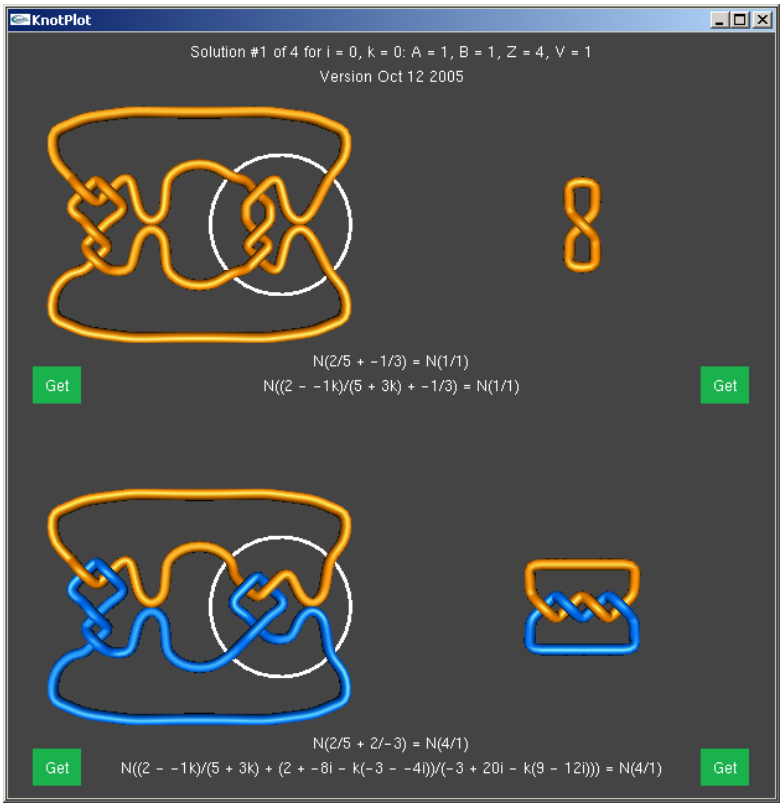
Hence we will assume the initial protein bound DNA configuration can be represented by the tangle

1/-3 = 

Use either load zoo or rollers to choose the initial protein bound DNA configuration:

We can now click on Solve: 

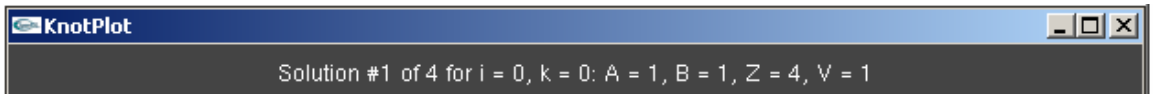
In the KnotPlot window, we see one method of changing the unknot into the four crossing right-handed torus link. The upper two figures show the unknot. On the right, the Xer protein complex is represented by the white circle. Inside this white circle, we see three vertical crossings. This represents the three negative supercoils that we assumed were trapped by Xer. The configuration outside of this circle represents the DNA not bound by Xer. In this case this outside configuration contains four crossings.



The bottom two figures show the right-handed four crossing torus link. The diagram on the left shows the DNA configuration after the protein has acted. In this case, the protein action changes the configuration inside the circle to contain three crossings, but in a different pattern than in the upper diagram. This software finds mathematically possible mechanisms, many of which will not be biologically likely. For this particular example, TopoICE-R finds all possible outside configurations as well as all possible post-recombination protein-bound configurations (represented by the tangle f2/g2) given any pre-recombination protein-bound configuration (represented by the tangle f1/g1). For more information on the types of configurations found by TopoICE-R see the section "For the mathematician" at the end of the TopoICE-R manual.

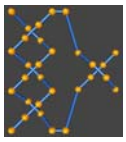
Observe that we assume that the configuration outside the circle is the same as in the top figure. This is always be assumed. We assume the protein complex changes only the DNA configuration inside the protein complex (note this only gives us one snapshot in time and ignores how the sites are brought together, etc.).

This is only one solution within 1 of 4 infinite families of solutions. For this family of solutions we have two variables we can work with i, k (as per the comment on the top of the KnotPlot window).

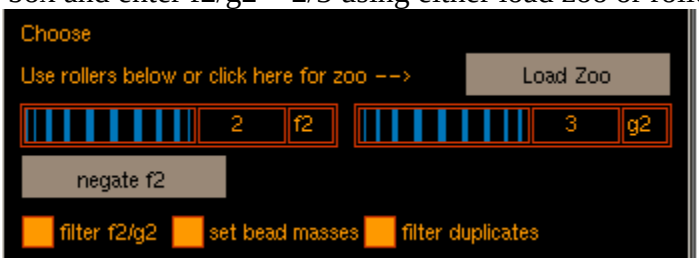


To see more solutions within this family click on "incr i", "decr i", "incr k", "decr k". To see a different family of solutions click on "up", "down".

It can be difficult to find biologically likely mechanisms within these infinite families of solutions. However, one can easily check if a particular mechanism is possible. A common protein mechanism is one in which the protein complex binds k supercoils (modeled by the 1/k tangle) and introduces another crossing. This can be modeled by replacing the 1/k tangle with either the (1+k)/k tangle or (1-k)/k tangle. In this case, k = 1/-3, so we will check if it is possible to replace the 1/-3 tangle with either the 2/3 tangle or the 4/-3 tangle.

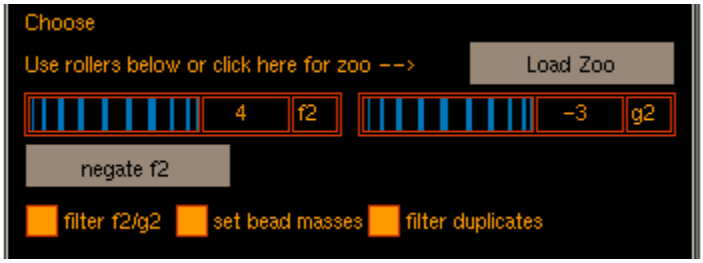
2/3 =  =  , 4/-3 = 

We can use the f2/g2 filter to determine if either of these are possible mechanisms. Click on the filter f2/g2 box and enter f2/g2 = 2/3 using either load zoo or rollers:

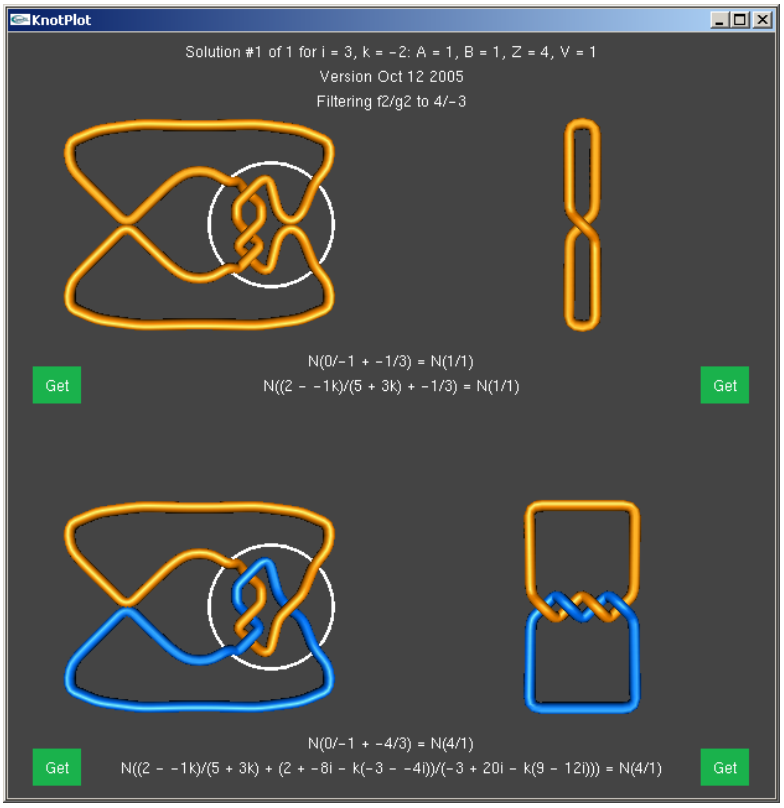


In this case there is no solution and hence the following appears in the KnotPlot Window:

Next we try f2/g2 = 4/-3:

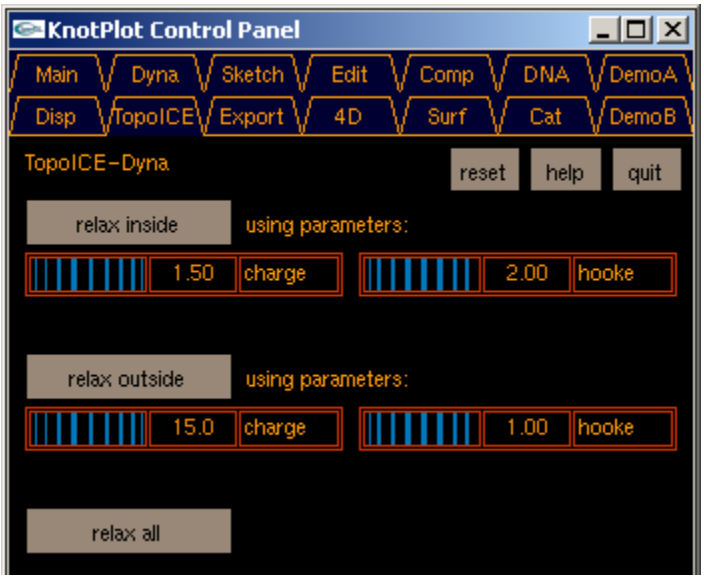


In this case we see that we have a possible mechanism (as per Colloms et al):



To see more 3-dimensional configurations, click on one of the green "Get" buttons to choose the configuration closest to this button.

This will take you to the TopoICE Dynamics control panel:



To relax the inside of the sphere, click on the "relax inside" button: 

To relax outside of the sphere, click on the "relax inside" button: 

To relax all, click on the "relax all" button: 

The following are more 3-dimensional models of pre and post- Xer recombination. Xer is modeled by the sphere.