# Tangle Analysis of Flp Recombination.

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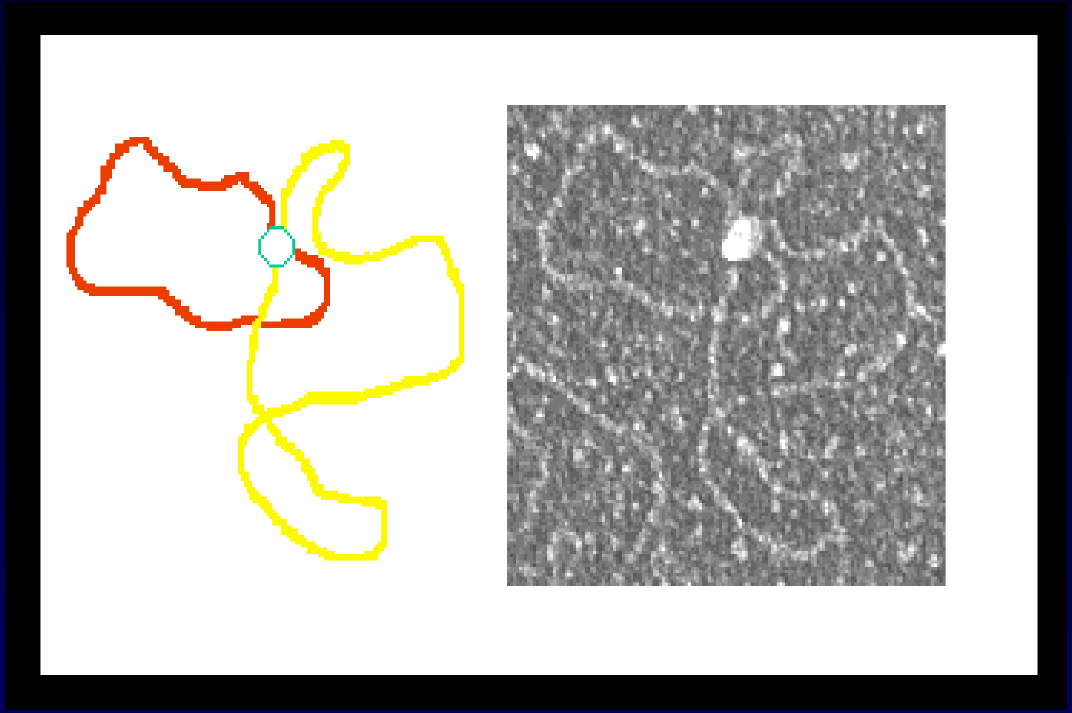
# An electron micrograph of the Flp DNA complex is shown below



Electron micrograph courtesy of Kenneth Huffman and Steve Levene

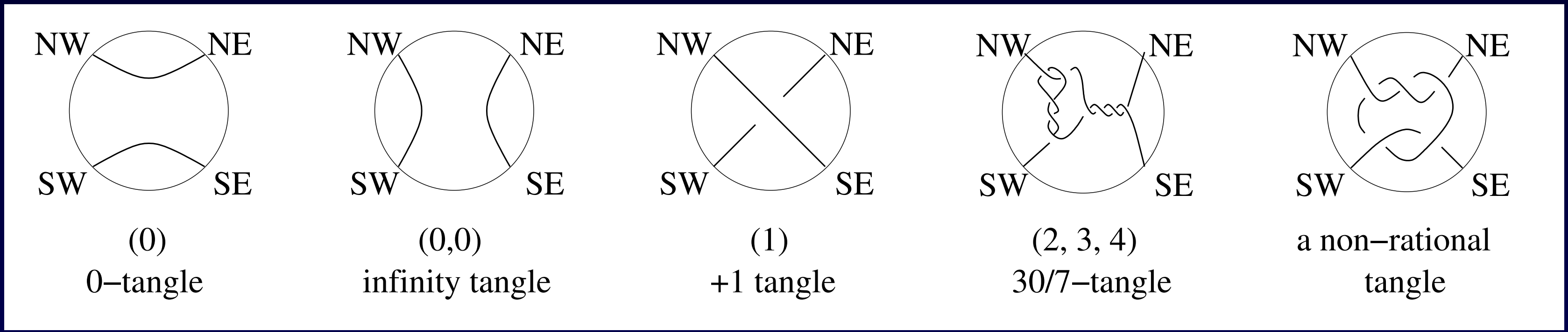
# Goal:

Determine the topology of the DNA segments bound by the protein Flp.

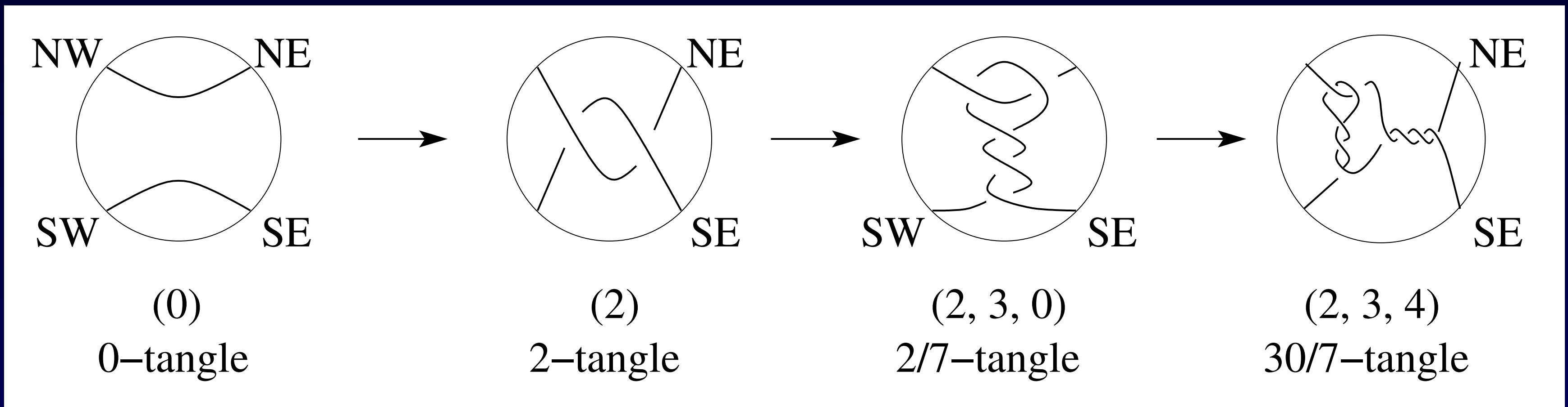
Note: We are studying the shape of the DNA bound by the protein, NOT the shape of the protein. Although we will not look at the protein structure, we can get information regarding the protein mechanism by determining what happens to the DNA it binds.

# Some notation:

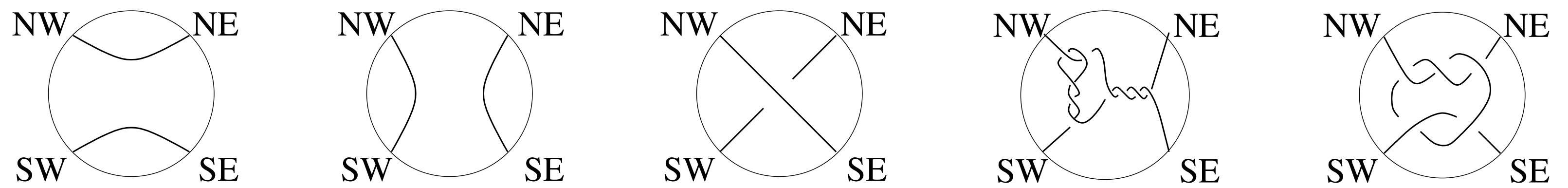
A 2-string tangle is a 3-dimensional ball containing two strings. Some examples:



# A tangle is rational if it is ambient isotopic to the zero tangle allowing the boundary of the 3-ball to move



# Tangle Examples




(0)
0−tangle

(0,0)
infinity tangle

(1)
+1 tangle

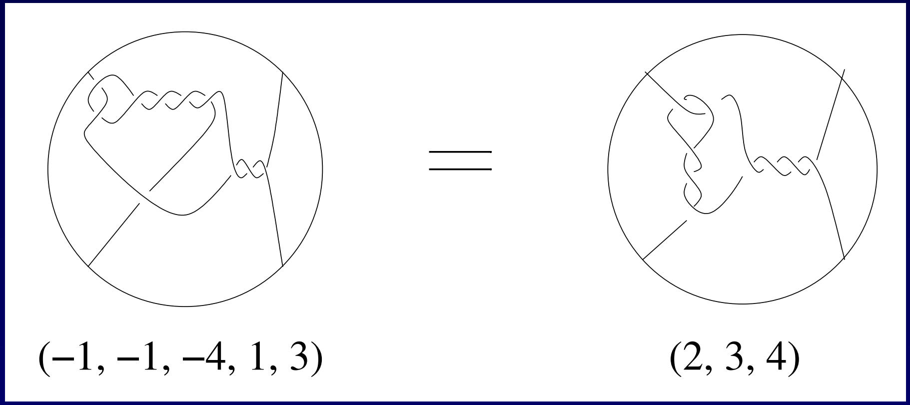
(2, 3, 4)
30/7−tangle

a non−rational
tangle

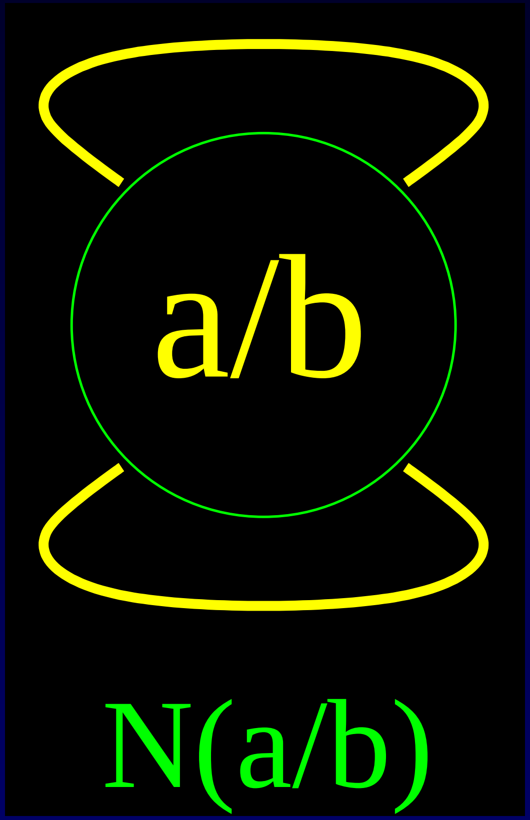
Rational tangles are uniquely identified by their corresponding continued fractions. For example the two tangles drawn below are equivalent since

$$4 + \frac{1}{3 + \frac{1}{2}} = \frac{30}{7} = 3 + \frac{1}{1 + \frac{1}{-4 + \frac{1}{-1 + \frac{1}{-1}}}}$$



Definition: The numerator closure of a rational tangle is a rational knot or link (also called 4-plat or 2-bridge knot/link).



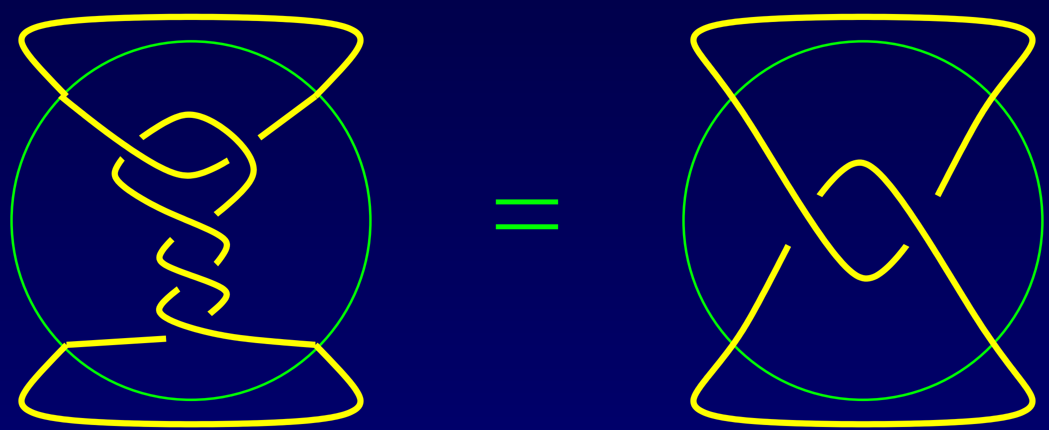
# For example,

$$N((2,3,0)) = N(0 + \frac{1}{3+\frac{1}{2}}) = N(\frac{2}{7})$$

and $N((2)) = N(\frac{2}{1}) = N((2))$

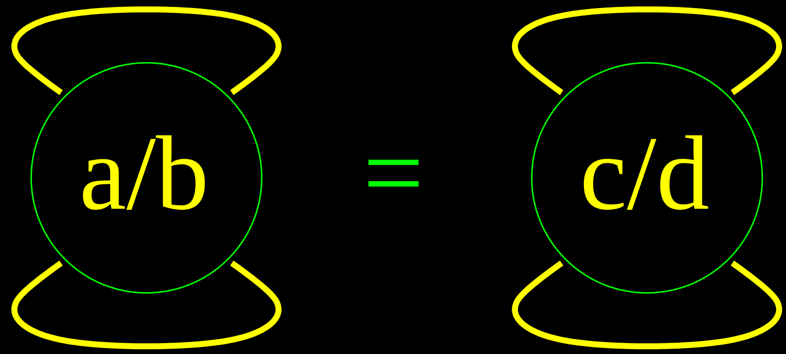
Thus, $N((2,3,0)) = N(\frac{2}{7}) = N(\frac{2}{1}) = N((2))$

since $7 = 1 + 2(3)$



# Rational knot/link equivalence

Take $a, c \geq 0$.




N(a/b) N(c/d)

if and only if

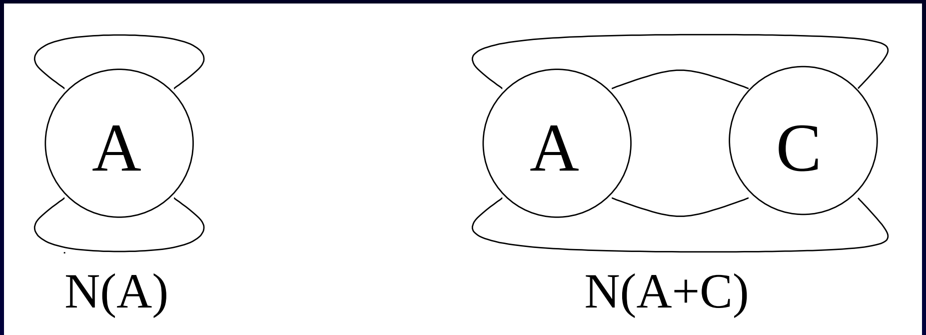
$a = c$

and

$bd^{\pm 1} = 1 \bmod a$

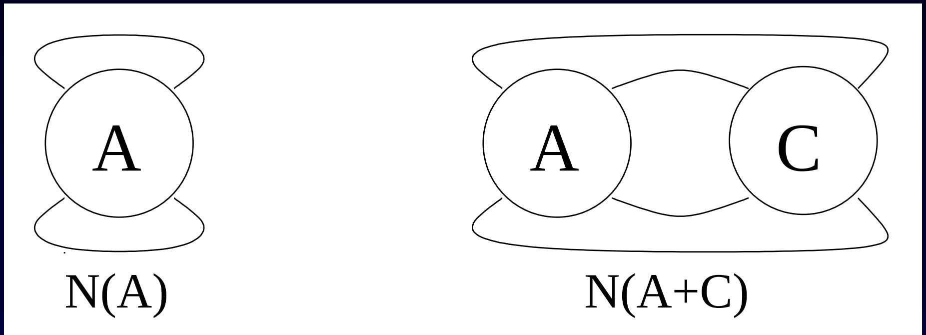
 

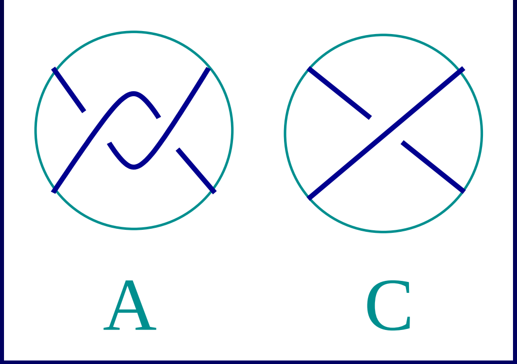
# Knots and links can be formed by taking the numerator closure of a tangle or a sum of tangles



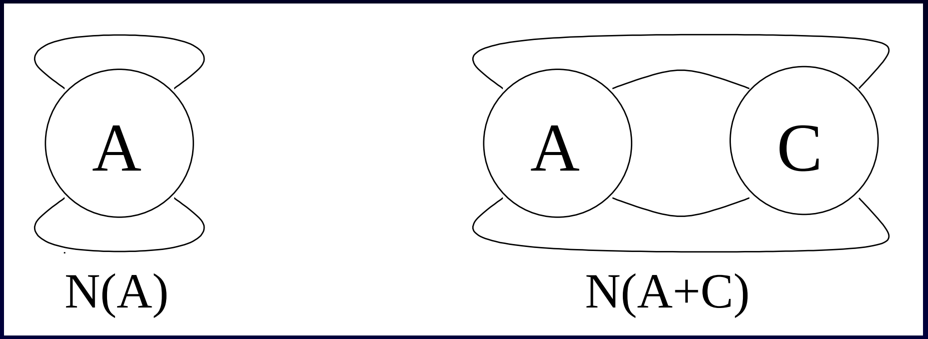
# Knots and links can be formed by taking the numerator closure of a tangle or a sum of tangles

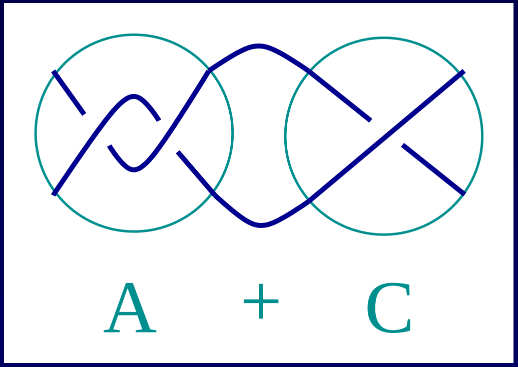


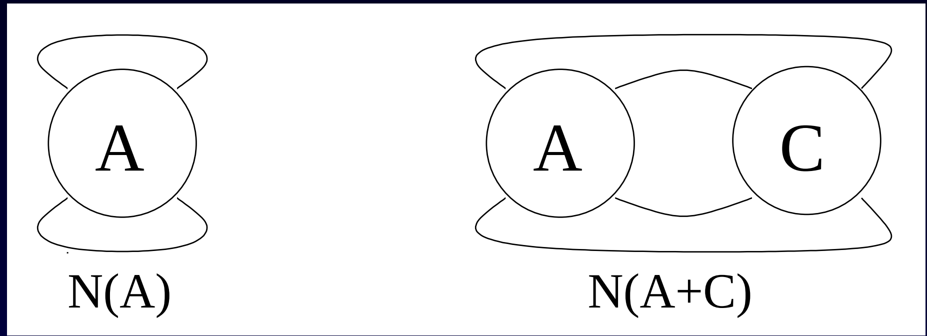

 

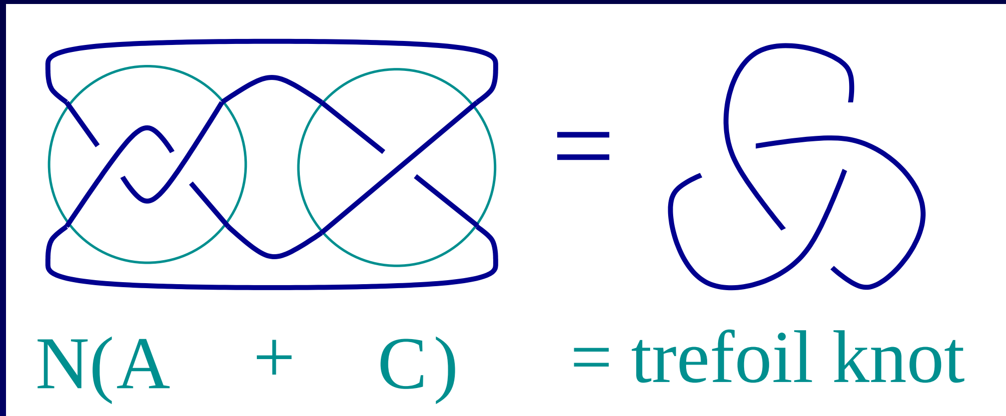
# Knots and links can be formed by taking the numerator closure of a tangle or a sum of tangles



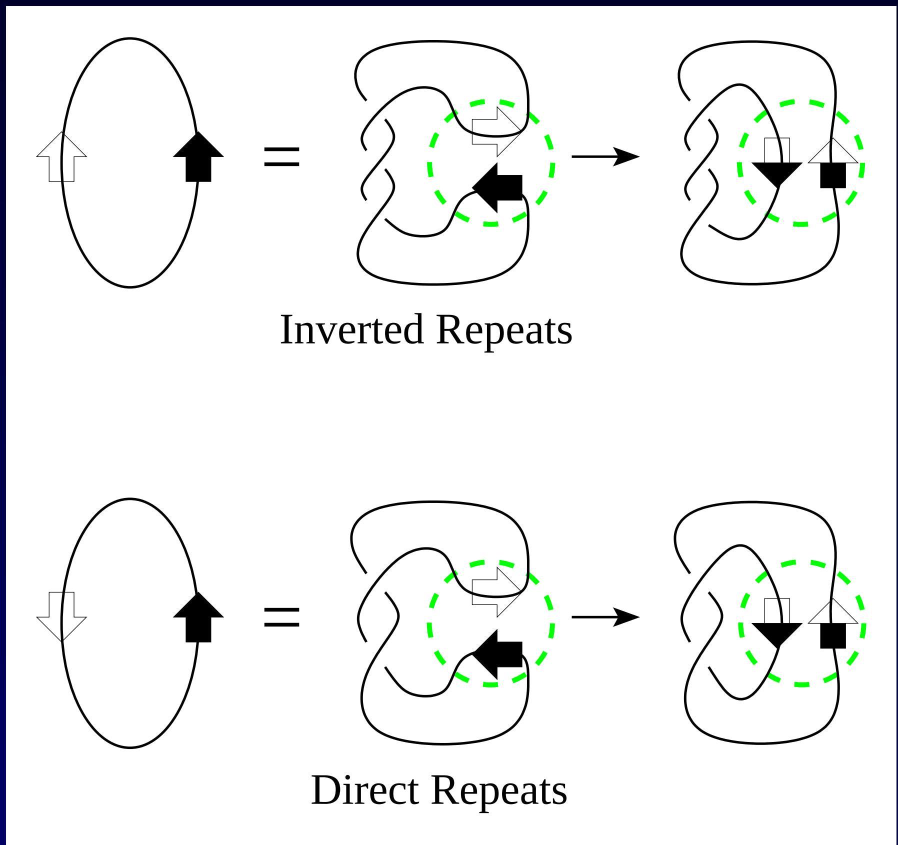
# Knots and links can be formed by taking the numerator closure of a tangle or a sum of tangles



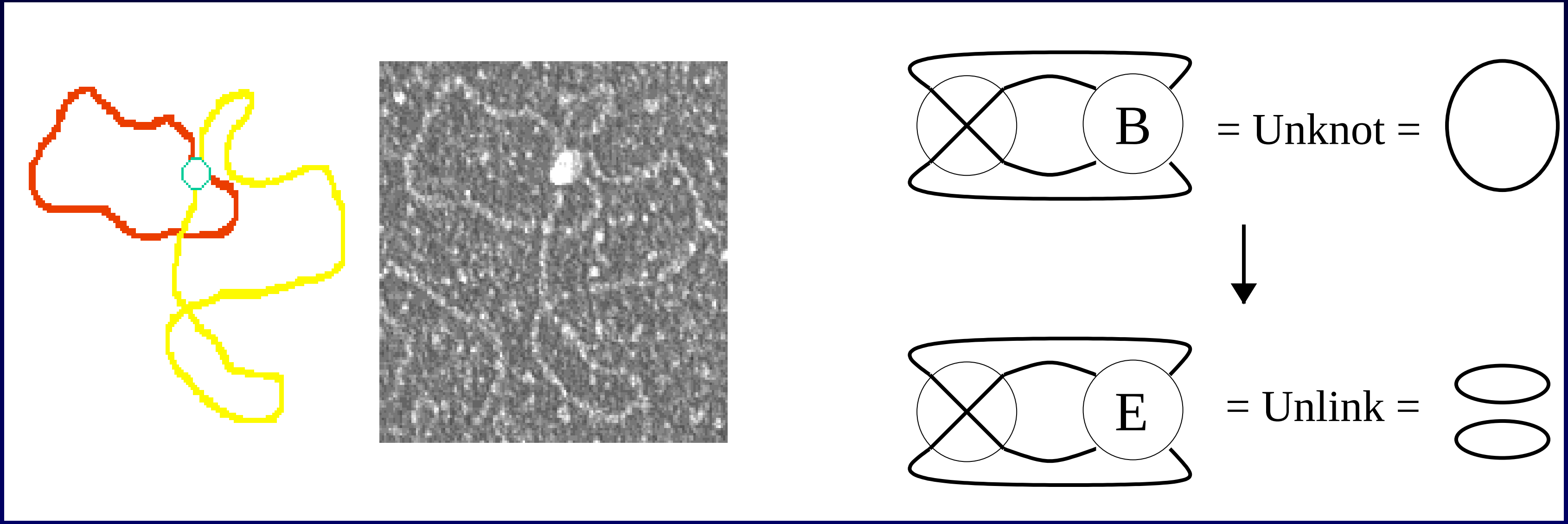

 

# Recombinases are proteins which cut two segments of DNA and interchange the ends resulting in the inversion or the deletion or insertion of a DNA segment



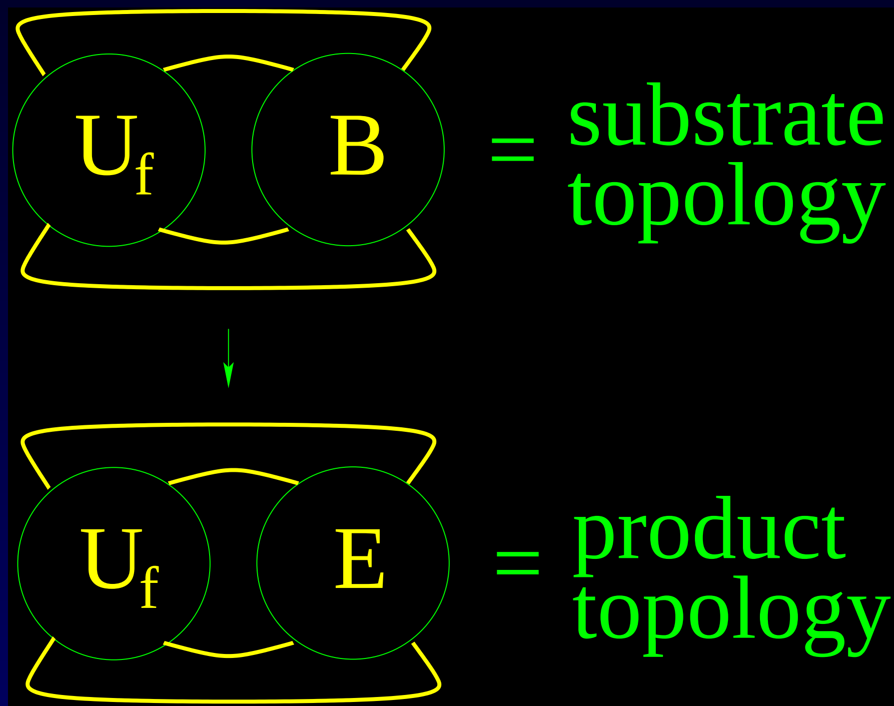
A protein bound to two segments of DNA can be modeled by a tangle. An electron micrograph of the Flp DNA complex and the corresponding tangle equations corresponding to the electron micrograph are shown below:




Electron micrograph courtesy of Kenneth Huffman and Steve Levene

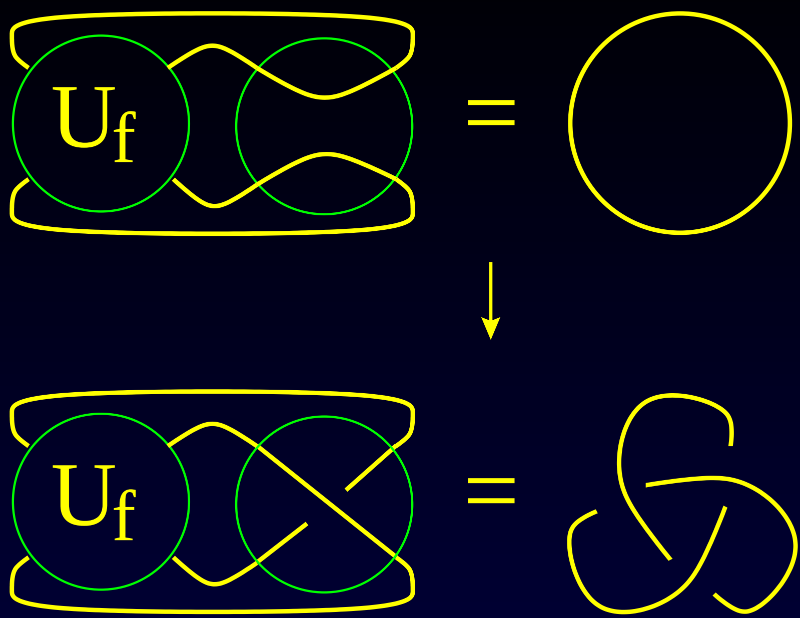
 

# In general, we are solving the tangle equations:

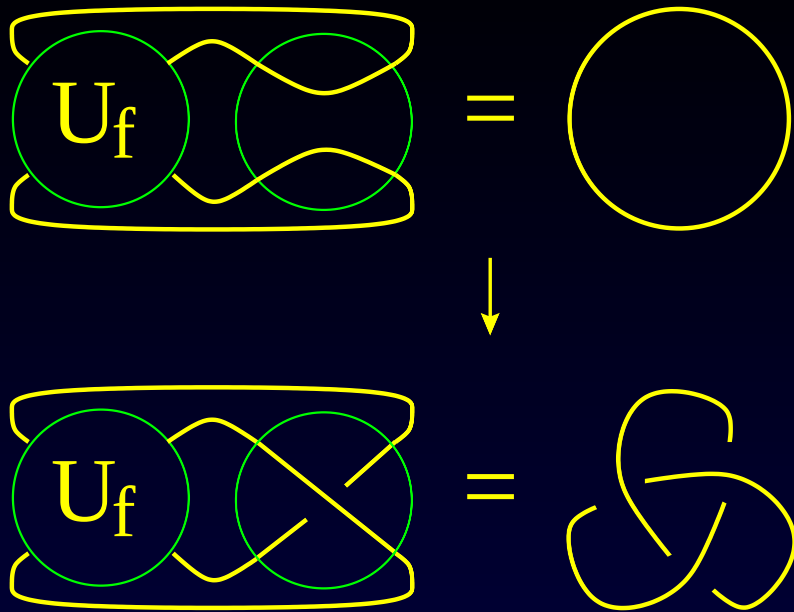


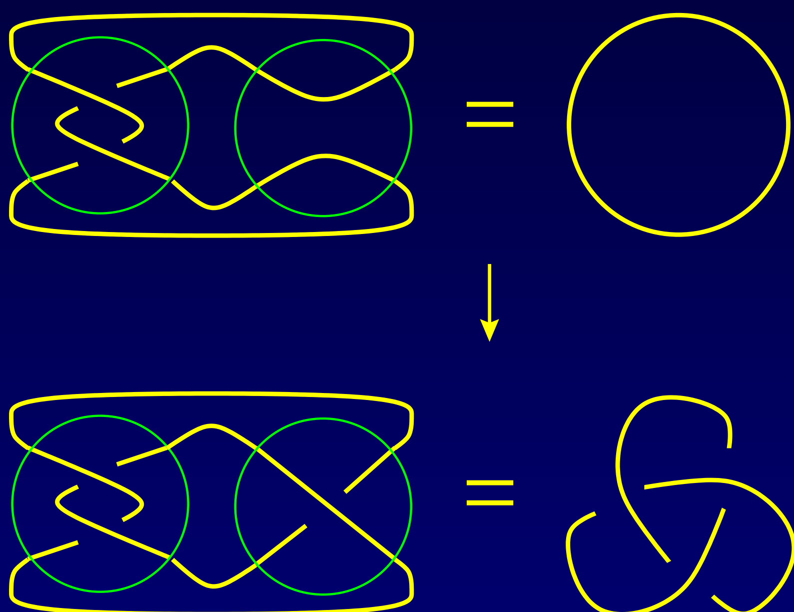
# Solve:



Solve:

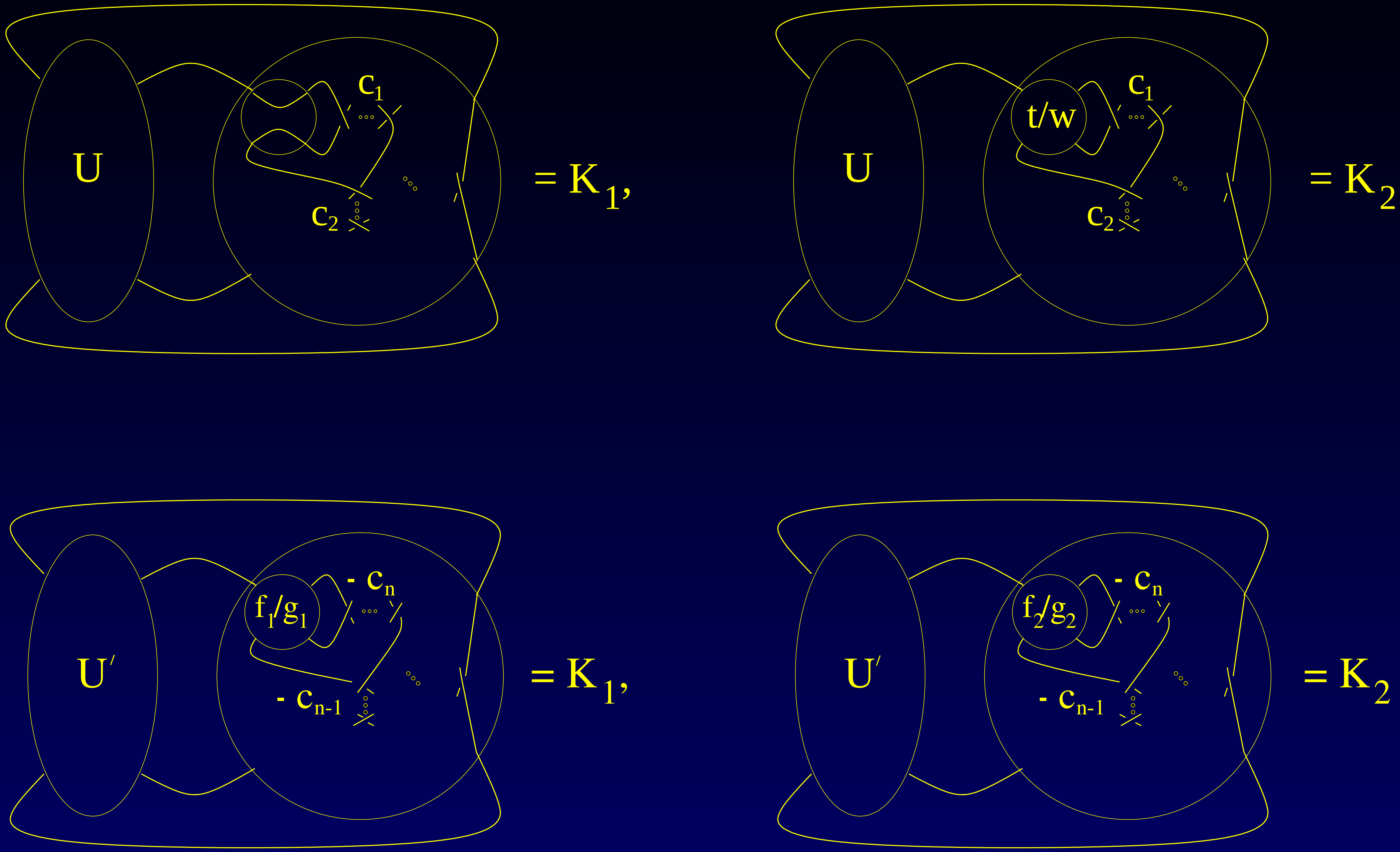



A solution:



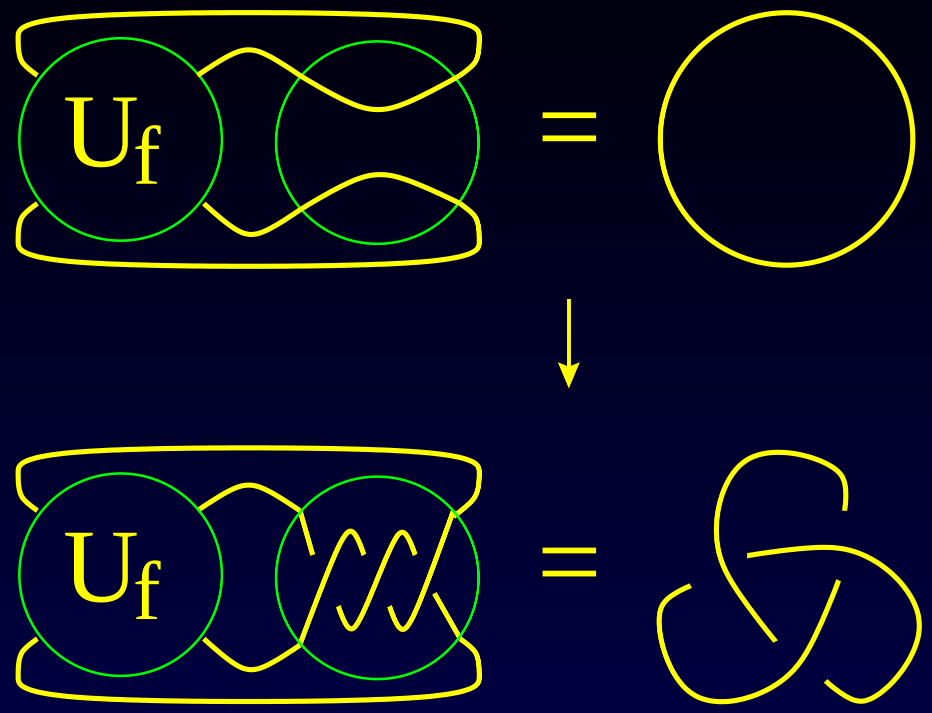

 

# Many moves are "equivalent":

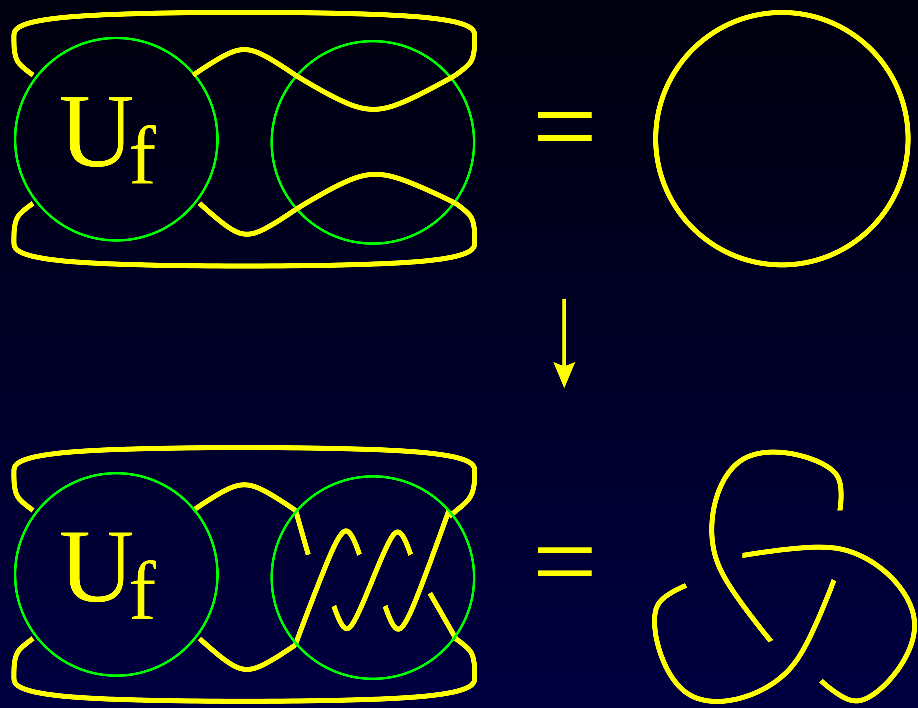


# Solve:

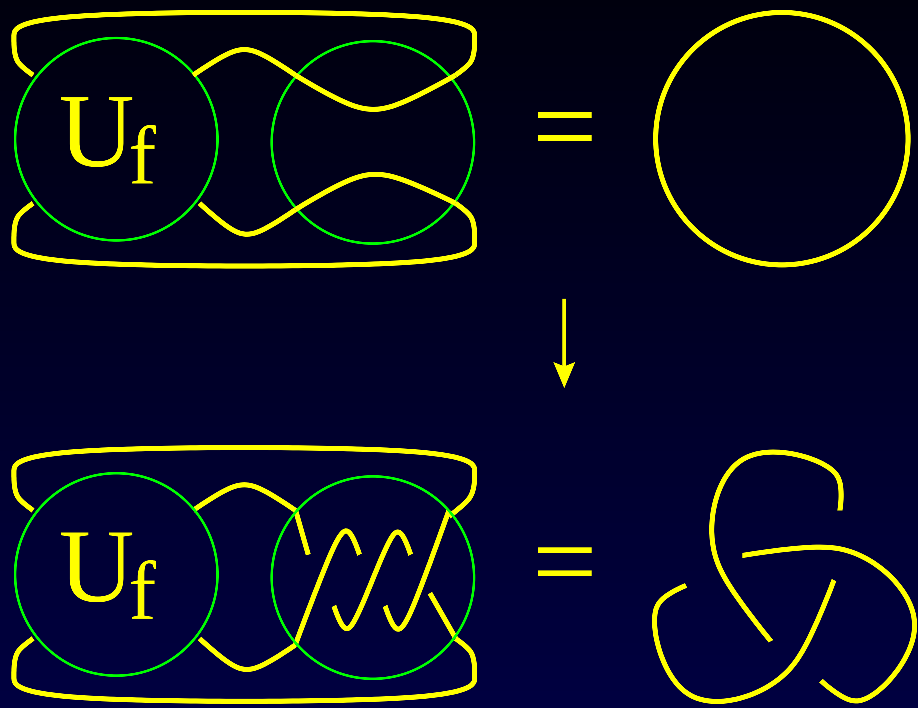


# Solve:




No Solution

# Solve:

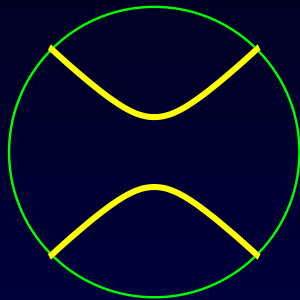
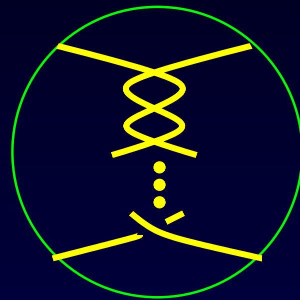



No Solution

Thus, not a possible protein mechanism.

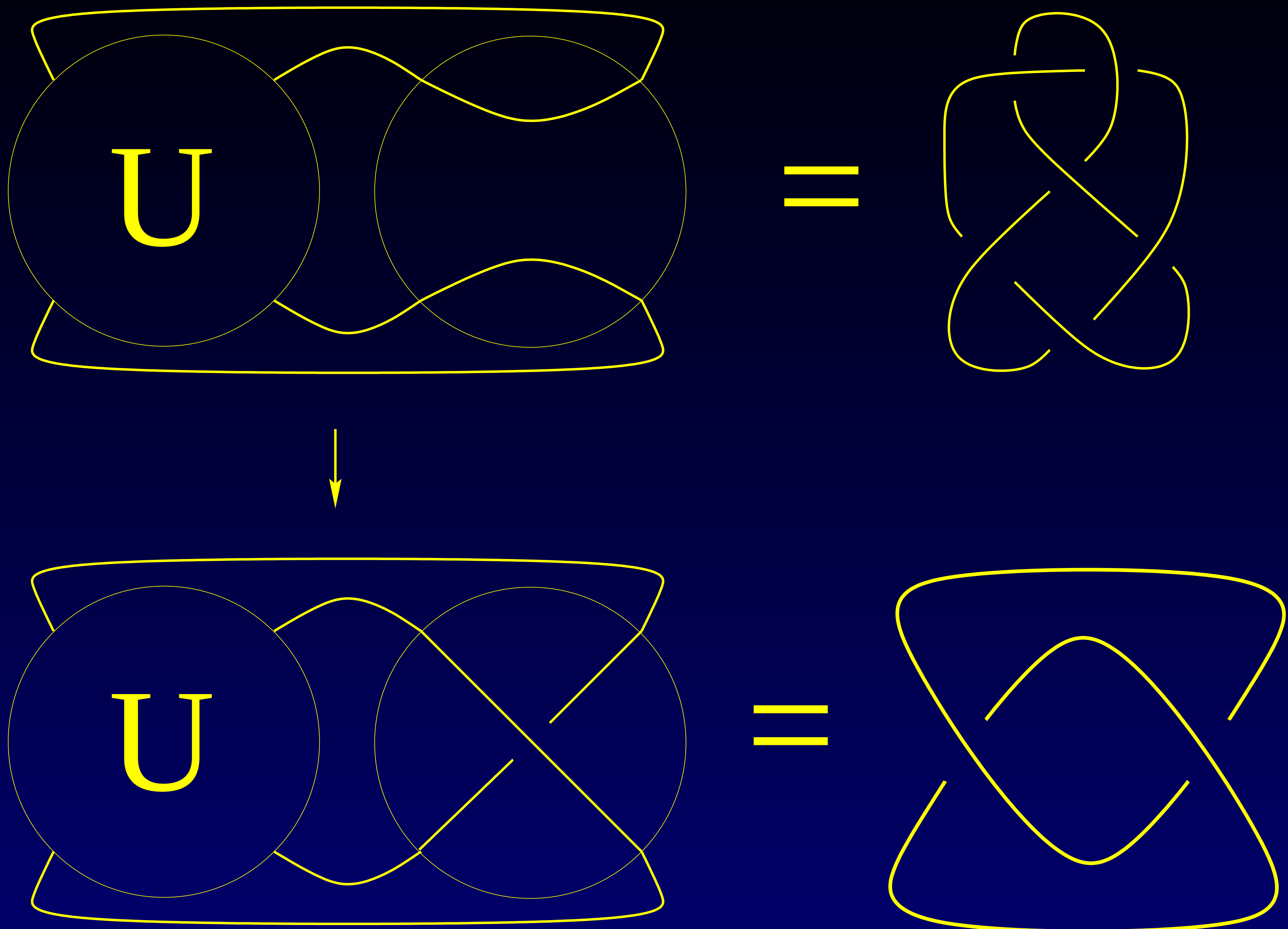
Unfortunately, when

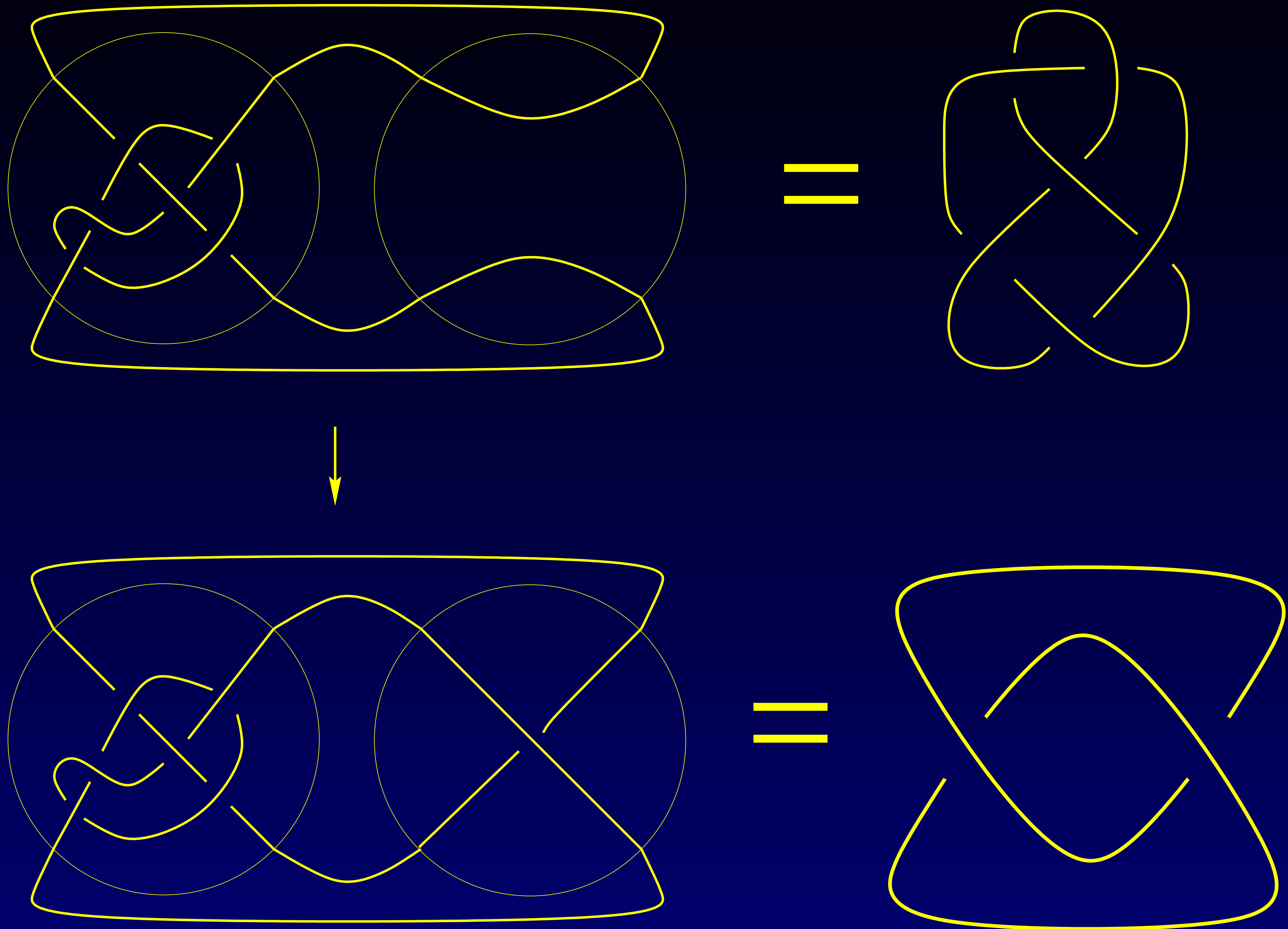
B =  and E = 

not all solutions are found.

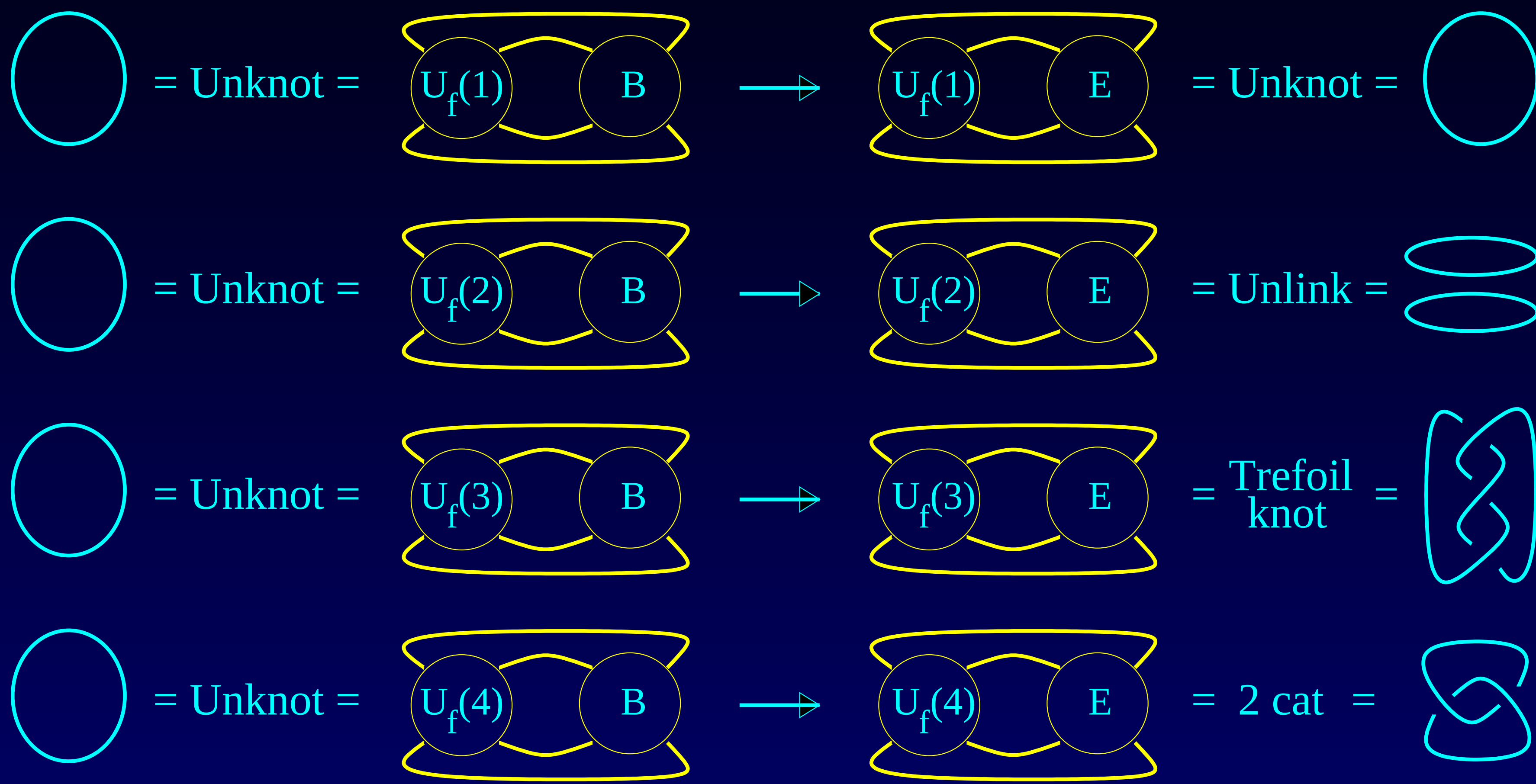
 

# For example,





# Flp recombinase produces a spectrum of knotted and linked products:



input A or 99 to exit
1

input B
0

input Z
0

input V
1

$N(1/(0 + 1k) + 0/1) = N(1/0)$

$N(1/(0 + 1k) + (-1 - 0i)/[0 + 0i - k(-1 - 0i)]) =$
$N(0/1)$

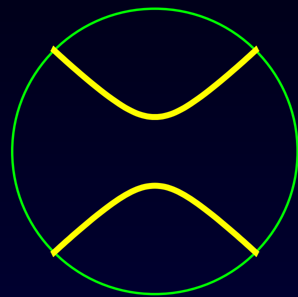
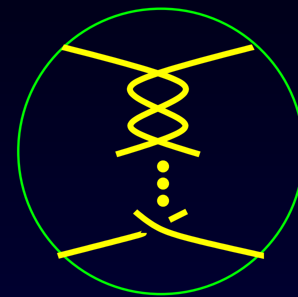
$t = 1, (p,q) = (1, 1)$

$N(1/(1h + -1) + 0/1) = N(1/0)$

$N(1/(1h + -1) + 1/(-1h + 1)) = N(0/1)$

# There are an infinite number of solutions.

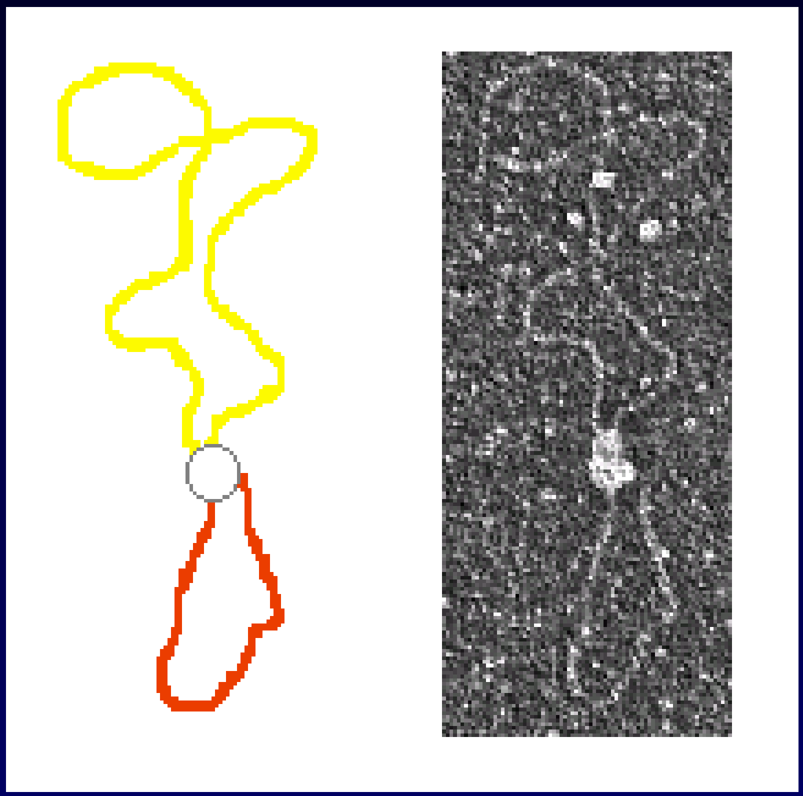
If B = , then E = 

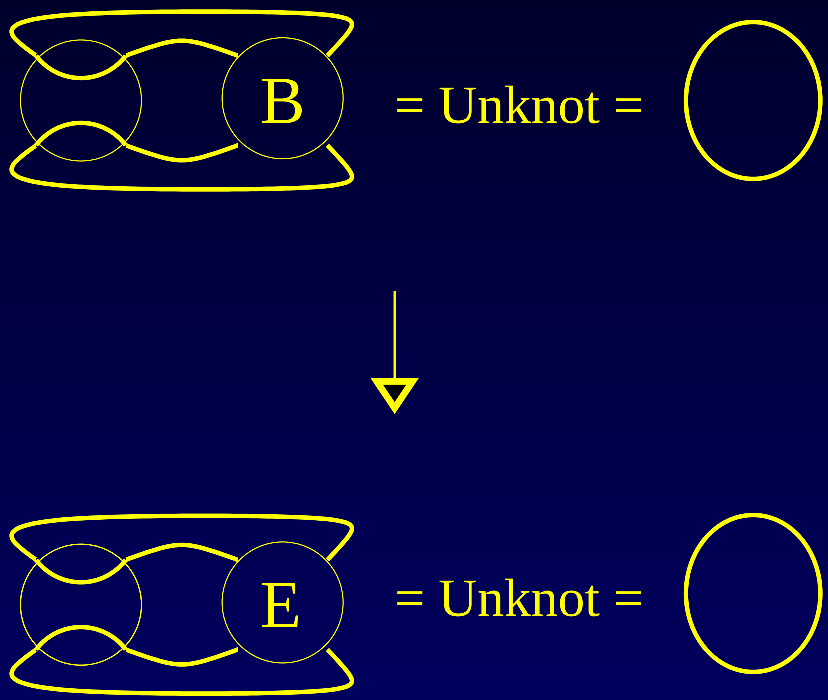
If $B = (c_1, ..., c_n)$,

then $E = (1, n-1, c_1, ..., c_n)$

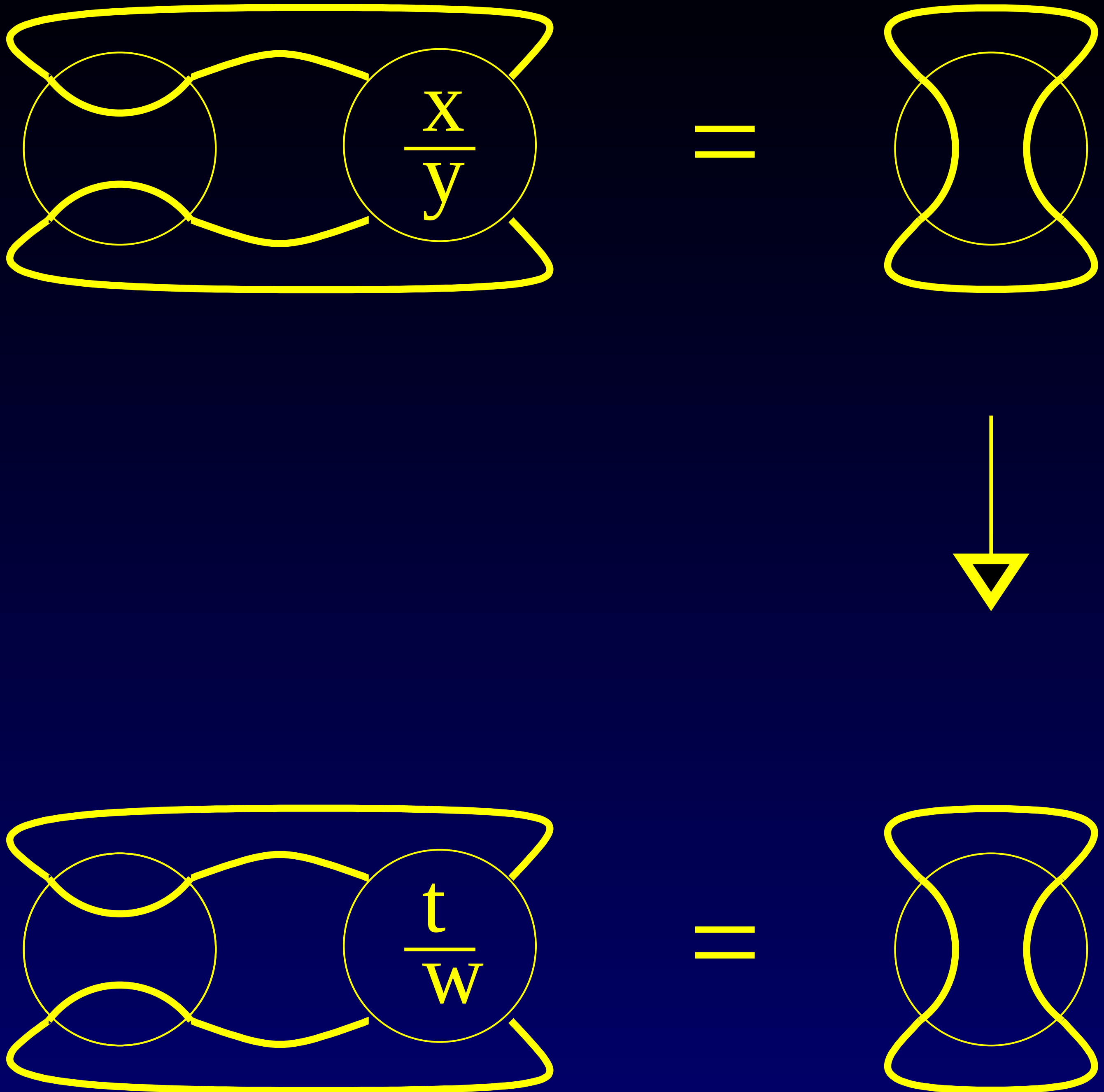
# Electron micrograph of Flp bound to nicked circular DNA containing inverted repeats and corresponding tangle equations

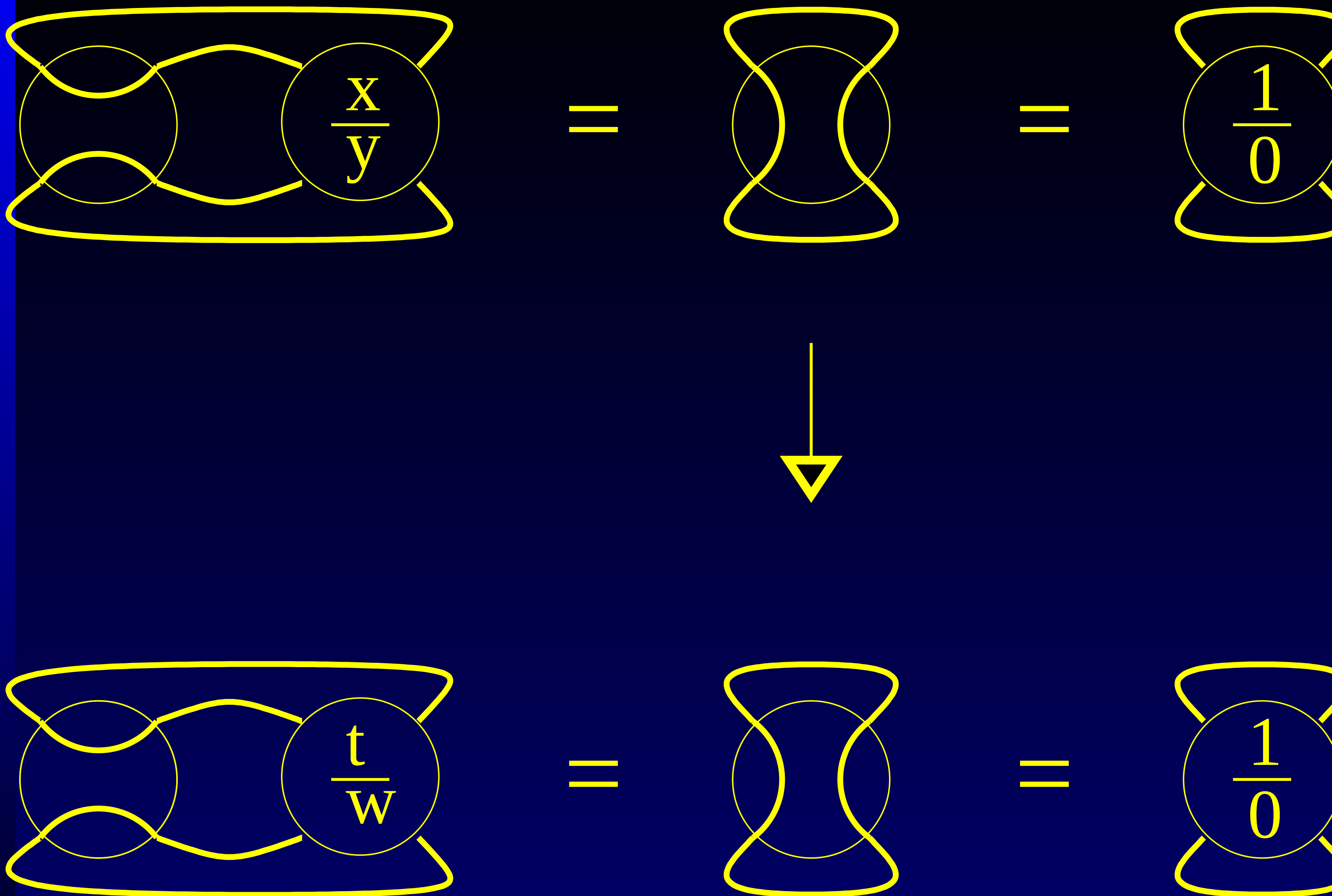





Electron micrograph courtesy of Kenneth Huffman and Steve Levene

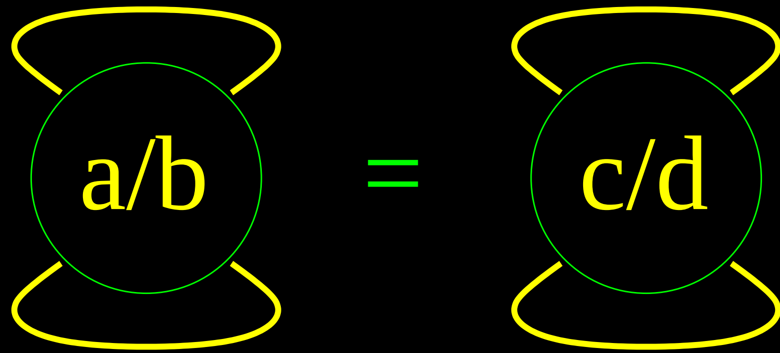
 


x
y
t
w


x/y
=
=
1/0
t/w
=
=
1/0

# Rational knot/link equivalence

Take a, c $\geq$ 0.




N(a/b) N(c/d)

if and only if

$a = c$

and

$bd^{\pm 1} = 1 \mod a$

Thus we are solving

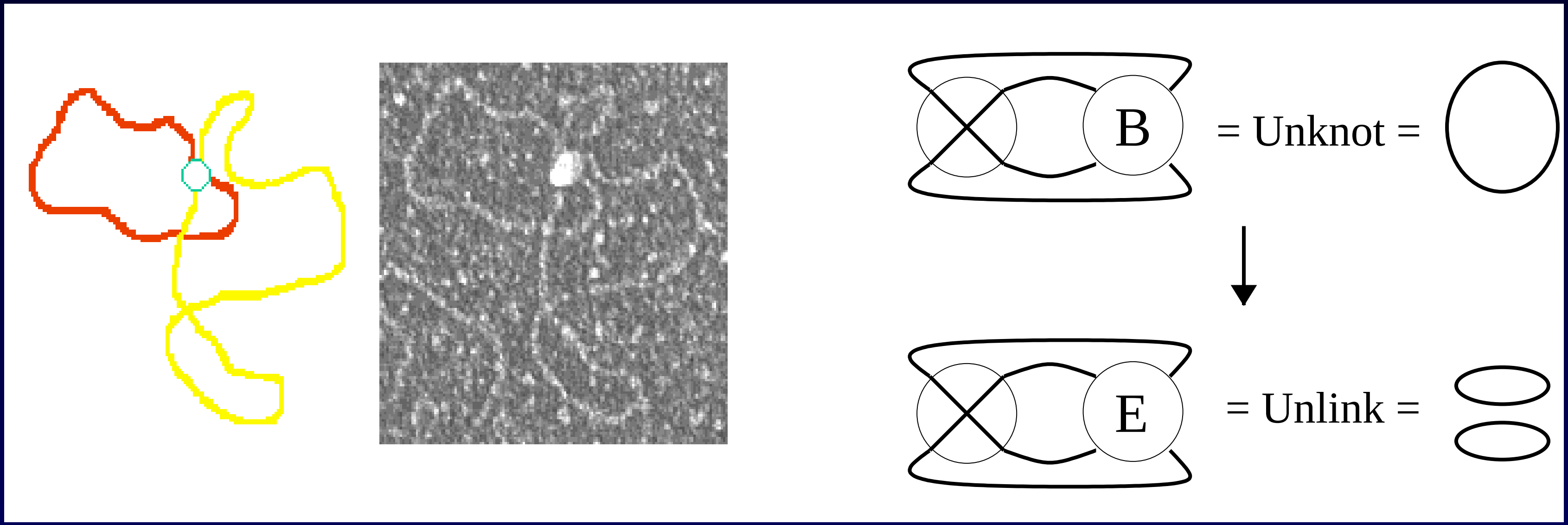
$$N(0 + \frac{x}{y}) = N(\frac{x}{y}) = N(\frac{1}{0})$$

$$N(0 + \frac{t}{w}) = N(\frac{t}{w}) = N(\frac{1}{0})$$

Thus, $x = 1$ and $y = 0 + 1n$. Hence $\frac{x}{y} = \frac{1}{y}$

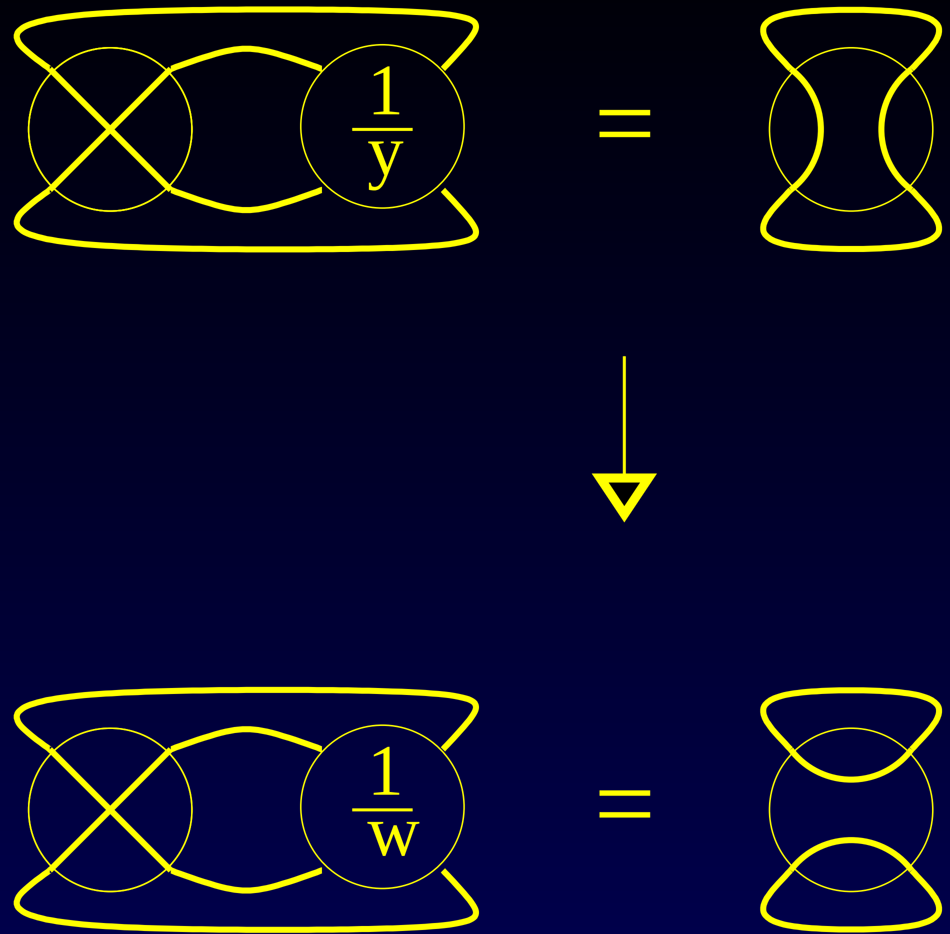
And $t = 1$ and $w = 0 + 1k$. Hence $\frac{t}{w} = \frac{1}{w}$

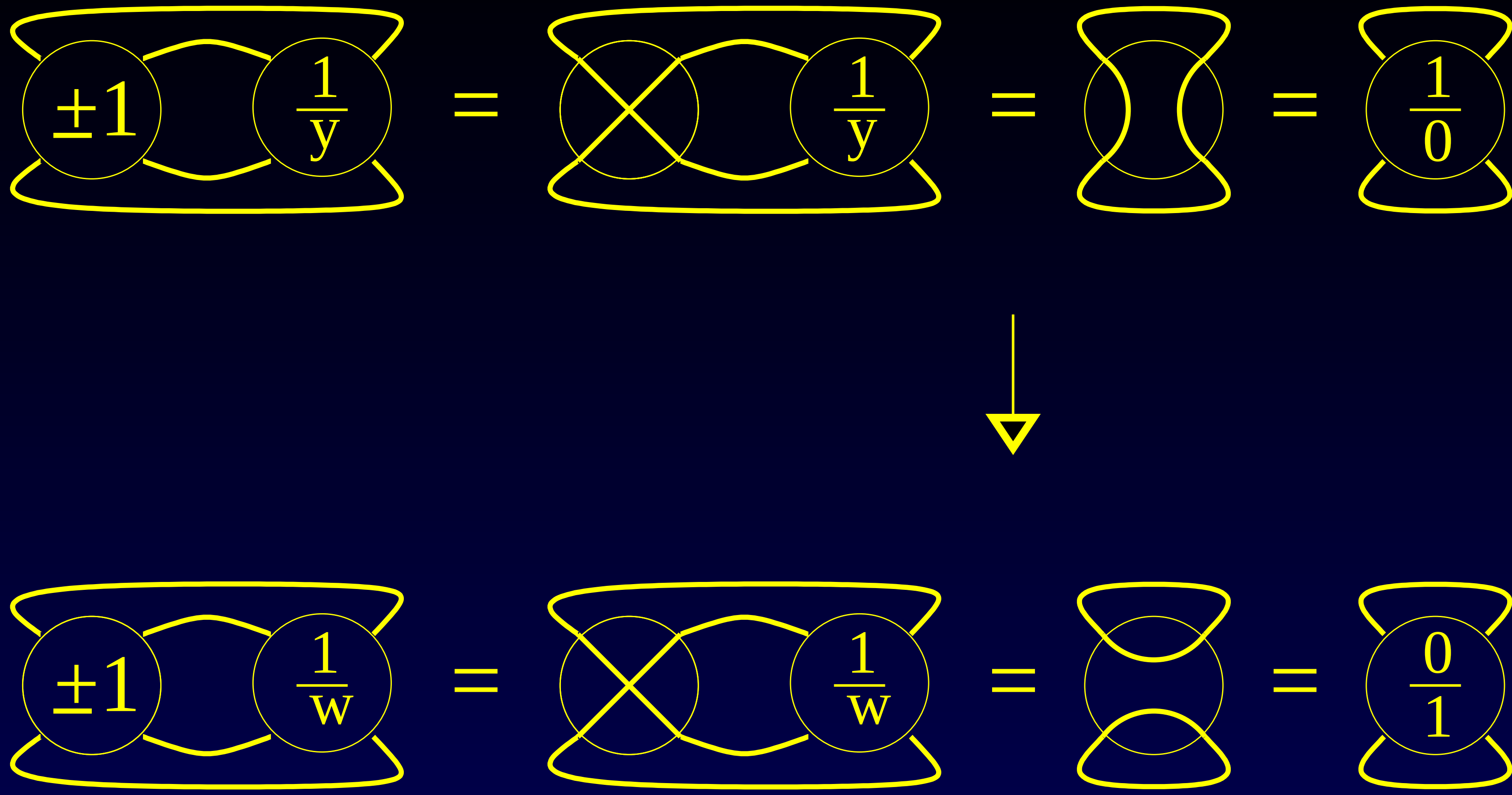
# Electron micrograph of Flp bound to nicked circular DNA containing direct repeats and corresponding tangle equations



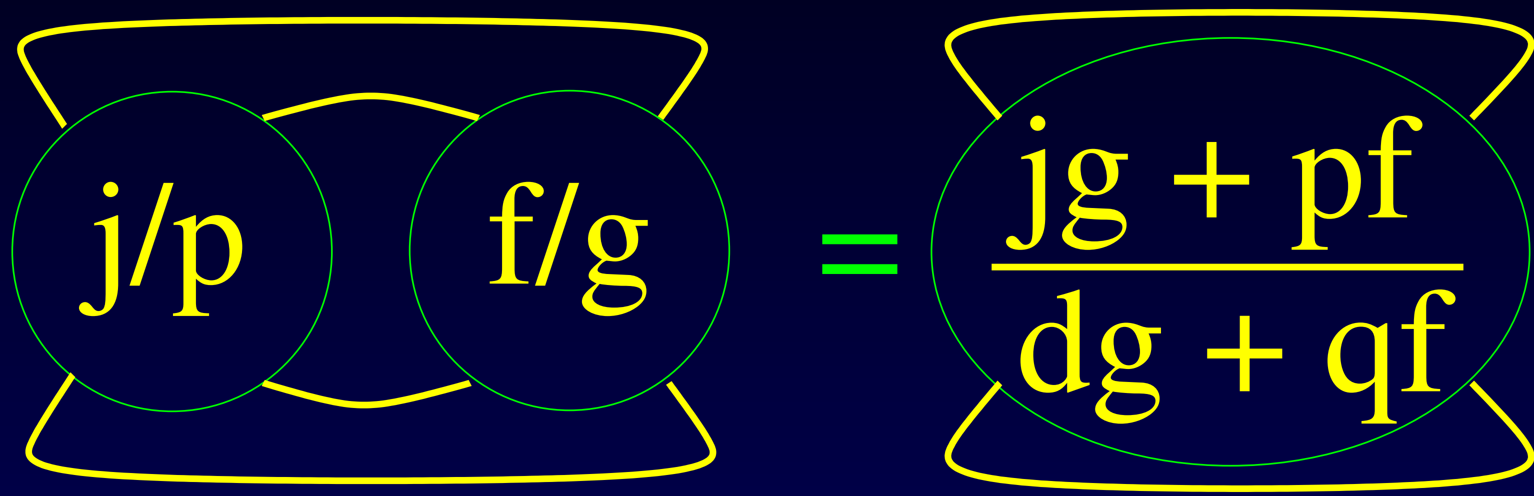

Electron micrograph courtesy of Kenneth Huffman and Steve Levene


1
y
=
1
w
=


±1
$\frac{1}{y}$
=
$\frac{1}{y}$
=
=
$\frac{1}{0}$
±1
$\frac{1}{w}$
=
$\frac{1}{w}$
=
=
$\frac{0}{1}$

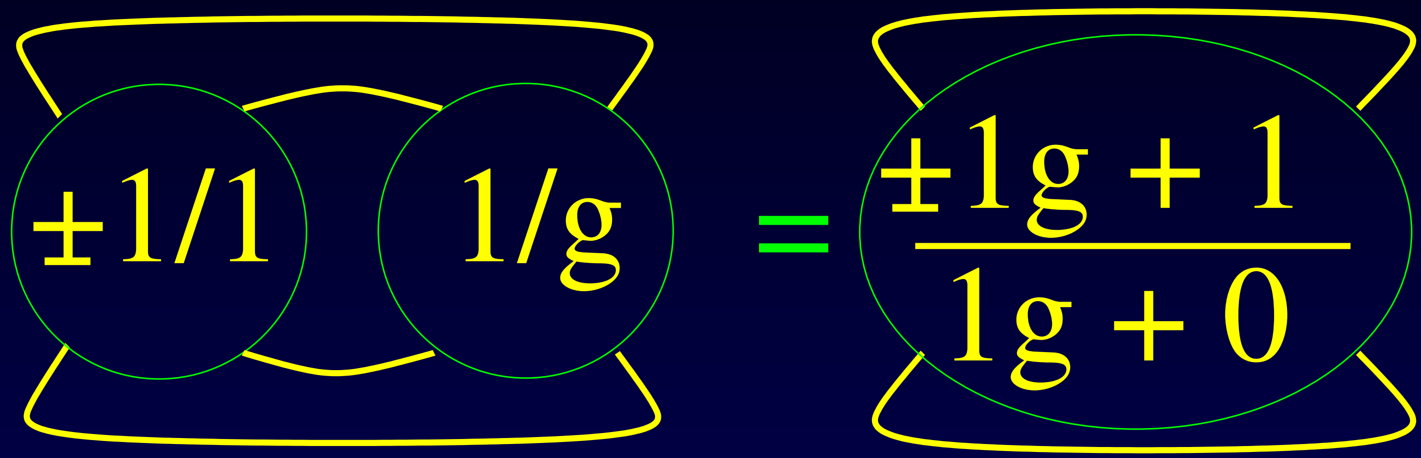
# The numerator closure of the sum of two rational tangles is a 4-plat




where dp - qj = 1

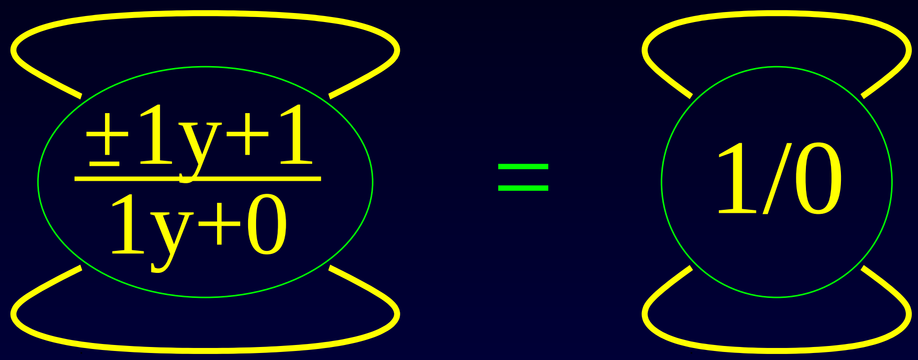
# The numerator closure of the sum of two rational tangles is a 4-plat




where 1(1) - 0(±1) = 1

# 4-plat equivalence

Take a, c $\geq$ 0.




N(a/b) N(c/d)

if and only if

$a = c$

and

$bd^{\pm 1} = 1 \bmod a$

Thus we are solving

$$N(\pm 1 + \frac{1}{y}) = N(\frac{1 \pm y}{y}) = N(\frac{1}{0})$$

$$N(\pm 1 + \frac{1}{w}) = N(\frac{1 \pm w}{w}) = N(\frac{0}{1})$$

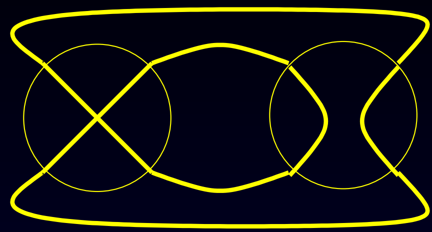
Thus, $1 \pm y = 1$ and $y = 0 + 1k$
OR $1 \pm y = -1$ and $y = -0 + 1k$

Hence $y = 0, \pm 2$

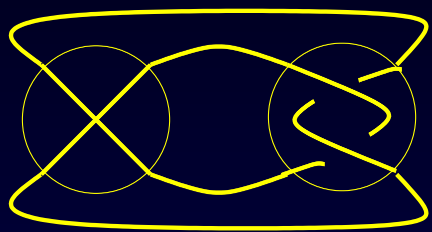
And $1 \pm w = 0$ and $w = \pm 1 + 0k$.

Hence $w = \pm 1$

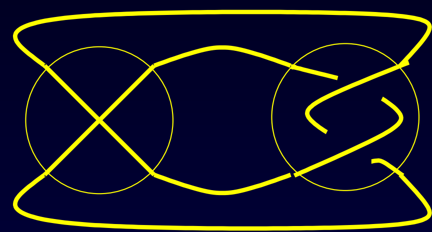
 



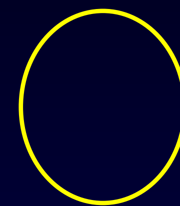
OR

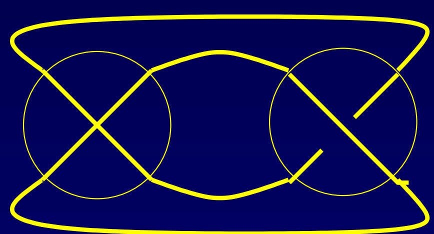


OR

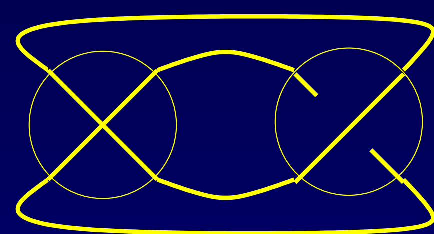


= Unknot =

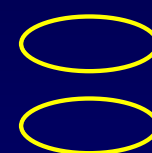




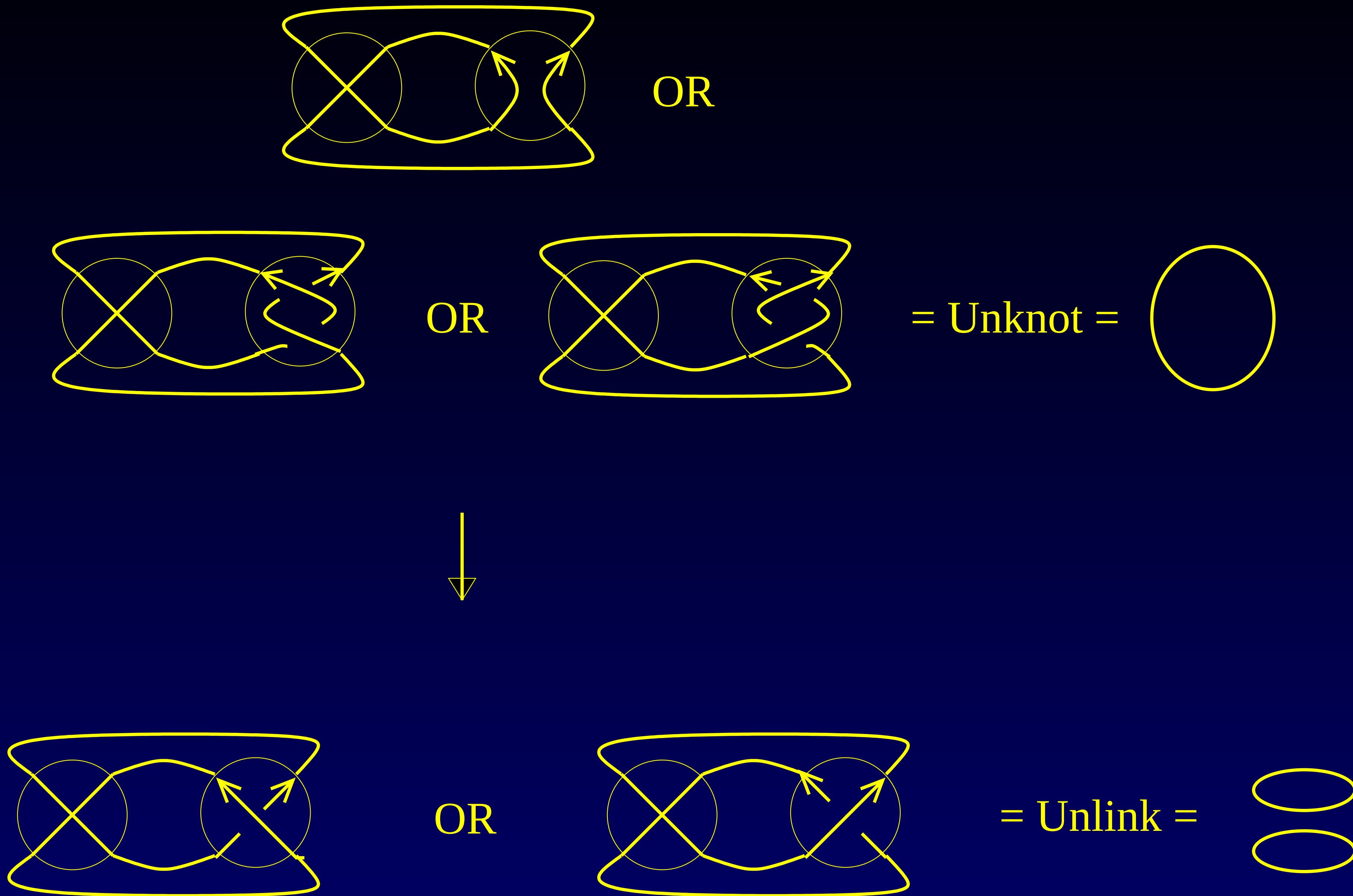
OR



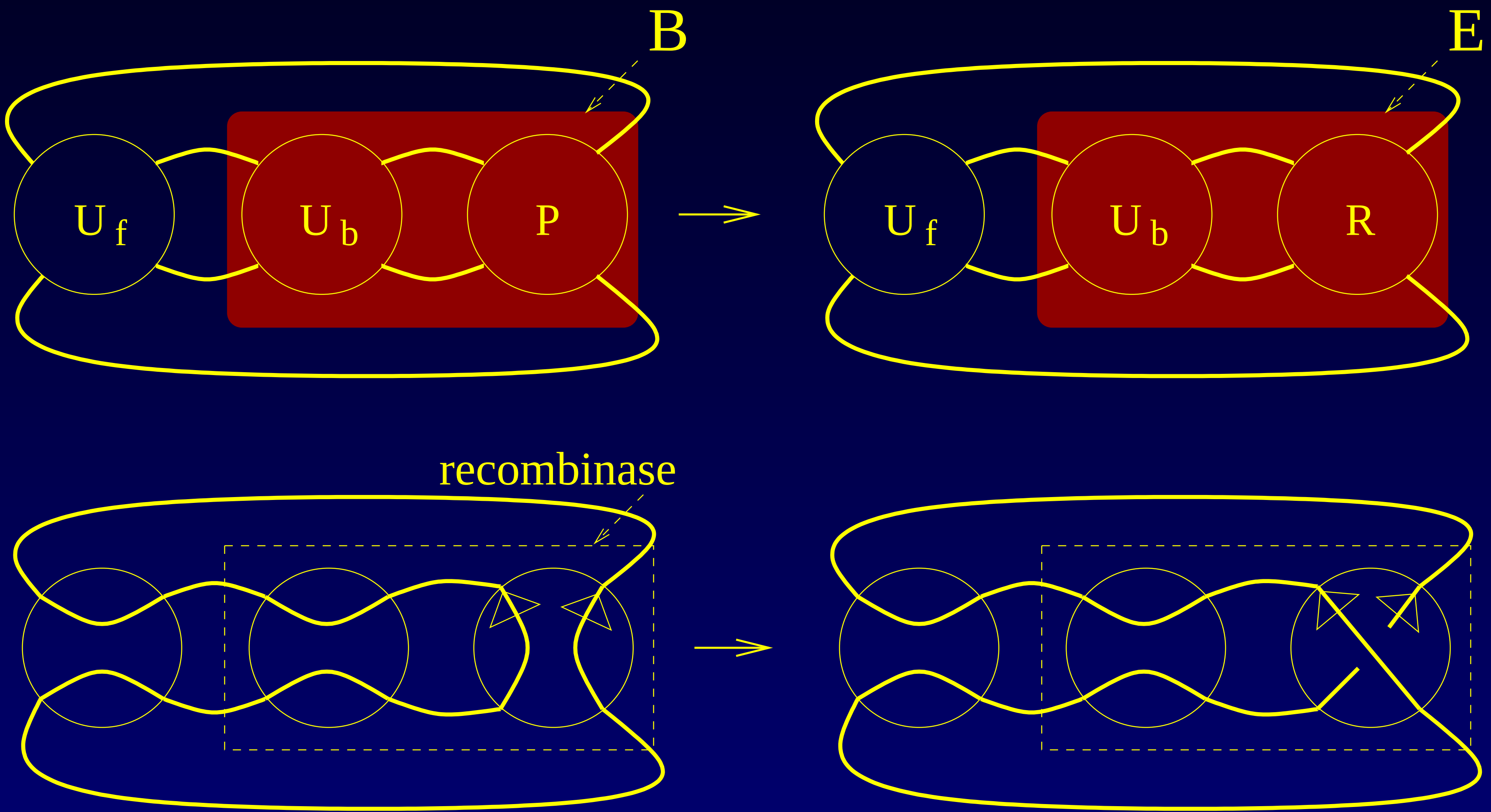
= Unlink =



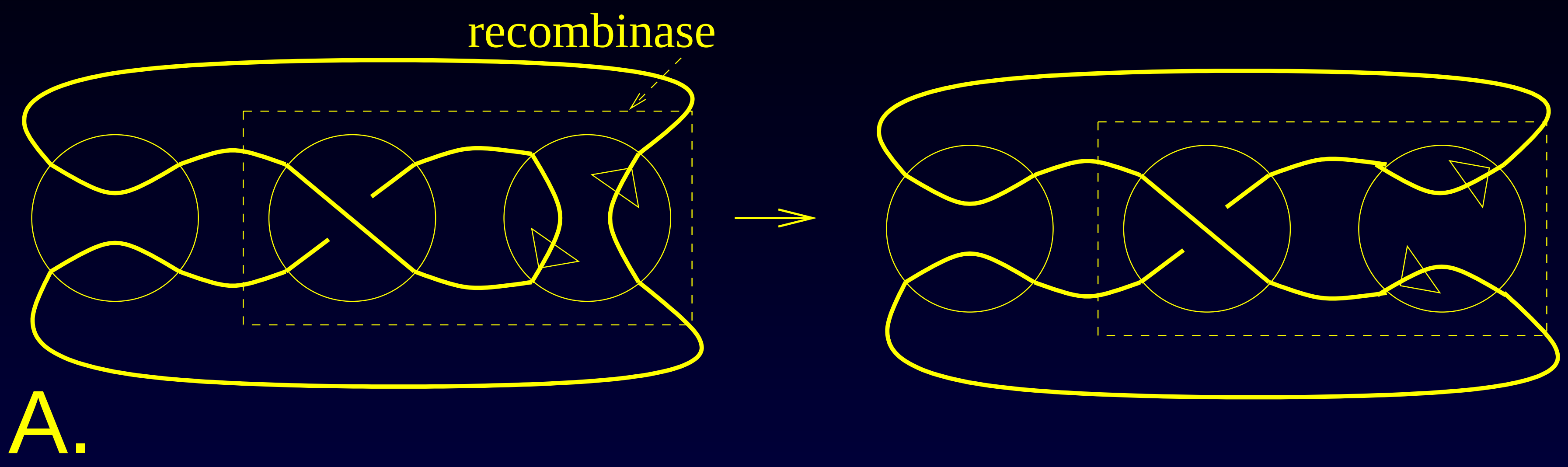

OR
OR
= Unknot =
OR
= Unlink =

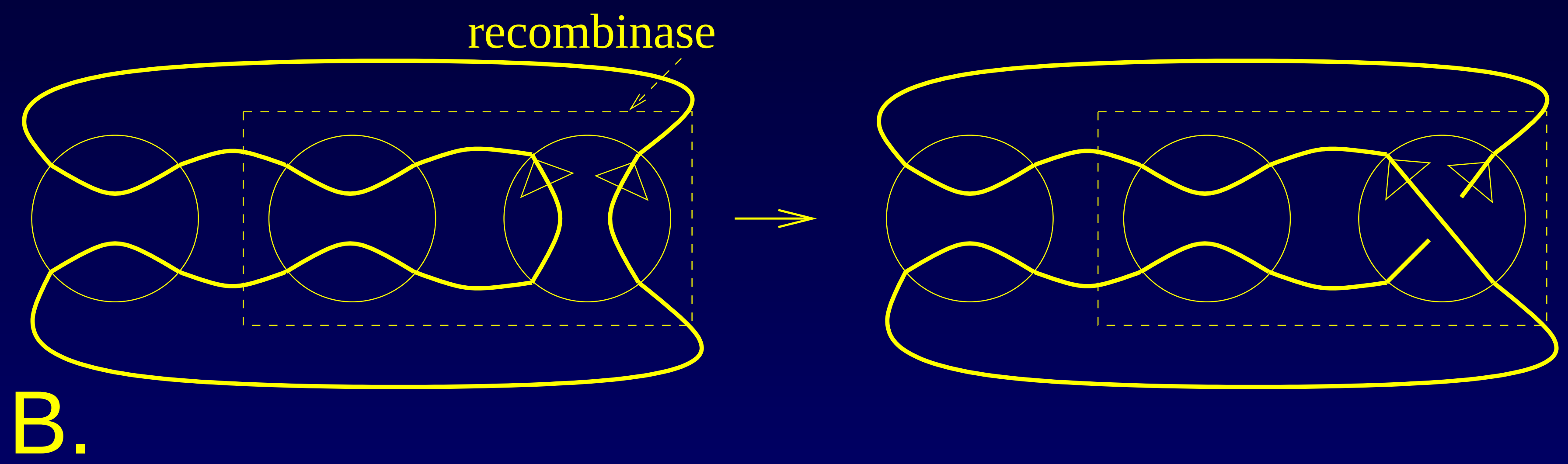
We can also divide the tangles $B$ into two other tangles $U_b$ and $P$. Similarly, $E$ can be divided into the tangles $U_b$ and $R$ respectively (Ernst and Sumners 1990):




B.

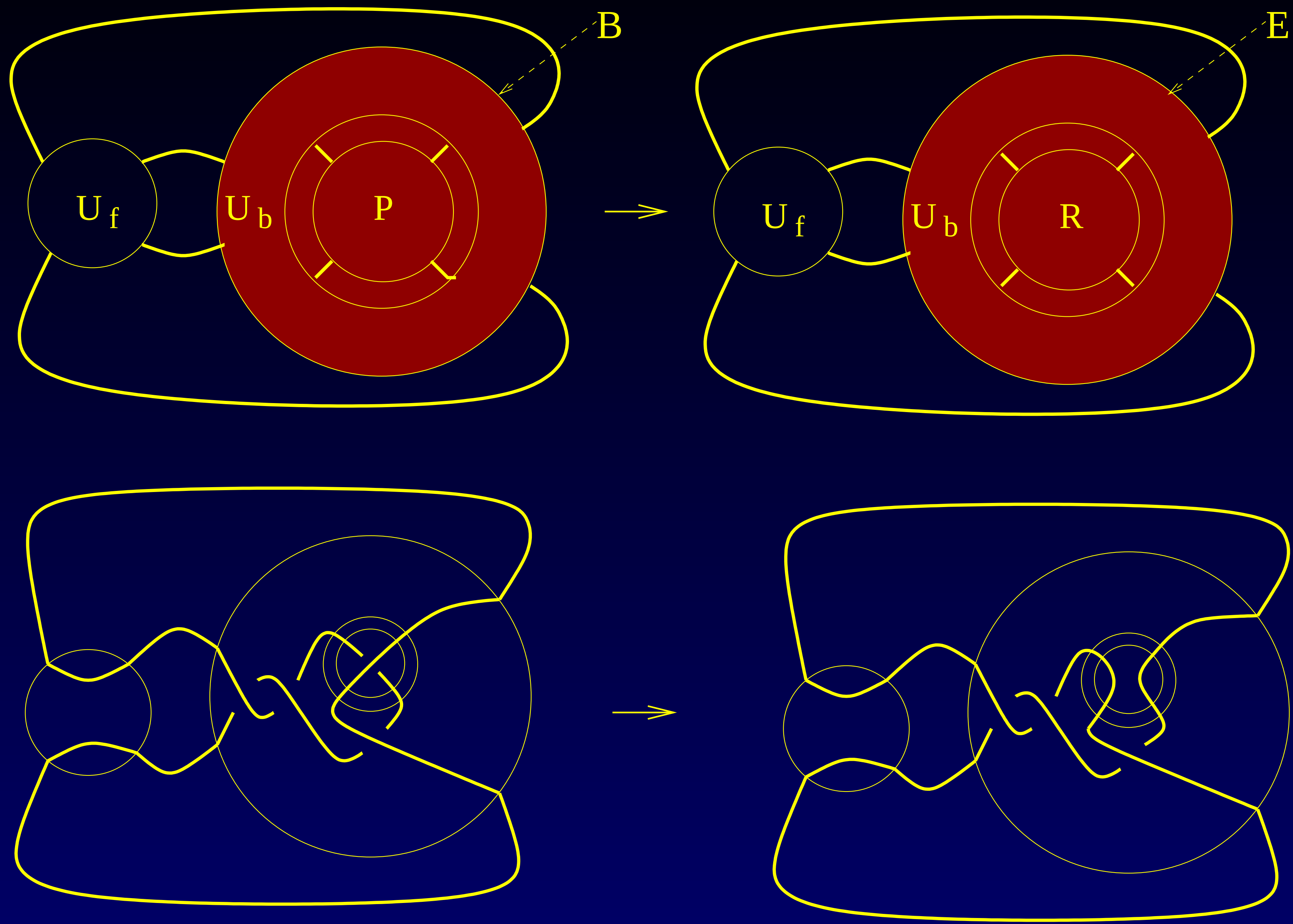
# Remember our solutions are topological



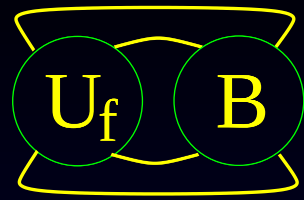

 

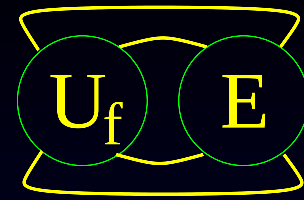
# Side Note: Alternate model



Summary

1.) Given 

= N(a/b), 

= N(z/v)

can solve for $E$ and $U_f$ in terms of $B$.

2.) Some solutions for $U_f$ are missed when $(B, E)$ "equivalent" to $(0, \frac{1}{n})$, but otherwise all solutions can be found and orientation determined when $B$ and $E$ are rational.

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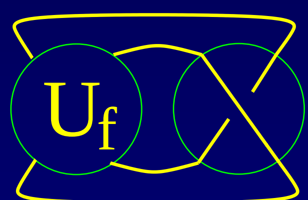
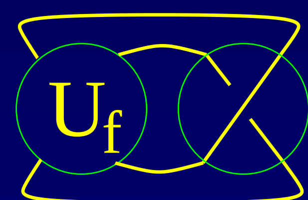
Side-note: Thus can find all solutions for $U_f$ when modeling a topoisomerase reaction



= N(a/b), 

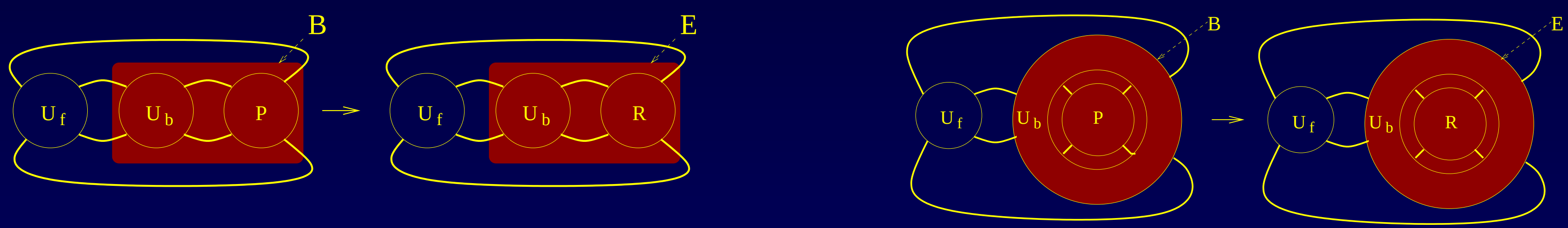
= N(z/v)

3.) There are an infinite number of solutions to the above system of tangle equations since many solutions are "equivalent".

4.) To get a unique solution, biologists can determine $U_f$ via electron microscopy.

5.) The solutions are topological. B and E can be divided into two other tangles.

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