The band surgery model for site-specific recombination along circular DNA molecules

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The circular, supercoiled chromosome of *Escherichia Coli* (Kavenoff, 1976)
Torus knots and links in DNA

$T(2, n)$ torus knots and links naturally occur during replication of circular DNA molecules.

(Right) DNA replication. (Center) The $T(2, n)$ torus link is the boundary of a twisted annulus. (Left) The $T(2, 8)$ torus link.

Two interlinked daughter chromosomes are produced, which must be separated for the cell line to survive.
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Example: Stepwise unlinking by site-specific recombination (Shimokawa et al., 2013). $T(2, n)$ torus knots and links occur as intermediate dimers.
Basic objects from knot theory in the model

Circular DNA is modeled as a topological knot or link.

Recombination events will be modeled by the band surgery operation.
Goal 1: understand recombination events involving $T(2, n)$ torus knots and links
A good starting place: the trefoil knot $T(2, 3)$.

Goal 2: do some interesting three-manifold topology

Our main results will provide both a classification of recombination events taking the trefoil to other $T(2, n)$ torus knots and links, obstructions to recombination, as well as a classification certain lens space surgeries.
Site-specific recombination in circular DNA molecules

Recombination sites (5-50 bp) are non-palindromic sequences of nucleotides.

- Sites in **direct repeat** induce **same** orientation along chain.
- Sites in **inverted repeat** induce **opposite** orientation along chain.

Schematically, recombination is a “head-to-tail” reconnection event.
Coherent and non-coherent band surgery

Let $b(I \times I)$ be any embedding of a unit square such that $L_1 \cap b(I \times I) = b(I \times \partial I)$. We say $L_2$ and $L_1$ are related by band surgery if $L_2 = (L_1 - b(I \times \partial I)) \cup b(\partial I \times I)$.

1. Sites in **direct** repeat $\leadsto$ **coherent** band surgery.
2. Sites in **inverted** repeat $\leadsto$ **non-coherent** band surgery.
Non-coherent and coherent band surgery are different beasts

*Coherent band surgery is controllable because the underlying surface cobordism is orientable.*

*Non-coherent band surgery less predictable because the underlying surface cobordism is non-orientable.*
Local operations on knots

- Crossing changes:
  \[ \xrightarrow{\text{\textbullet}} \xrightarrow{\text{\textbullet}} \xrightarrow{\text{\textbullet}} \xrightarrow{\text{\textbullet}} \]

- Resolutions (smoothings):
  \[ \xrightarrow{\text{\textbullet}} \xrightarrow{\text{\textbullet}} \xrightarrow{\text{\textbullet}} \xrightarrow{\text{\textbullet}} \]

Observe: band surgery realized as a skein resolution and vice-versa.
Local operations and knot invariants

Example: determinant and signature

Knot invariants:

\[ K \sim p(K) \]
\[ K \neq K' \iff p(K) \neq p(K') \]

e.g. **Determinant** and **Signature**:

\[ \det(\bigcirc) = 1 \quad \det(\bigotimes) = 3 \]
\[ \sigma(\bigcirc) = 0 \quad \sigma(\bigotimes) = -2 \]

*(Easy to compute via Gordon-Litherland.)*
Signature obstructions to band surgery

Theorem (Murasugi, 1965)

Let $L$ and $L'$ be links related by coherent band surgery. Then

$$|\sigma(L) - \sigma(L')| \leq 1.$$

Theorem (Moore-Vazquez, 2018)

Let $K$ and $K'$ be alternating knots with $\det K = m = \det K'$ for $m$ square-free. If $K$ and $K'$ are related by non-coherent band surgery, then

$$|\sigma(K) - \sigma(K')| = 8 \text{ or } 0.$$
Band surgeries relating $T(2, 3)$ to other $T(2, n)$'s

Non-coherent bandings from $T(2, 3)$ to $T(2, 7)$, from $T(2, 3)$ to itself, and from $T(2, 3)$ to the unknot.

Coherent bandings from $T(2, 3)$ to $T(2, −6)$, $T(2, 3)$ to $T(2, 2)$, and $T(2, 3)$ to $T(2, 4)$ (see also Darcy et al. (2012)).
Band surgery along the trefoil

**Theorem (Lidman-Moore-Vazquez, 2017)**

The torus knot or link $T(2, n)$ is obtained from $T(2, 3)$ by a (coherent or non-coherent) banding if and only if

$$n \in \{ \pm 1, \pm 2, 3, 4, -6, 7 \}.$$
How to prove the other bandings do not exist?

The above classification of band surgeries on the trefoil is a corollary of:

**Theorem (Lidman-Moore-Vazquez)**

*The lens space $L(n, 1)$ is obtained by a distance one surgery along any knot in the lens space $L(3, 1)$ if and only if*

$$n \in \{ \pm 1, \pm 2, 3, 4, -6, 7 \}.$$  

Note: This is a partial generalization of the *lens space realization problem*
The “Montesinos Trick”

Fact

1. The branched double cover of $K = T(2, n)$ is the lens space $L(n, 1)$.


Therefore: A band surgery from $T(2, 3)$ to $T(2, n)$ ‘lifts’ to an integral Dehn surgery along a knot from $L(3, 1)$ to $L(n, 1)$. 
Dehn surgery in lens spaces

In our setting: $K$ is a knot in the lens space $L(3,1)$.

- $M = L(3,1) - \text{nbhd}(K)$
- $\mu$ is a meridian of $K$.
- $M(\mu) = L(3,1)$
- $M(\alpha) = L(n,1)$

We say $\alpha$ and $\mu$ are distance one in $\partial M$ because they intersect geometrically once.
Key ingredients of proof: Heegaard Floer $d$-invariants

(Ozsváth and Szabó, 2001): Heegaard Floer homology for closed, oriented three-manifolds.

\[ Y \leadsto \bigoplus_{t \in \text{Spin}^c(Y)} \text{HF}^+(Y, t) \]

- $Y$ is a rational homology sphere.
- $d(Y, t)$ is the minimal grading of any non-torsion class in $\text{HF}^+(Y, t)$.
- Example: The $d$-invariants of $L(3, 1)$ are $\frac{1}{2}, -\frac{1}{6}, -\frac{1}{6}$
The $d$-invariants of manifolds related by surgery

**Theorem (Ni-Wu, 2015)**

Let $S^3_p(K)$ denote $p$-surgery along $K$ in $S^3$. Then:

$$d(S^3_p(K), i) = d(L(p, 1), i) - 2V_i.$$  \(1\)

**Theorem (Lidman-Moore-Vazquez, 2017)**

Several technical adaptations of equation (1) for surgery along knots in $L(3, 1)$.

We then use these formulas to analyze when $L(n, 1)$ is obtained by surgery along any $K$ in $L(3, 1)$. 
Summary of the strategy:
Summary of the results relevant to site-specific recombination:

1. Classification of recombination events taking $T(2,3)$ to $T(2,n)$ for any $n$.

2. Easy to evaluate criterion on banding along alternating knots of the same determinant.
Plus computer simulations!

3 Analytical results indicate that chirally cosmetic banding (\(K\) to its mirror) are unusual.

4 Monte Carlo simulations also demonstrate that chirally cosmetic bandings are rare.

5 Via simulation we have discovered new band moves (e.g. \(8_8\) to \(8_8^*\)).

6 ... More Monte Carlo simulations to come.
Thank you for listening!

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References


Knots and links in DNA molecules

Trefoil knots made by T4 topoisomerase and observed using electron microscopy, Wasserman and Cozzarelli (1991).

Supercoiled E. coli plasmid pBP90 was reacted with the enzyme λ-Int and nicked by DNAase I. Product is a $T(2, 13)$ torus knot, observed using electron microscopy, Spengler et al. (1985).