Avoiding binary patterns with reversal

James D. Curie & Phillip Lafrance

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MathStats Seminar
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Outline

DNA as a sequence of symbols

A DNA sequence from a normal human heart:

AGAAAAGCGCCTCCACGGAGACGGTAACACCACTCAC
ATGGATGGATAATCCTATAGAATTAAATGTTAAGGATAGTG
TATGGGTACCTGGCCCCACAGATGATCACTGCCCTGCC
AAACCTGAGGAAGAAGGGATGATGATAAATATTTCCATTG
GGTATCGTTATTCTCCTATTTGCCTAGGAAGAGCACCAGG
ATGCTTAATGCCTGCATTCCAAAATTGGTTGGTAGAAGTA
CCTACTGCCGGTCCTAACAGTAGACTCACTTATCACATGG
TGTACCCAACAGCTCGGAAGAGACAGCGACCATCGAGA
ACGGGCCATGATGACGATGGCGGTTTTGTCGAAAAGAA
AAGGGGGAAATGTGGGGAAAAGCAAGAGAGATCAGATT
GTTACTGTGTCTGTGTAGAAAGAAGTAGACATAGGAGAC
TCCCTTTTGTTCTGTACTAAGAAAAATTATTCTGCCTTGA
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ACGGGCCATGATGACGATGGCGGTTTTGTCGAAAAGAA
AAGGGGGAAATGTGGGGAAAAGCAAGAGAGATCAGATT
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Patterns in DNA

- We see that this sequence has a pattern embedded in it, of the form *xxyy*, where $x = CTGTGT$, $y = AGGA$.
- We may wonder whether these repetitions are functionally significant.
- Perhaps the occurrence of *xxyy* is just coincidence.
- To what extent are various patterns avoidable?
- Does every pattern (e.g., *xx*, *xyx*, *xxyyy*, ...) show up in every long enough sequence of symbols?

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Patterns with reversal

- In the context of DNA, we may be interested, not just in identical repetitions of some string, but in coded repetitions.
- The four bases in DNA are arranged in complementary pairs: $\phi : C \leftrightarrow G$, $\phi : A \leftrightarrow T$
- Also of importance are **reversals**: $(CCAGATT)^R = TTAGACC$.
- For example, geneticists study **hairpins**: structures of the form $xy\phi(x^R)$
- A hair pin structure

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- A sequence over a 1-letter alphabet eventually encounters whatever pattern you like.
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- Over a 2-letter alphabet, some patterns can be avoided
- Let $w_0 = 0$, $w_{n+1} = w_n \bar{w}_n$, where $\bar{w}$ is the binary complement of w
- Iterating $w_0 \to w_1 \to w_2 \to w_3 \cdots$ gives the **Thue-Morse sequence** t
- $t = 0110100110010110 \cdots$
- Sequence t **avoids** (i.e., does not encounter) xxx and $xyxyx$ (Thue, 1906).
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Avoidability of binary patterns

- A pattern over the alphabet $\{x, y\}$ is called a **binary pattern.**
- Cassaigne (1993) completely classified binary patterns as unavoidable, 2-avoidable or 3-avoidable.
- For example, all binary patterns of length at least 6 are 2-avoidable.
- Let Σ be the alphabet $\Sigma = \{x, x^R, y, y^R\}$. We call a word $p \in \Sigma^*$ a **binary pattern with reversal.**
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Observing symmetries

- A first step in a classification is to notice symmetries, to reduce unnecessary work.
- If a finite word w avoids p, then w^R avoids p^R. Thus p and p^R are equally avoidable on any given alphabet.
- An instance of $xyyx^Rx$ is also an instance of $yxxy^Ry$ (switching x and y) and of x^Ryyxx^R (switching x and x^R).
- We thus observe symmetries: $p \leftrightarrow p^R$; $x \leftrightarrow y$; $x \leftrightarrow x^R$.
- Consider the lexicographic order on Σ^* generated by $x < x^R < y < y^R$.
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Some 2-avoidable patterns

- The following patterns are 2-avoidable for various reasons:
- $S_{2,1} = \{xxx, xxyxyy, xxyyx, xyxxy, xyxyx\}$ (Cassaigne)
- $S_{2,2} = \{xyxyx^R\}$
- $S_{2,3} = \{xxyxy^R, xxyx^Ry, xxyx^Ry^R, xxyyx^R, xx^R, xyx^Rx^Ry, xyyx^R\}$
- $S_{2,4} = \{xyxy^Rx^R, xyx^Ry^Rx, xyxy^Rx, xyx^Ryx\}$.

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- $S_{2,3} = \{xxyxy^R, xxyx^Ry, xxyx^Ry^R, xxyyx^R, xx^R, xyx^Rx^Ry, xyyx^R\}$
- $S_{2,4} = \{xyxy^Rx^R, xyx^Ry^Rx, xyxy^Rx, xyx^Ryx\}$.

Some 2-avoidable patterns

- Recall that $S_{2,2} = \{xyxyx^R\}$.
- Fraenkel and Simpson (1995) constructed a binary sequence f in which the only instances of xx are 00, 11 and 0101.
- Suppose that f contains a factor $XYXYX^R$, where X and Y are non-empty words.
- Since $XYXY$ is a square of length greater than 2, we must have $XYXY = 0101$, forcing $X = 0$, $Y = 1$.
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- The notation $(01)^\omega$ stands for the infinite alternating binary string $(01)^\omega = 01010101\cdots$
- Let p be a binary pattern with reversal.
- Define $G(p)$ to be the graph with vertex set Σ, and an edge between a^R and b whenever ab is a length two factor of p.

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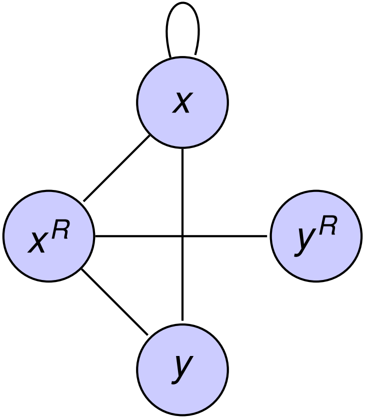
Figure: The graph $G(p)$, where $p = x^R xyx^R x^R y$.



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Let $p \in \{x, x^R, y, y^R\}^*$. An instance of p appears in $(01)^\omega$ if and only if $G(p)$ is bipartite.

For each $p \in S_{2,3}$, $G(p)$ contains an odd cycle, so that p is avoided by $(01)^\omega$.

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- New constructions had to be found for each of the patterns of $S_{2,4}$.
- For example, let h be the binary morphism given by $h(0) = 0$, $h(1) = 00101101111$, and let $\mathbf{w_1} = h(\mathbf{t})$.
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Let $S_2 = \cup_{i=1}^{4} S_{2,i}$.

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- For each non-negative integer n, let A_n be defined by
- $A_n = \{q : |q| = n, q = \ell(q)$, and if u is a factor of q then $\ell(u) \notin S_2\}$.
- If q is in A_n, then $q = ra$, where r is equivalent to a word of A_{n-1}, $a \in \Sigma$.
  - $A_0 = \{\epsilon\}$, $A_1 = \{x\}$, $A_2 = \{xx, xy\}$, $A_3 = \{xxy, xyx, xyx^R\}$, $A_4 = \{xxyx, xxyx^R, xxyy, xyxy, xyxy^R, xyx^Ry^R, xyyx\}$, $A_5 = \{xxyxx, xxyxy, xxyx^Rx^R\}$, $A_6 = \phi$.
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Let $S_3 = \{xx, xyxy, xyxy^R, xyx^Ry^R\}$.

Theorem

The patterns of S_3 are 3-avoidable.

- The pattern xx was shown to be 3-avoidable by Thue.
- The other patterns of S_3 are avoided by a 3-letter word built from the word f of Fraenkel and Simpson.
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Theorem

Let p be a binary pattern with reversal. If $\ell(p)$ is a prefix of one of xyx and xyx^R, then p is unavoidable; otherwise p is 3-avoidable.

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