10th International Conference on
Unconventional Computation

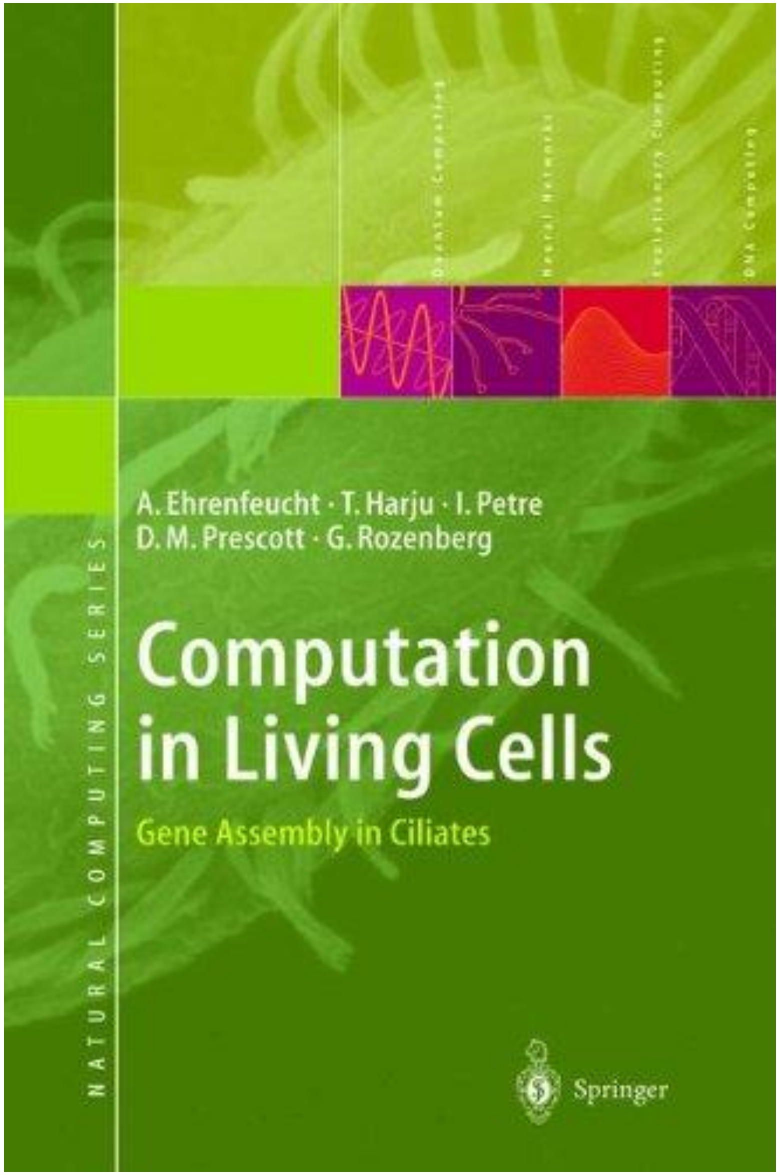
Workshop on
Language Theory in Biocomputing
Turku, June 9, 2011

The Algebra of Ciliates

Robert Brijder Hasselt

Hendrik Jan Hoogeboom
Leiden

image: http://www.depts.ttu.edu/hillcountry/research/protozoa.php

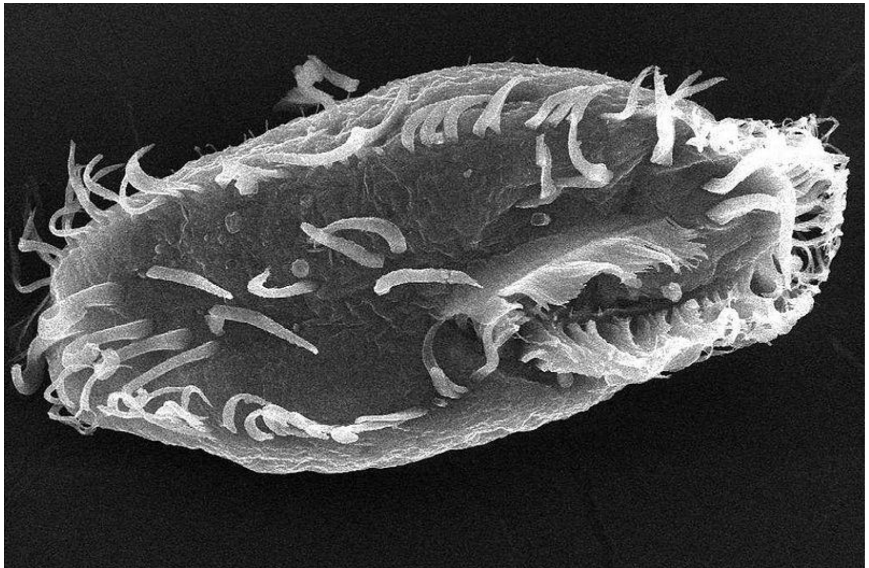


Computation in Living Cells
Gene Assembly in Ciliates

A. Ehrenfeucht, T. Harju, I. Petre,
D.M. Prescott, G. Rozenberg

Natural Computing Series, Springer,
2004.

ciliates



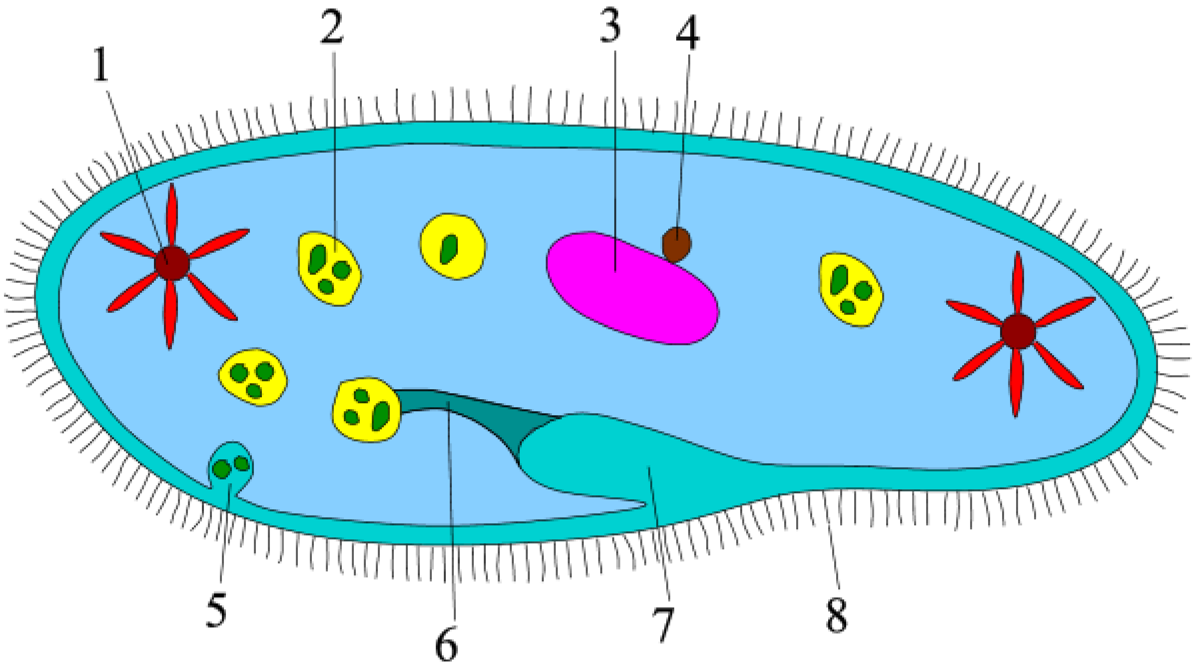
Oxytricha trifallax

The **ciliates** are a group of protozoans characterized by the presence of hair-like organelles called **cilia**, [...] variously used in swimming, crawling, attachment, feeding, and sensation.

Ciliates are one of the most important groups of protists, common almost everywhere there is water — in lakes, ponds, oceans, rivers, and soils. Ciliates have many ectosymbiotic and endosymbiotic members, as well as some obligate and opportunistic parasites. Ciliates tend to be large protozoa, a few reach 2 mm in length, and are some of the most complex protozoans in structure

http://en.wikipedia.org/wiki/Ciliate

micro and macro



cell structure:

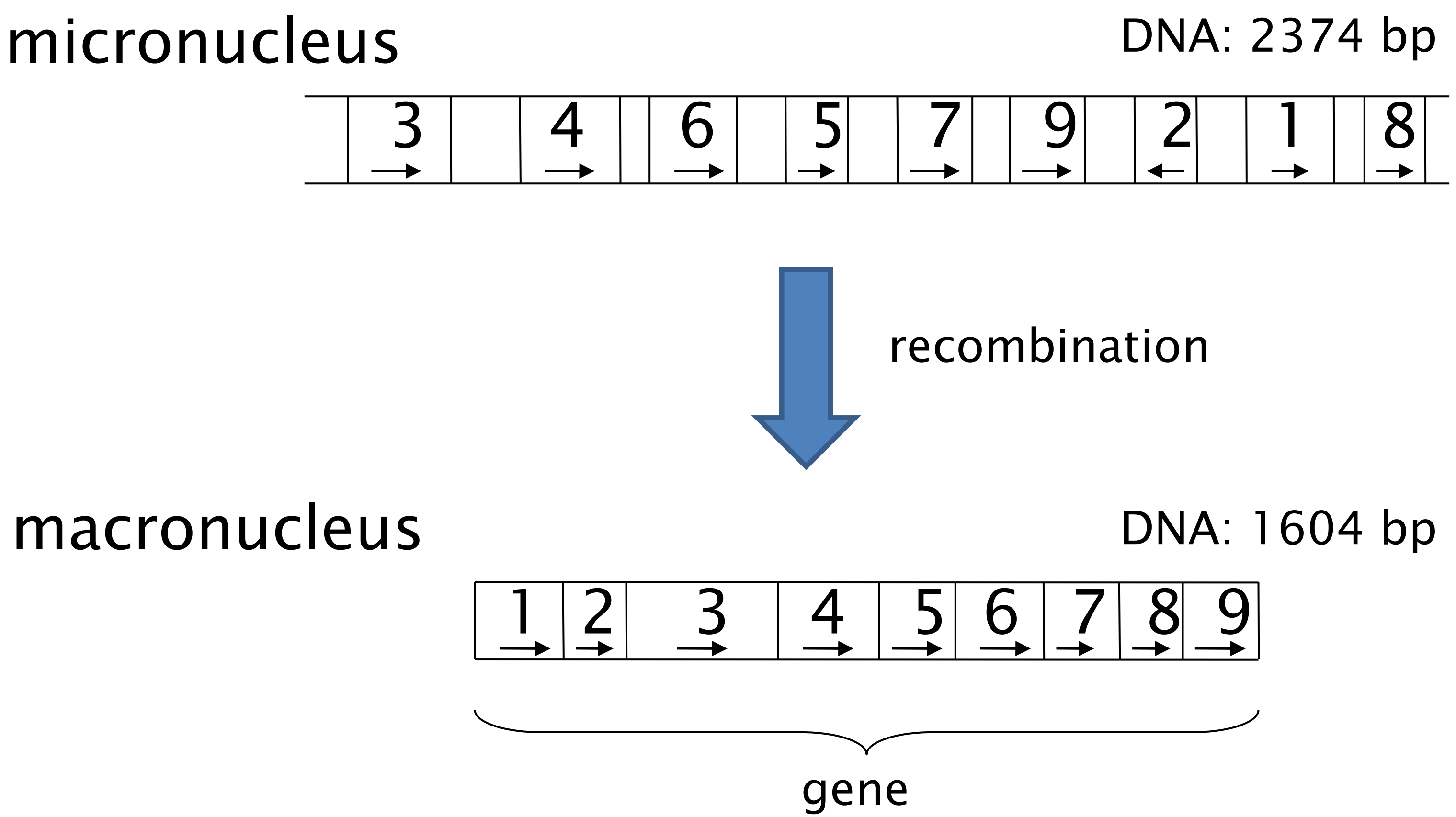
3. macronucleous
4. micronucleous
8. cilium

Unlike most other eukaryotes, ciliates have two different sorts of nuclei: a small, diploid **micronucleus** (reproduction), and a large, polyploid **macronucleus** (general cell regulation). The latter is generated from the micronucleus by amplification of the genome and heavy editing.

http://en.wikipedia.org/wiki/Ciliate

from micro to macro

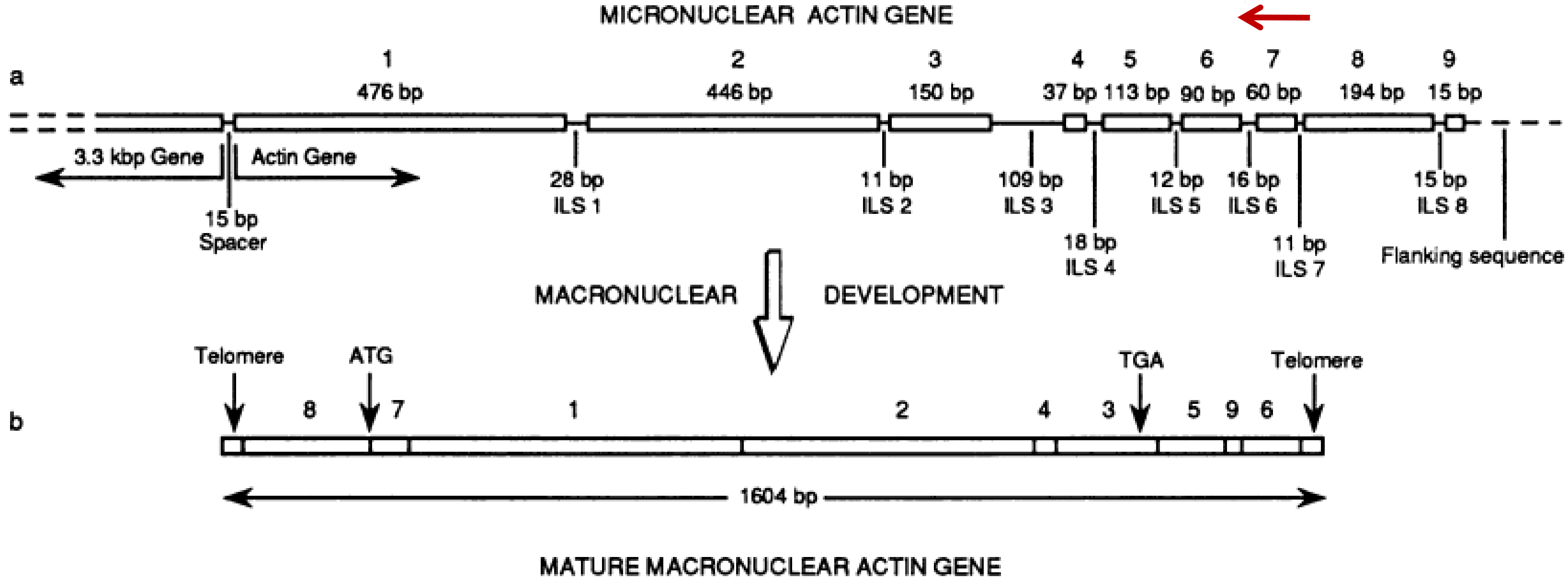
http://oxytricha.princeton.edu/cgi-bin/get_MDS_IES_Info.cgi?num=38



here: segment numbers in sorted order

micronucleus

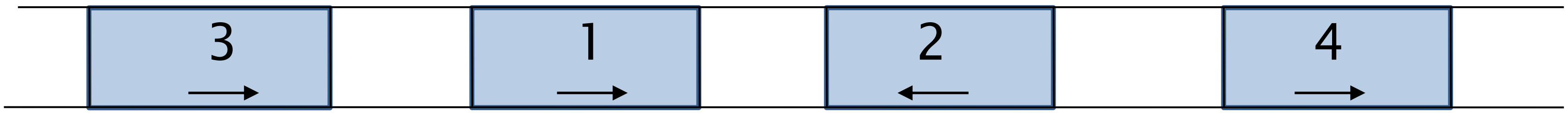
9 exons



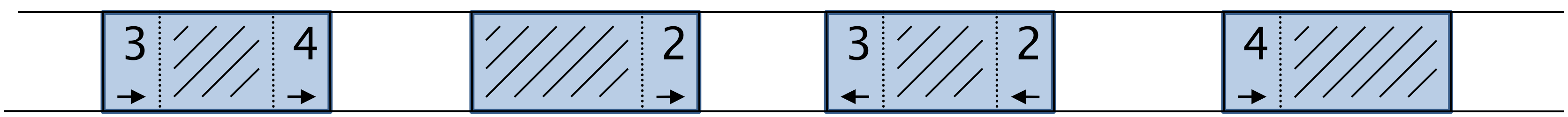
macronucleus

Greslin, Prescott etal. Reordering of nine exons is necessary to form a functional actin gene in Oxytricha nova. PNAS 86, 6264-6268, Aug 1989.

pointers

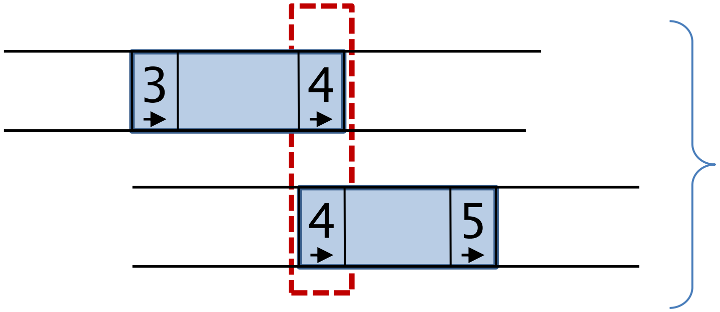


pointers – overlapping segments (for glueing)

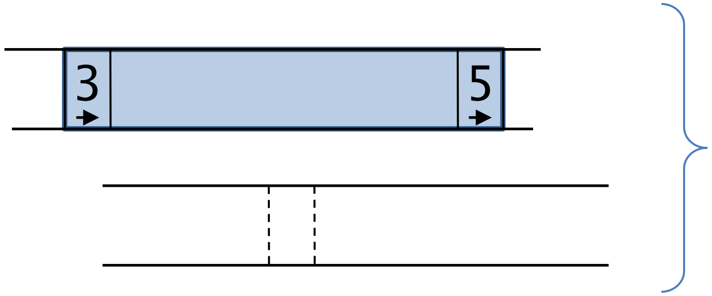


e.g., pointer 5 of actin gene: 13 bp

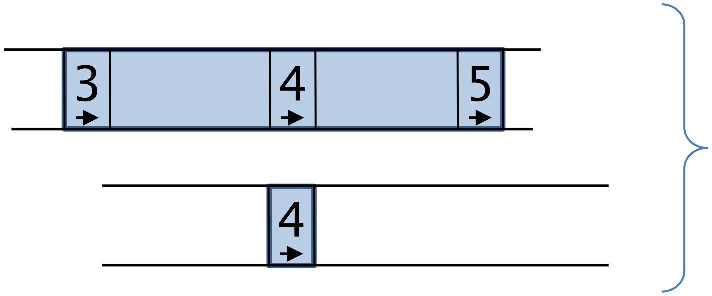
rc_4 recombination on pointer 4 'generic'



before



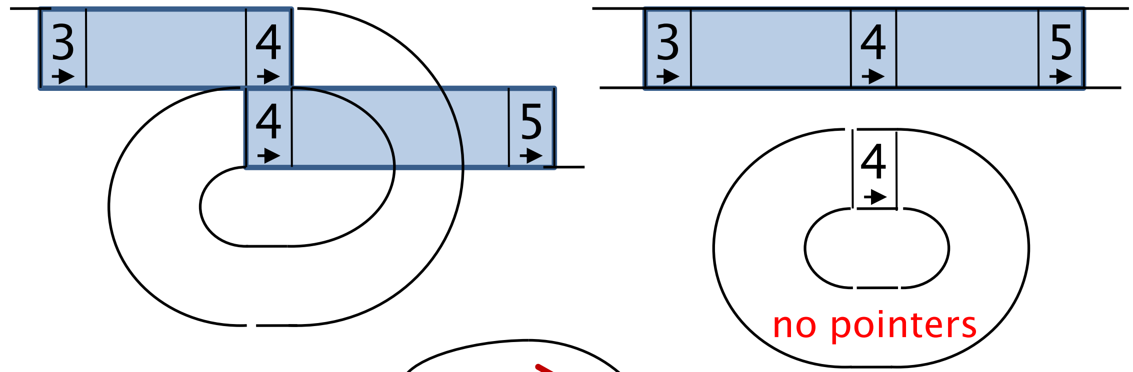
after 'ciliate view'



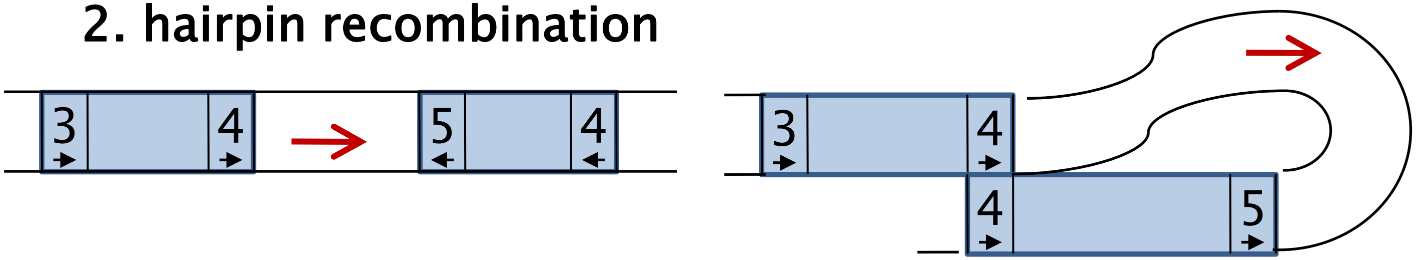
after 'math view'

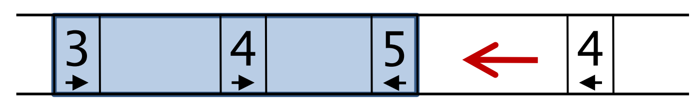
recombination on pointers

1. loop recombination

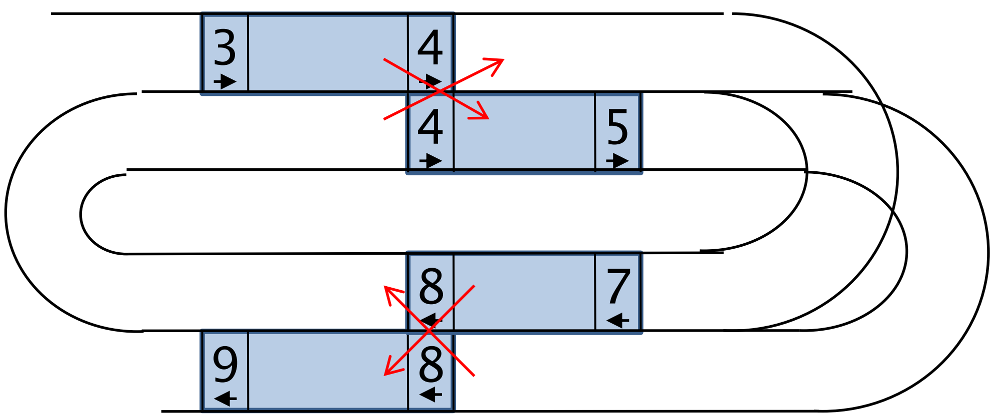


2. hairpin recombination





3. double-loop recombination

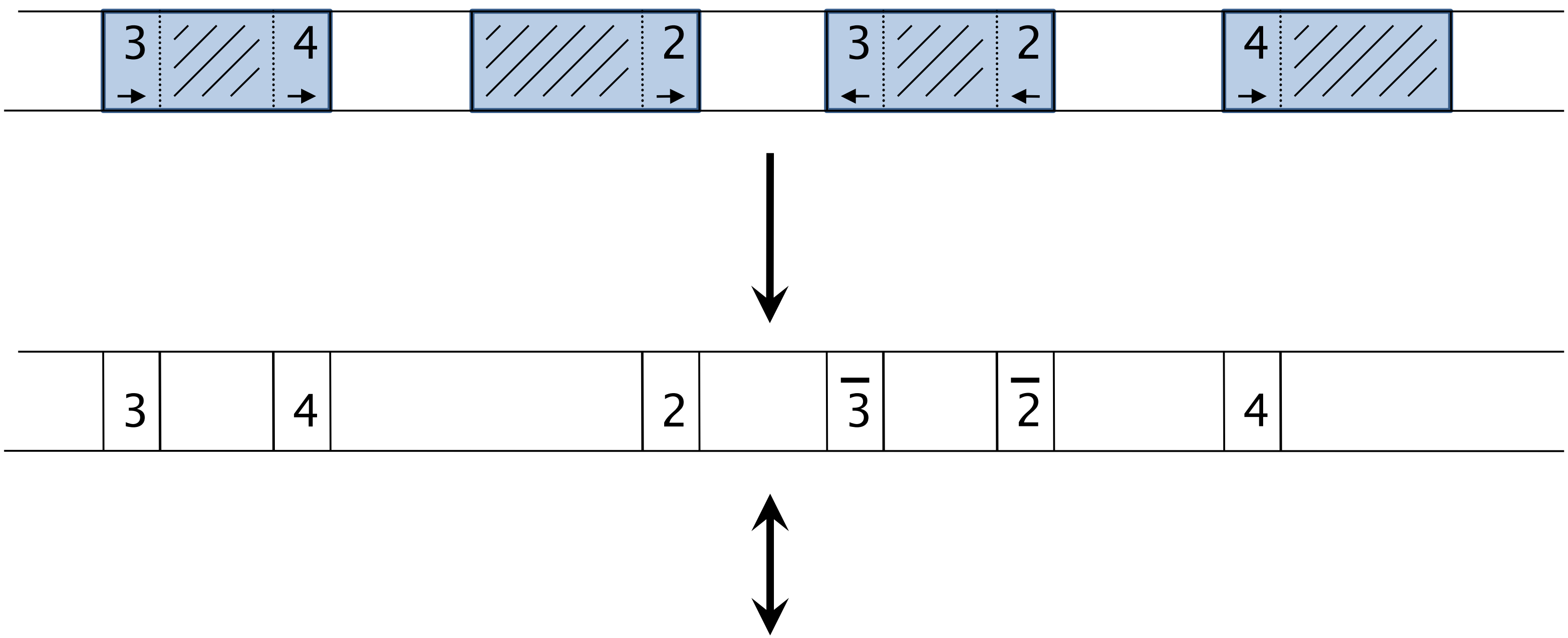


quest for the "right" model

- strings
- graphs
- matrices
- set systems

1

abstraction: pointers

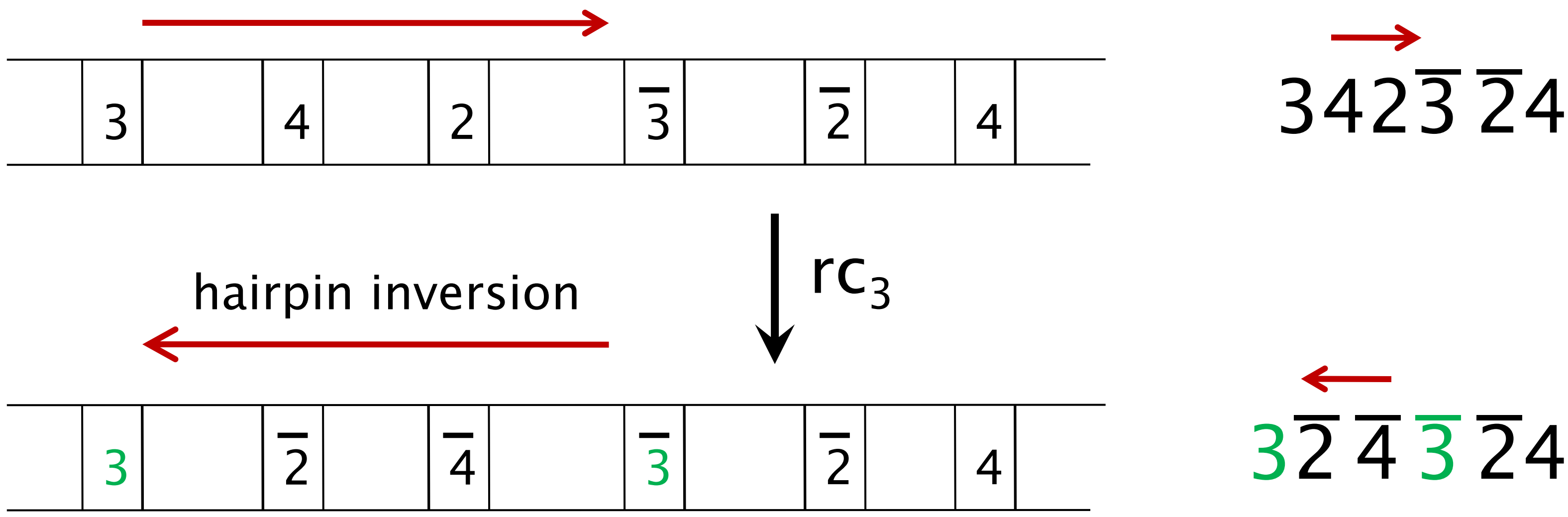


$342\bar{3}\bar{2}4$ ‘legal’ string

... 4774 ... realistic strings vs. generalizations

string positive rule

translating recombinations into string operations



$$rc_p(\ u_1 p u_2 \overline{p} u_3\ ) = u_1 p \overline{u}_2 \overline{p} u_3$$

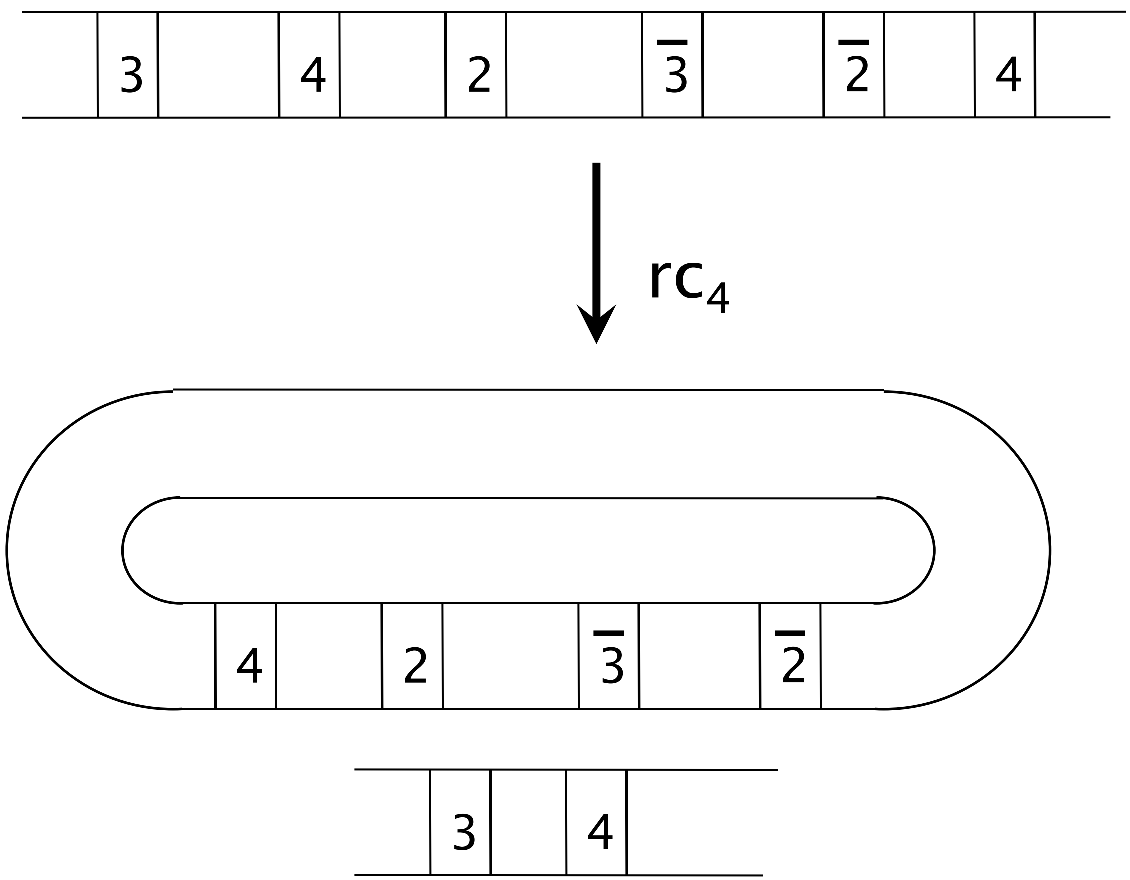
string pointer reduction systems

$$rc_p(\ u_1 pp u_2\ ) = u_1 pp u_2$$

no rearrangement
excision circular molecule

$$rc_p(\ u_1 p u_2 \overline{p} u_3\ ) = u_1 p \overline{u}_2 \overline{p} u_3$$

$$rc_{p,q}(\ u_1 p u_2 q u_3 p u_4 q u_5\ ) = u_1 p u_4 q u_3 p u_2 q u_5$$



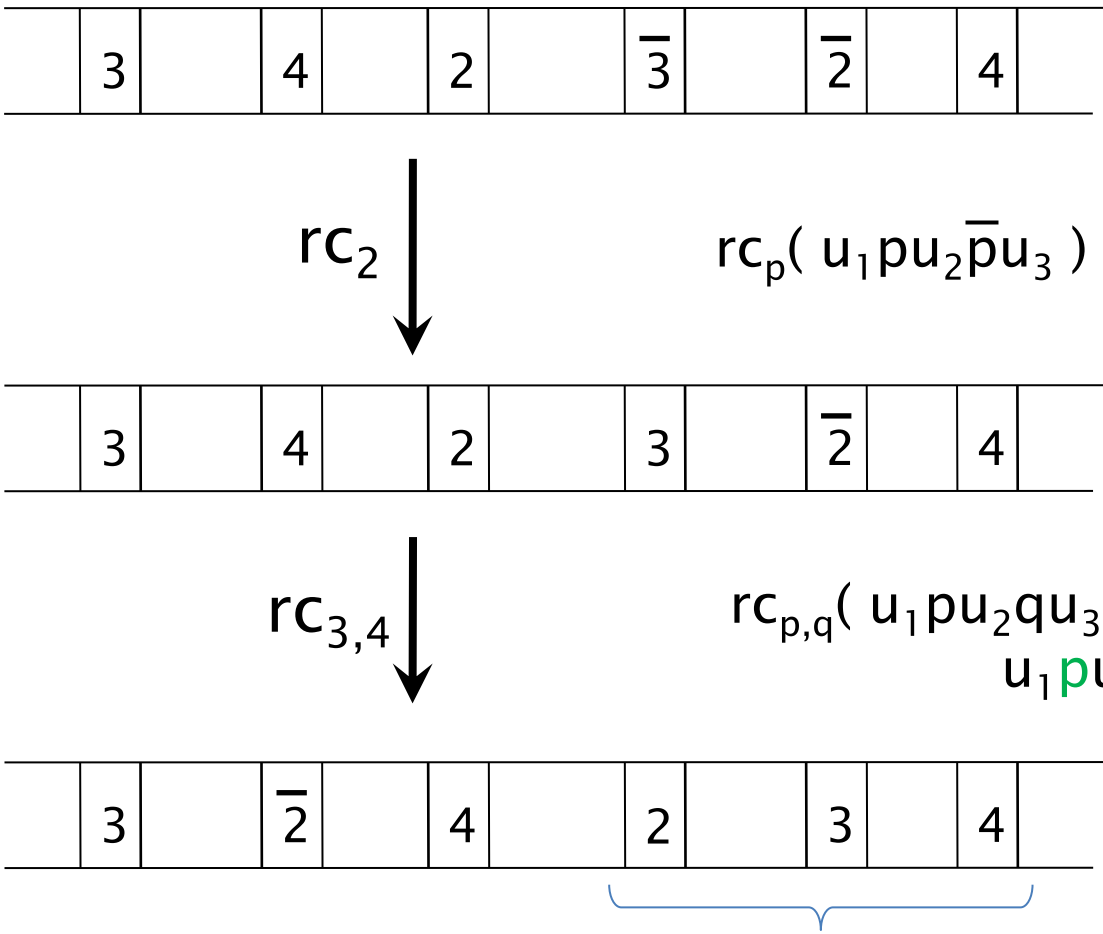
$34 2\bar{3}\,\bar{2}4$

undefined

(we will come beack to this)

sorting = reduction

Micronuclear DNA



$3 4 2 \bar{3}\, \bar{2} 4$

$rc_p(\, u_1 p u_2 \bar{p} u_3 \,) = u_1 p \bar{u}_2 \bar{p} u_3$

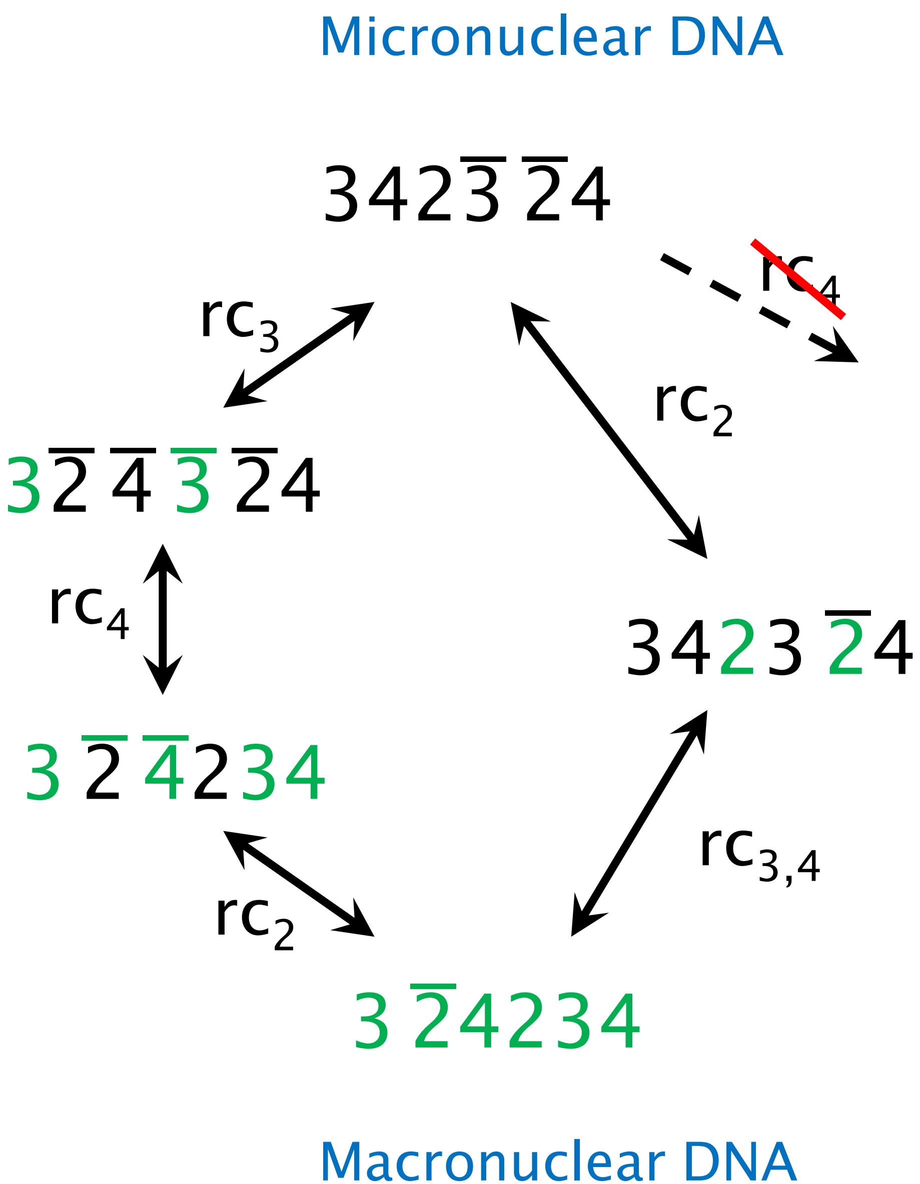
$3 4 2 3\, \bar{2} 4$

$rc_{p,q}(\, u_1 p u_2 q u_3 p u_4 q u_5 \,) =$
$u_1 p u_4 q u_3 p u_2 q u_5$

$3\, \bar{2} 4 2 3 4$

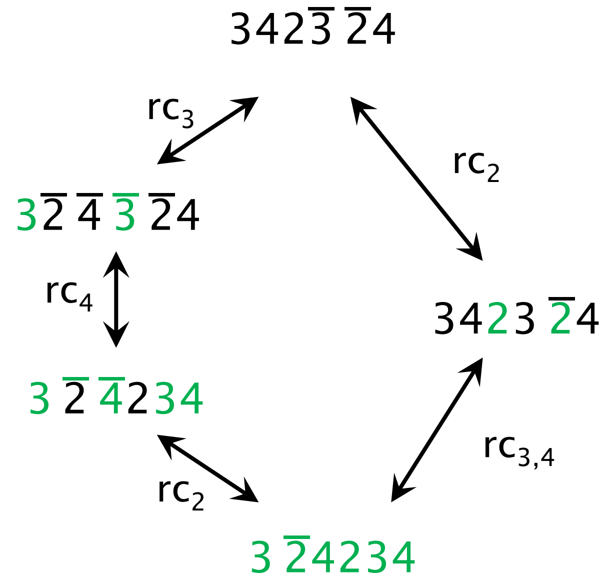
Macronuclear DNA

nondeterministic



$$rc_p(\, u_1 p u_2 \bar{p} u_3 \,) = u_1 p \bar{u}_2 \bar{p} u_3$$

$$rc_{p,q}(\, u_1 p u_2 q u_3 p u_4 q u_5 \,) = u_1 p u_4 q u_3 p u_2 q u_5$$



question:

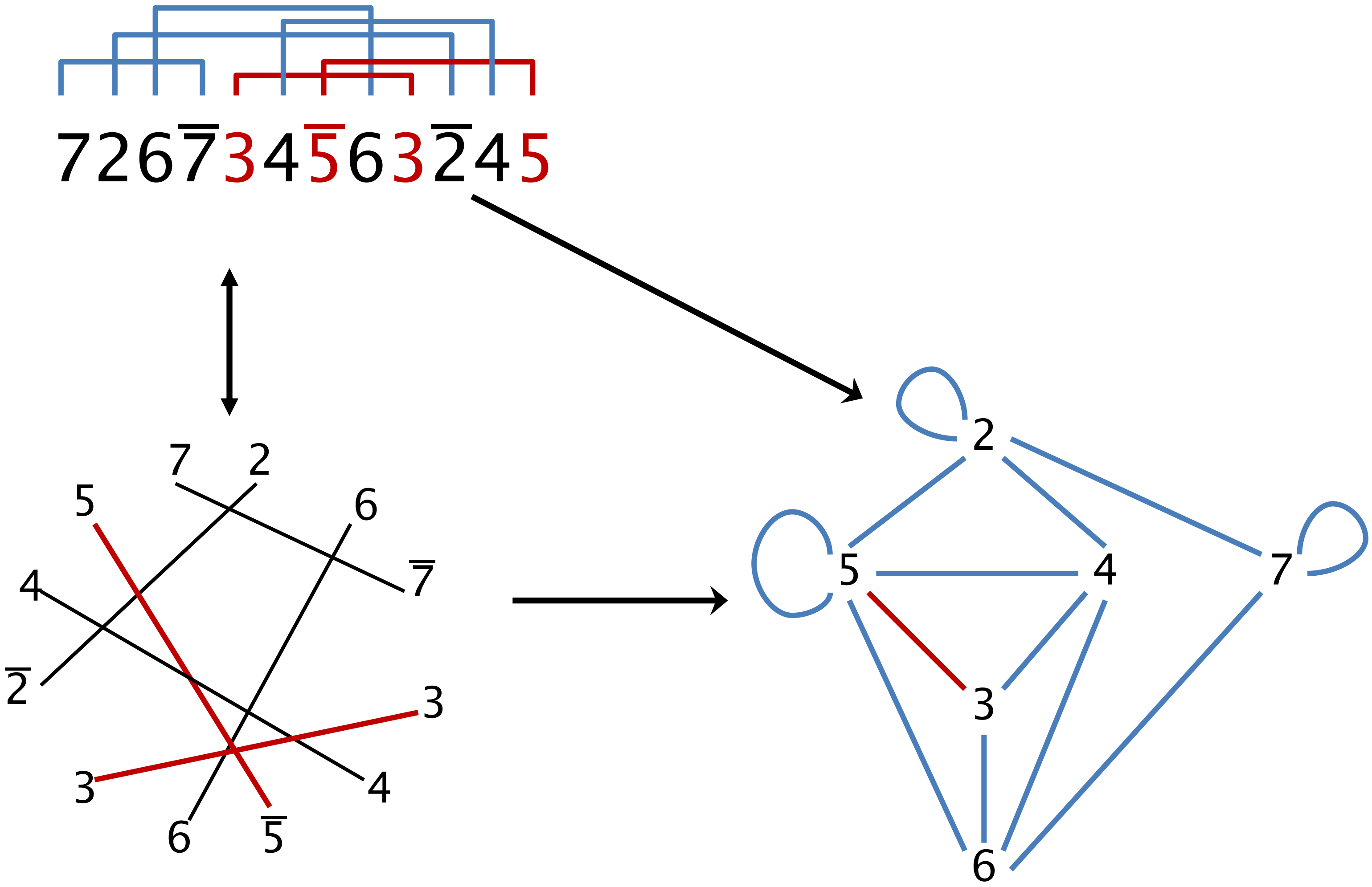
is the result of reductions independent of operations chosen?

2

quest for the "right" model

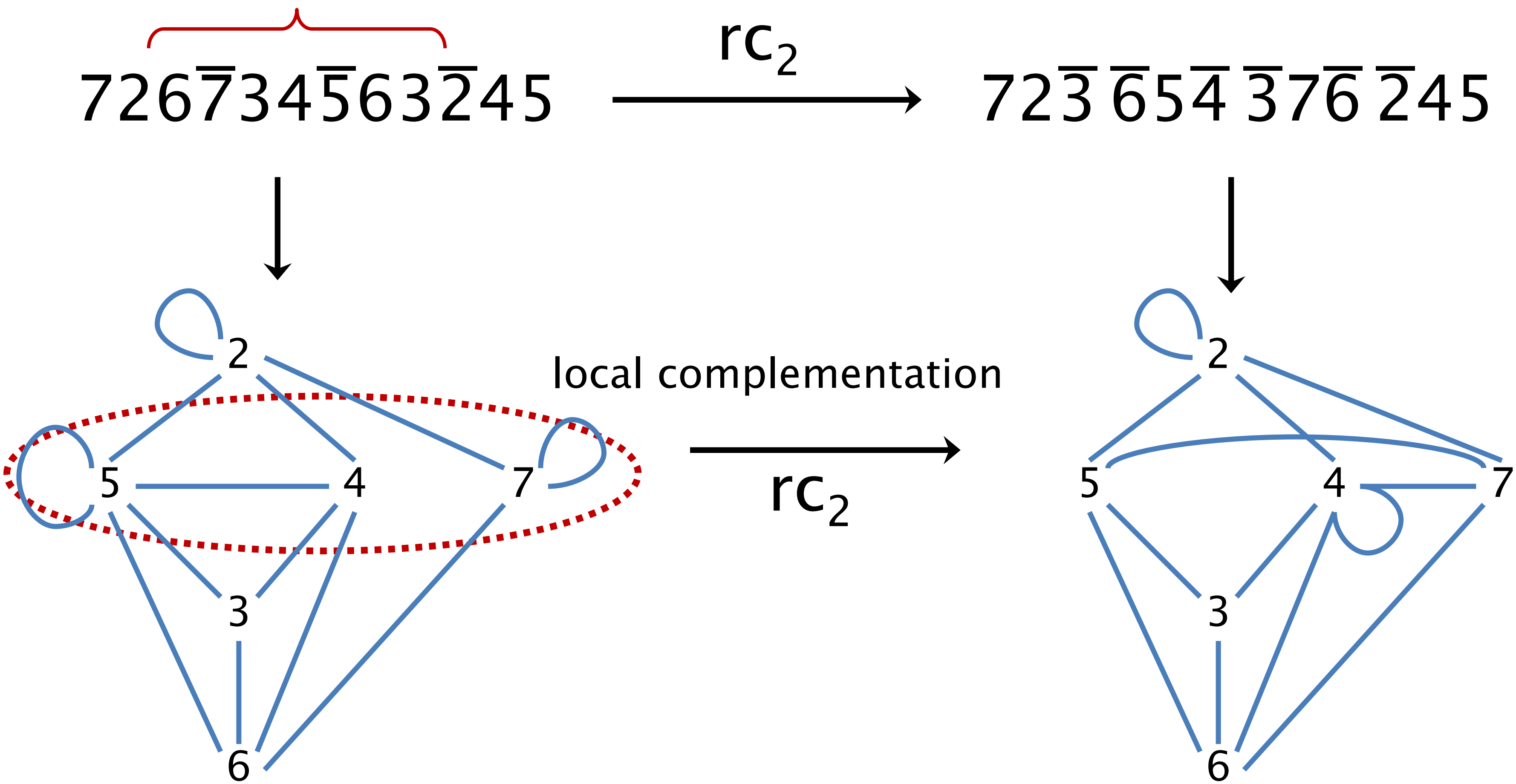
- strings
- graphs
- matrices
- set systems

circle & overlap graph



string to overlap graph

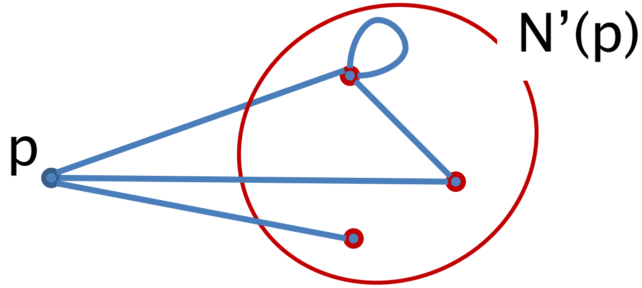
real generalization

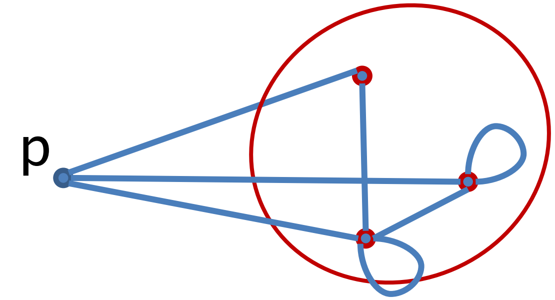


Ehrenfeucht etal, *Theor. Comp. Sci.*, 2003

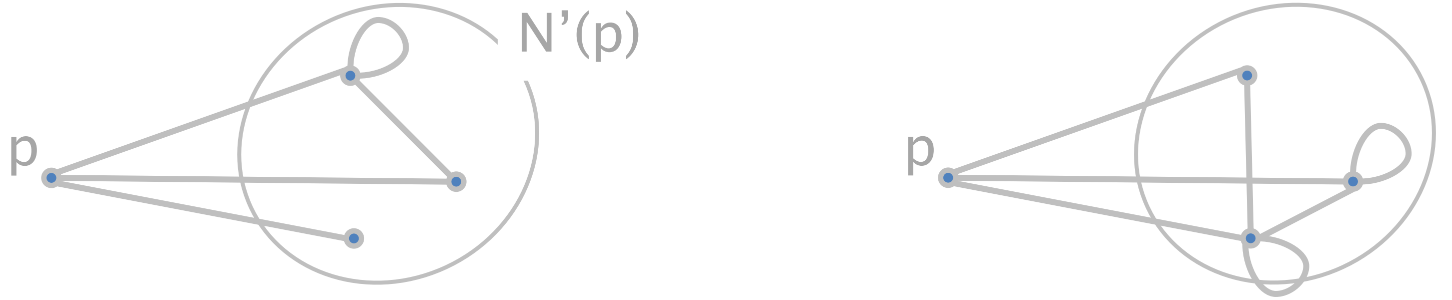
(for signed graphs instead of looped graphs)

rc_p *local complementation* looped vertex p

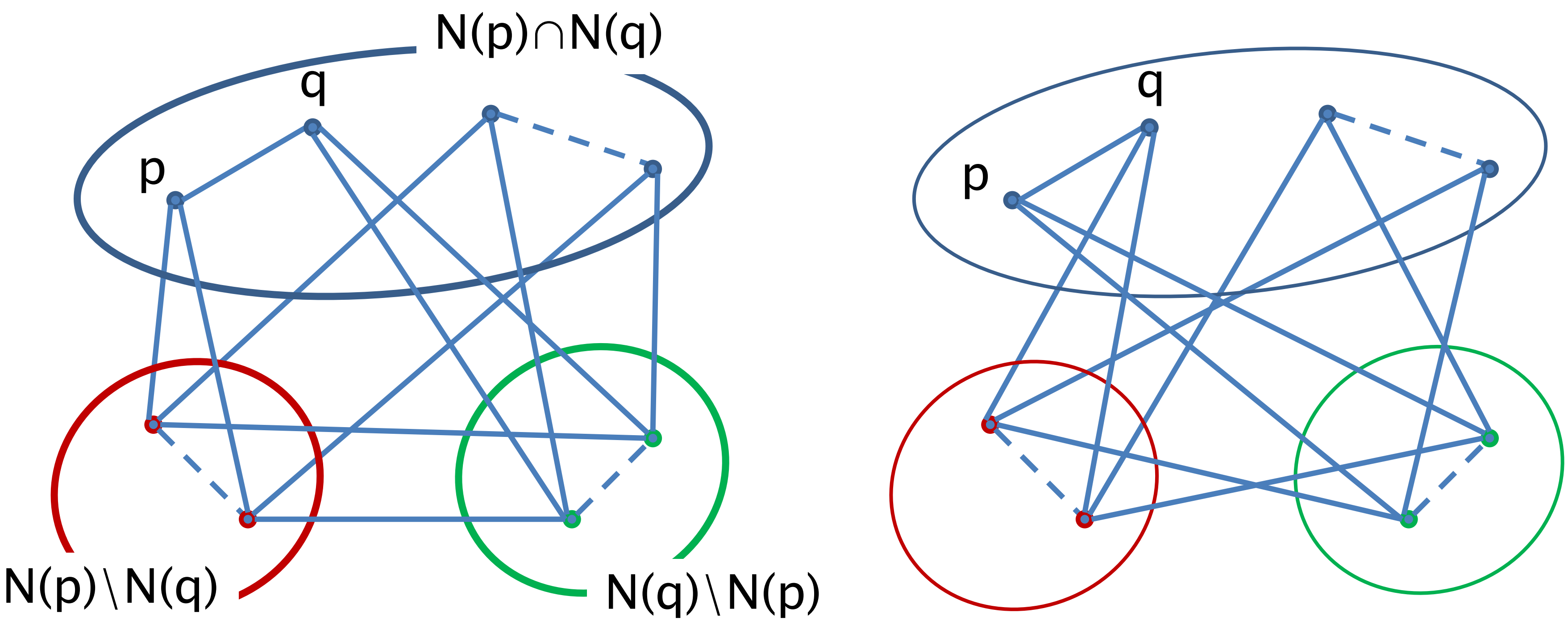




rc_p *local complementation* looped vertex p

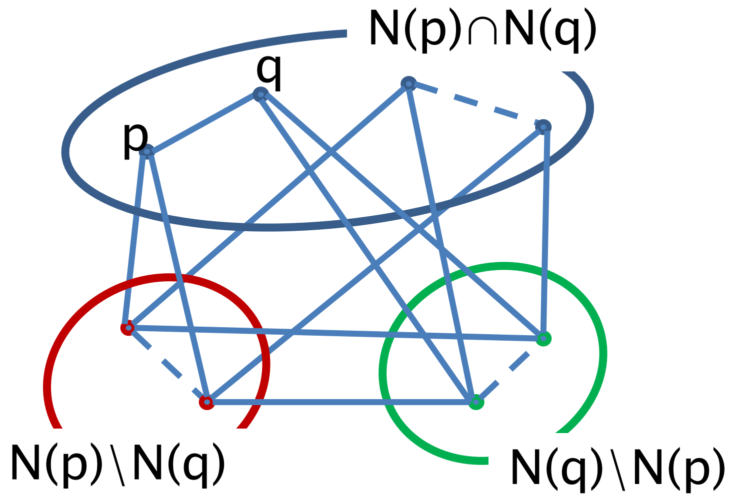


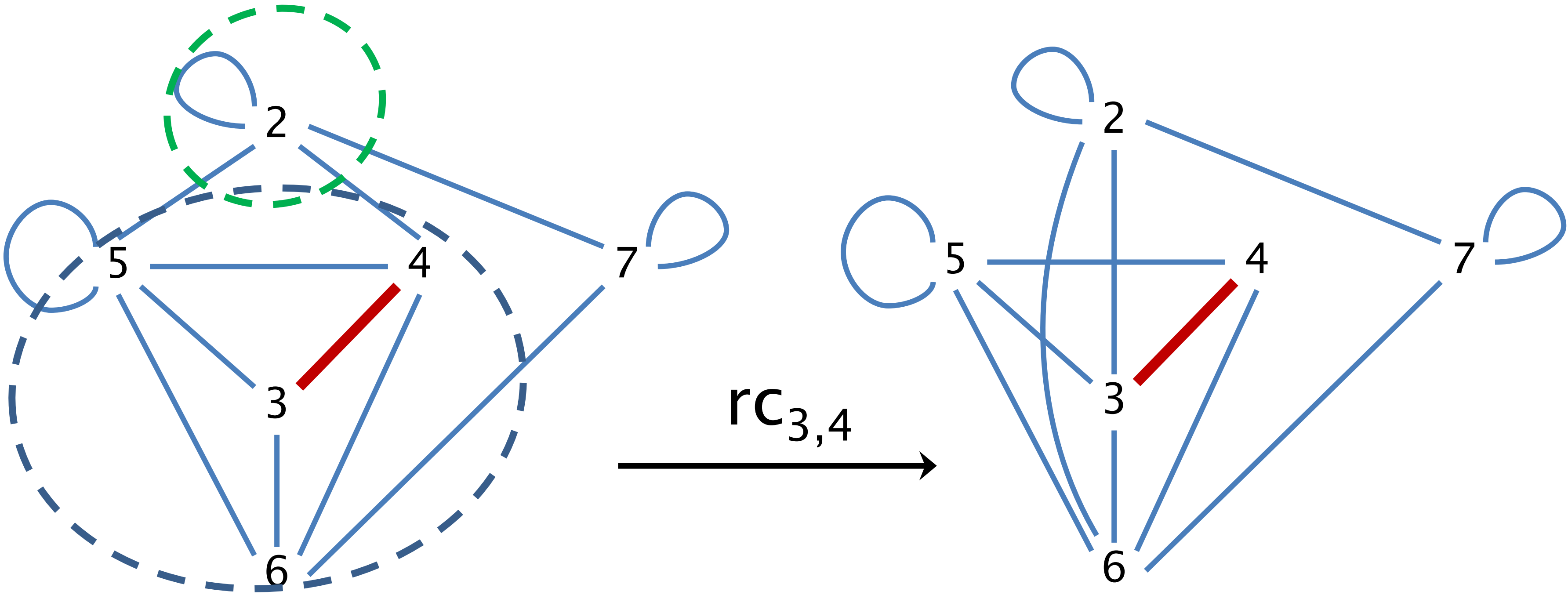
$rc_{p,q}$ *edge complementation* unlooped edge pq



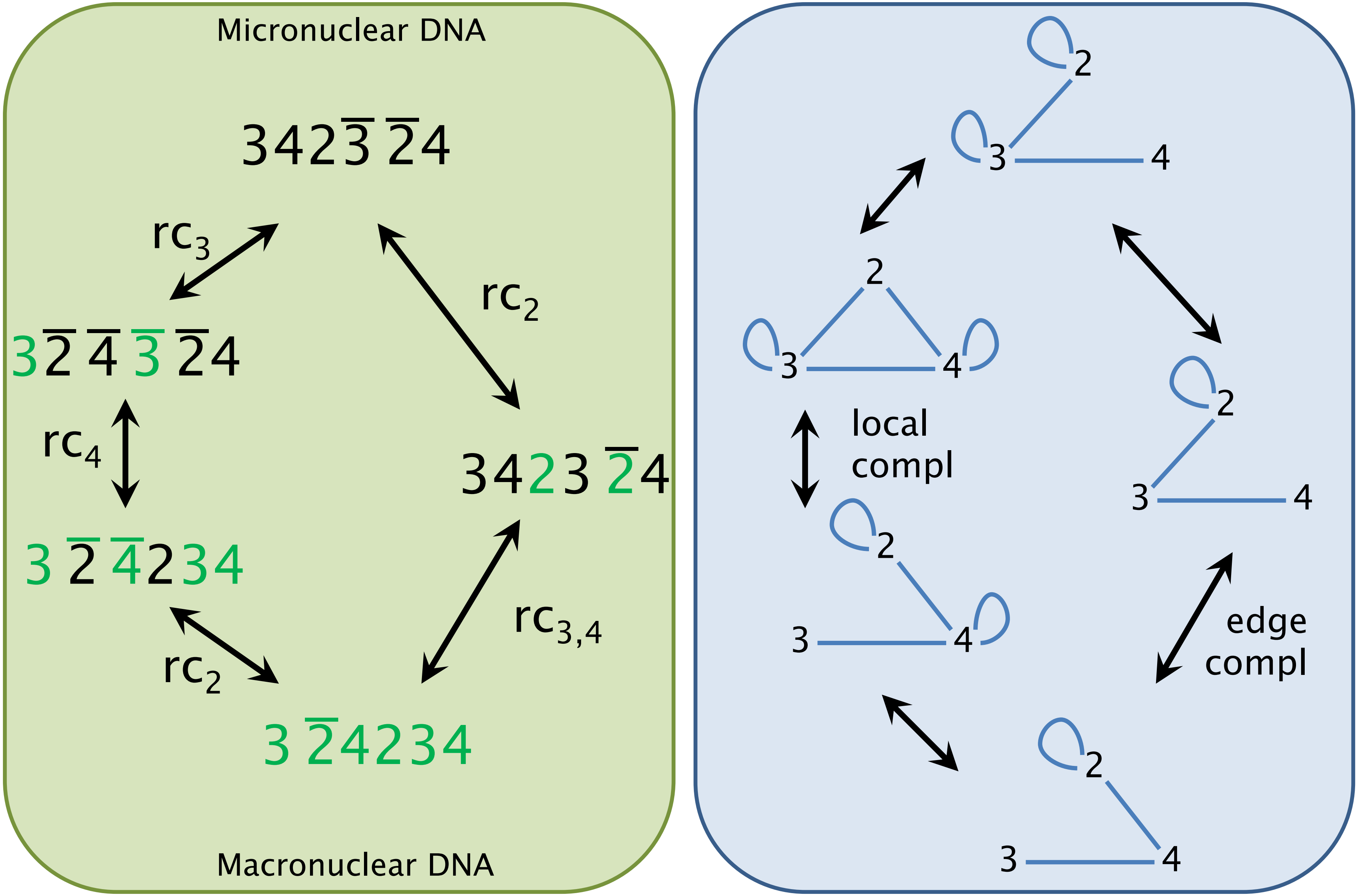
example edge complement

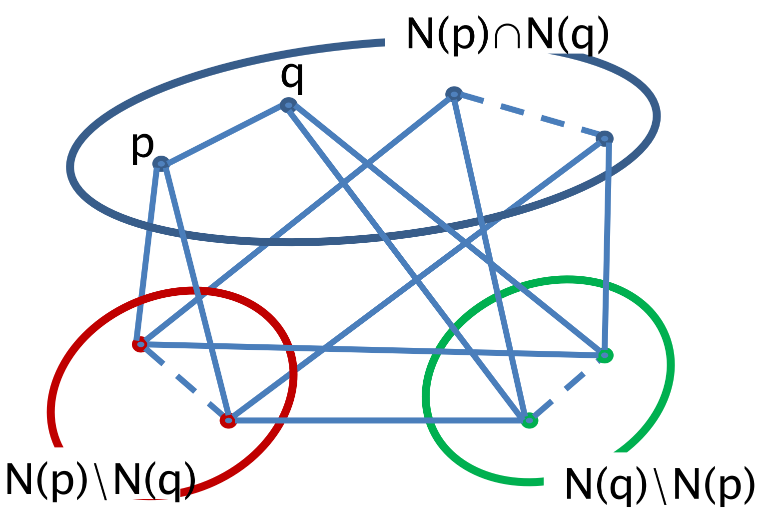
$rc_{3,4}$ on edge 3,4





two worlds


Micronuclear DNA
$3 4 2 \bar{3} \bar{2} 4$
rc3
rc2
$3 \bar{2} \bar{4} \bar{3} \bar{2} 4$
rc4
$3 4 2 3 \bar{2} 4$
$3 \bar{2} \bar{4} 2 3 4$
rc3,4
rc2
$3 \bar{2} 4 2 3 4$
Macronuclear DNA
2
3
4
local
compl
edge
compl



question:

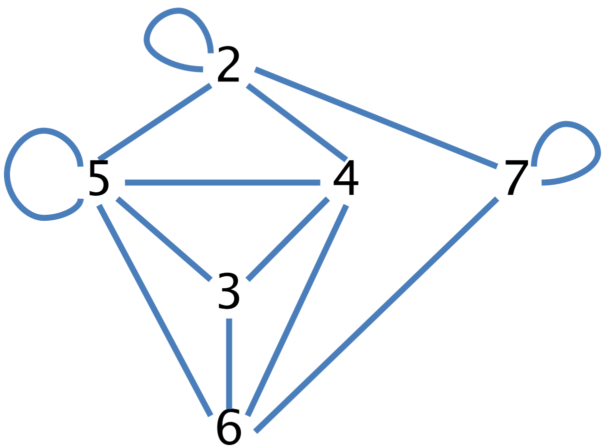
how do $rc_{p,q}$ and $rc_{p',q'}$ interact ?

3

quest for the “right” model

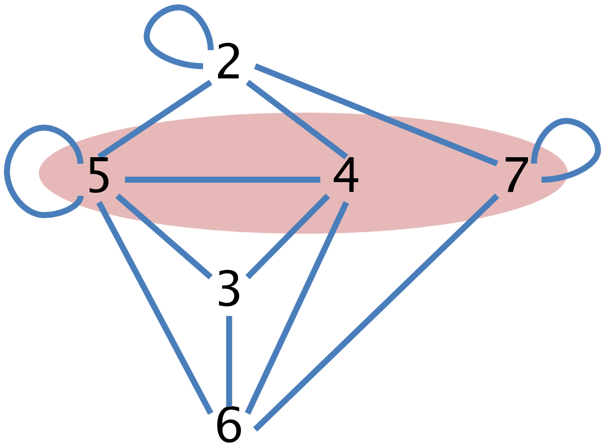
- strings
- graphs
- matrices
- set systems

graphs and matrices



	2	3	4	5	6	7
2	1	0	1	1	0	1
3	0	0	1	1	1	0
4	1	1	0	1	1	0
5	1	1	1	1	1	0
6	0	1	1	1	0	1
7	1	0	0	0	1	1

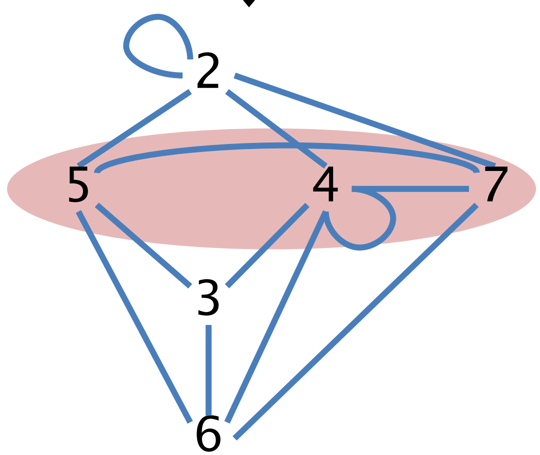
reconsider local/edge complementation



	2	3	4	5	6	7
2	1	0	1	1	0	1
3	0	0	1	1	1	0
4	1	1	0	1	1	0
5	1	1	1	1	1	0
6	0	1	1	1	0	1
7	1	0	0	0	1	1

rc_2

rc_2



	2	3	4	5	6	7
2	1	0	1	1	0	1
3	0	0	1	1	1	0
4	1	1	1	0	1	1
5	1	1	0	0	1	1
6	0	1	1	1	0	1
7	1	0	1	1	1	0

what *is* happening?

$3 4 2 \bar{3} \bar{2} 4$ $\xrightarrow{rc_3\ rc_4\ rc_2}$ $3 \bar{2} 4 2 3 4$

$$\begin{array}{c|ccc} & 2 & 3 & 4 \\ \hline 2 & 1 & 1 & 0 \\ 3 & 1 & 1 & 1 \\ 4 & 0 & 1 & 0 \end{array} \qquad \xrightarrow{rc_3\ rc_4\ rc_2} \qquad \begin{array}{c|ccc} & 2 & 3 & 4 \\ \hline 2 & 1 & 0 & 1 \\ 3 & 0 & 0 & 1 \\ 4 & 1 & 1 & 0 \end{array}$$

multiply (over the binary numbers)

$$\underbrace{\begin{pmatrix} 1 & 1 & 0 \\ 1 & 1 & 1 \\ 0 & 1 & 0 \end{pmatrix}}_{\text{micro}} \underbrace{\begin{pmatrix} 1 & 0 & 1 \\ 0 & 0 & 1 \\ 1 & 1 & 0 \end{pmatrix}}_{\text{macro}} = \begin{pmatrix} & & \\ & & \\ & 0 & \end{pmatrix}$$

$+$ xor $\oplus$ $1+1=0$

$*$ and $\wedge$

what *is* happening? inversion

$3\,4\,2\,\bar{3}\,\bar{2}\,4 \xrightarrow{rc_3\ rc_4\ rc_2} 3\,\bar{2}\,4\,2\,3\,4$

$$\begin{array}{c|ccc} & 2 & 3 & 4 \\ \hline 2 & 1 & 1 & 0 \\ 3 & 1 & 1 & 1 \\ 4 & 0 & 1 & 0 \end{array} \quad \xrightarrow{rc_3\ rc_4\ rc_2} \quad \begin{array}{c|ccc} & 2 & 3 & 4 \\ \hline 2 & 1 & 0 & 1 \\ 3 & 0 & 0 & 1 \\ 4 & 1 & 1 & 0 \end{array}$$

multiply (over the binary numbers)

$$\underbrace{\begin{pmatrix} 1 & 1 & 0 \\ 1 & 1 & 1 \\ 0 & 1 & 0 \end{pmatrix}}_{\text{micro}} \underbrace{\begin{pmatrix} 1 & 0 & 1 \\ 0 & 0 & 1 \\ 1 & 1 & 0 \end{pmatrix}}_{\text{macro}} = \begin{pmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{pmatrix}$$

$$\begin{pmatrix} 1 & 1 & 0 \\ 1 & 1 & 1 \\ 0 & 1 & 0 \end{pmatrix} = \begin{pmatrix} 1 & 0 & 1 \\ 0 & 0 & 1 \\ 1 & 1 & 0 \end{pmatrix}^{-1}$$

sorting DNA = computing the inverse

partial inverse

$A\,x = y$ iff $A^{-1}\,y = x$

principal pivot transform

$$A\begin{bmatrix} x_1 \\ x_2 \end{bmatrix} = \begin{bmatrix} y_1 \\ y_2 \end{bmatrix} \quad \text{iff} \quad A{*}X\begin{bmatrix} y_1 \\ x_2 \end{bmatrix} = \begin{bmatrix} x_1 \\ y_2 \end{bmatrix}$$

← X pointers

← other

$A * X$ is defined iff $A[X]$ is invertible

real recipe (which we do not need)

$$A = \begin{matrix} & X & \\ X & \left(\begin{array}{c|c} P & Q \\ \hline R & S \end{array}\right) \end{matrix} \qquad A * X = \left(\begin{array}{c|c} P^{-1} & -P^{-1}\,Q \\ \hline R\,P^{-1} & S - R\,P^{-1}\,Q \end{array}\right)$$

$P = A[X]$ invertible / nonsingular i.e. $\det P \neq 0$

M.J. Tsatsomeros. Principal pivot transforms: properties and applications.
Linear Algebra and its Applications, 307(1-3):151-165, 2000

principal pivot transform

$$A \begin{pmatrix} x_1 \\ x_2 \end{pmatrix} = \begin{pmatrix} y_1 \\ y_2 \end{pmatrix} \quad \text{iff} \quad A{*}X \begin{pmatrix} y_1 \\ x_2 \end{pmatrix} = \begin{pmatrix} x_1 \\ y_2 \end{pmatrix}$$

using partial inversion

xor

$$(A * X) * Y = A * (X \oplus Y)$$ (when defined)

$$A * \{p_1, p_2\} \ldots * p_n = A * V = A^{-1}$$ (all pointers)

this shows

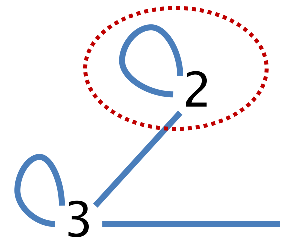
- how the rc_p and $rc_{p,q}$ interact
- result does not depend on order of operations

applicability

A * X is defined iff A[X] is invertible

rc_2

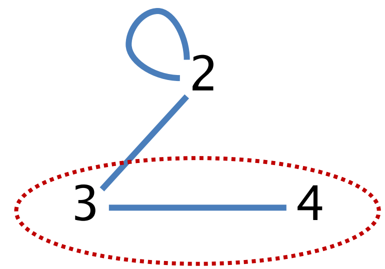
$3\,4\,2\,\overline{3}\,\overline{2}\,4$



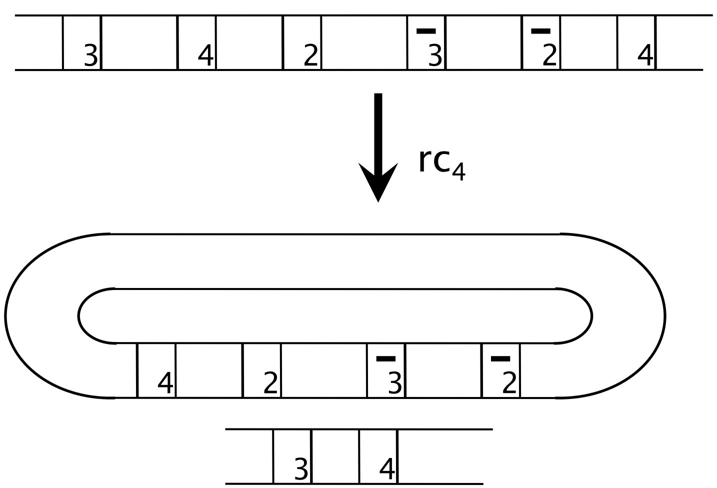
$$\begin{pmatrix} 1 & 1 & 0 \\ 1 & 1 & 1 \\ 0 & 1 & 0 \end{pmatrix}$$

$rc_{3,4}$

$3\,4\,2\,3\,\overline{2}\,4$

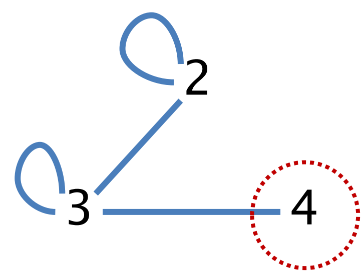


$$\begin{pmatrix} 1 & 1 & 0 \\ 1 & 0 & 1 \\ 0 & 1 & 0 \end{pmatrix}$$



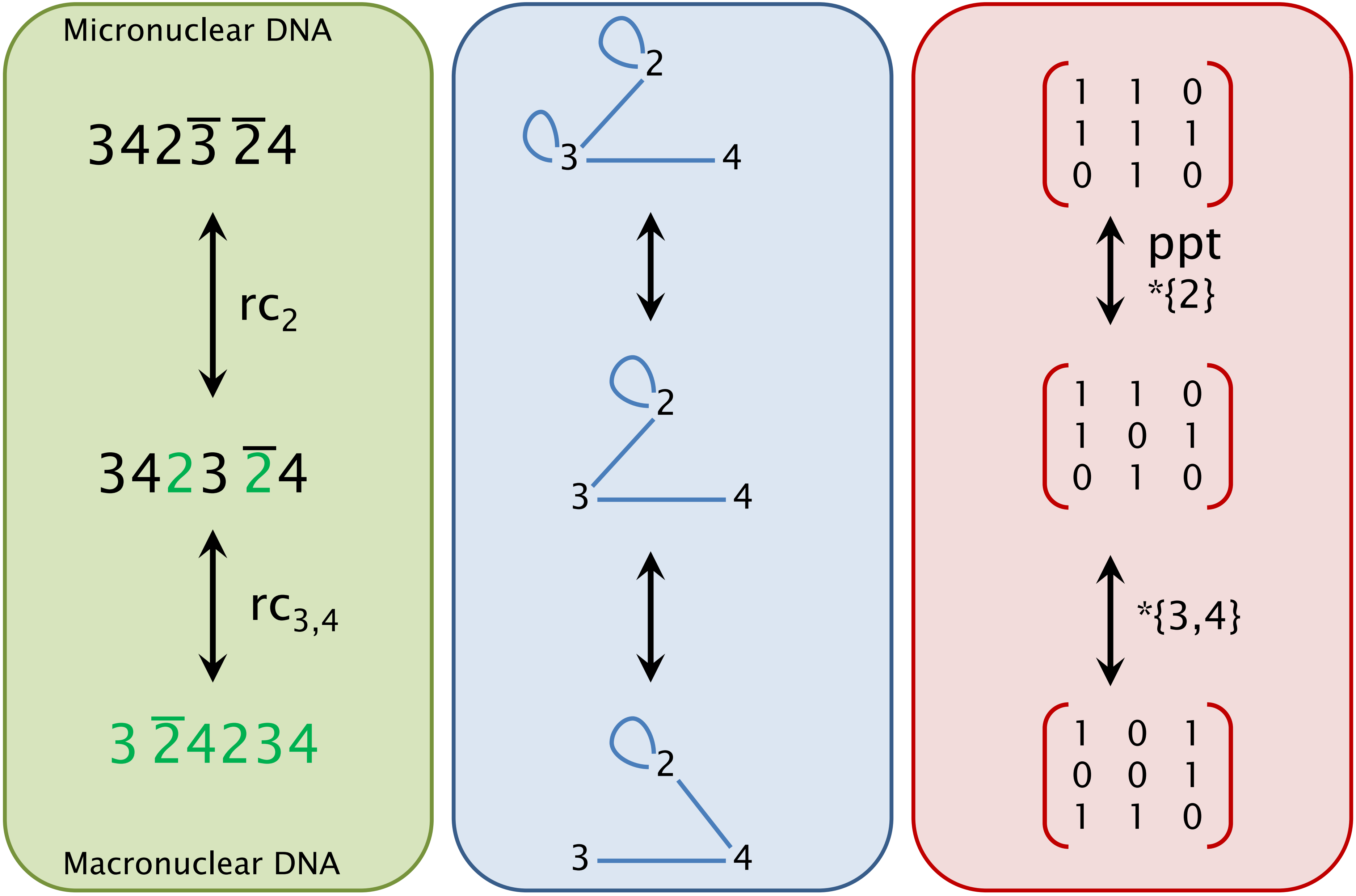
$3\,4\,2\,\overline{3}\,\overline{2}\,4$

undefined



	2	3	4
2	1	1	0
3	1	1	1
4	0	1	0

three worlds



conclusion (for now)

- by careful modeling we find that gene assembly is *actually* principal pivot transform (ppt)
- we can use results about ppt to know more about gene assembly
  - independent order operations
  - interaction operations

quest for the "right" model

- strings
- graphs
- matrices
- set systems

the most elegant model was hidden

4

applicable sets

A * X is defined iff A[X] is invertible

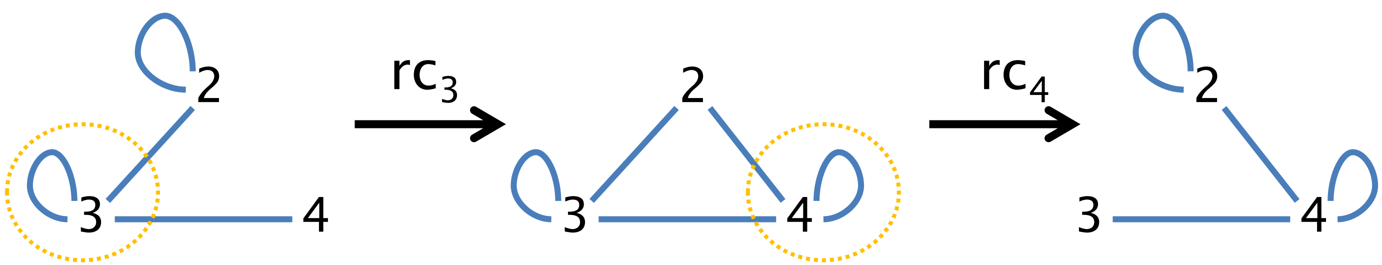
$$\begin{array}{c|ccc} & 2 & 3 & 4 \\ \hline 2 & 1 & 1 & 0 \\ 3 & 1 & 1 & 1 \\ 4 & 0 & 1 & 0 \end{array} \quad \longleftrightarrow$$

A[{3,4}]

set system

V = {2,3,4}

D = { ∅, {2}, {3}, {2,4}, {3,4}, {2,3,4} }



which operation ?

graphs $\subseteq$ set systems (strict)

$342\bar{3}\bar{2}4$

$$\begin{array}{c|ccc} & 2 & 3 & 4 \\ \hline 2 & 1 & 1 & 0 \\ 3 & 1 & 1 & 1 \\ 4 & 0 & 1 & 0 \end{array} \quad \longleftrightarrow \quad \begin{array}{l} V = \{2,3,4\} \\ D = \{\, \emptyset, \{2\}, \{3\}, \{2,4\}, \{3,4\}, \{2,3,4\} \,\} \end{array}$$

$\updownarrow$ rc_3 $\qquad\qquad$ $\updownarrow$?

$3\bar{2}\bar{4}\bar{3}\bar{2}4$

$$\begin{array}{c|ccc} & 2 & 3 & 4 \\ \hline 2 & 0 & 1 & 1 \\ 3 & 1 & 1 & 1 \\ 4 & 1 & 1 & 1 \end{array} \quad \longleftrightarrow \quad \begin{array}{l} V = \{2,3,4\} \\ D' = \{\, \emptyset, \{3\}, \{4\}, \{2,3\}, \{2,4\}, \{2,3,4\} \,\} \end{array}$$

graphs $\subseteq$ set systems (strict)

$3\,4\,2\,\overline{3}\,\overline{2}\,4$

$$\begin{array}{c|ccc} & 2 & 3 & 4 \\ \hline 2 & 1 & 1 & 0 \\ 3 & 1 & 1 & 1 \\ 4 & 0 & 1 & 0 \end{array} \longleftrightarrow \begin{array}{l} V = \{2,3,4\} \\ D = \{ \emptyset, \{2\}, \{3\}, \{2,4\}, \{3,4\}, \{2,3,4\} \} \end{array}$$

$\updownarrow$ rc_3 $\qquad\qquad$ $\updownarrow$?

$3\,\overline{2}\,\overline{4}\,\overline{3}\,\overline{2}\,4$

$$\begin{array}{c|ccc} & 2 & 3 & 4 \\ \hline 2 & 0 & 1 & 1 \\ 3 & 1 & 1 & 1 \\ 4 & 1 & 1 & 1 \end{array} \longleftrightarrow \begin{array}{l} V = \{2,3,4\} \\ D' = \{ \{3\}, \{2,3\}, \emptyset, \{2,3,4\}, \{4\}, \{2,4\} \} \end{array}$$

graphs $\subseteq$ set systems (strict)

$3\,4\,2\,\overline{3}\,\overline{2}\,4$

$$\begin{array}{c|ccc} & 2 & 3 & 4 \\ \hline 2 & 1 & 1 & 0 \\ 3 & 1 & 1 & 1 \\ 4 & 0 & 1 & 0 \end{array} \quad \longleftrightarrow \quad \begin{array}{l} V = \{2,3,4\} \\ D = \{\, \emptyset, \{2\}, \{3\}, \{2,4\}, \{3,4\}, \{2,3,4\} \,\} \end{array}$$

rc_3 $\updownarrow$ $\oplus 3$ $\updownarrow$ xor 3

$3\,\overline{2}\,\overline{4}\,\overline{3}\,\overline{2}\,4$

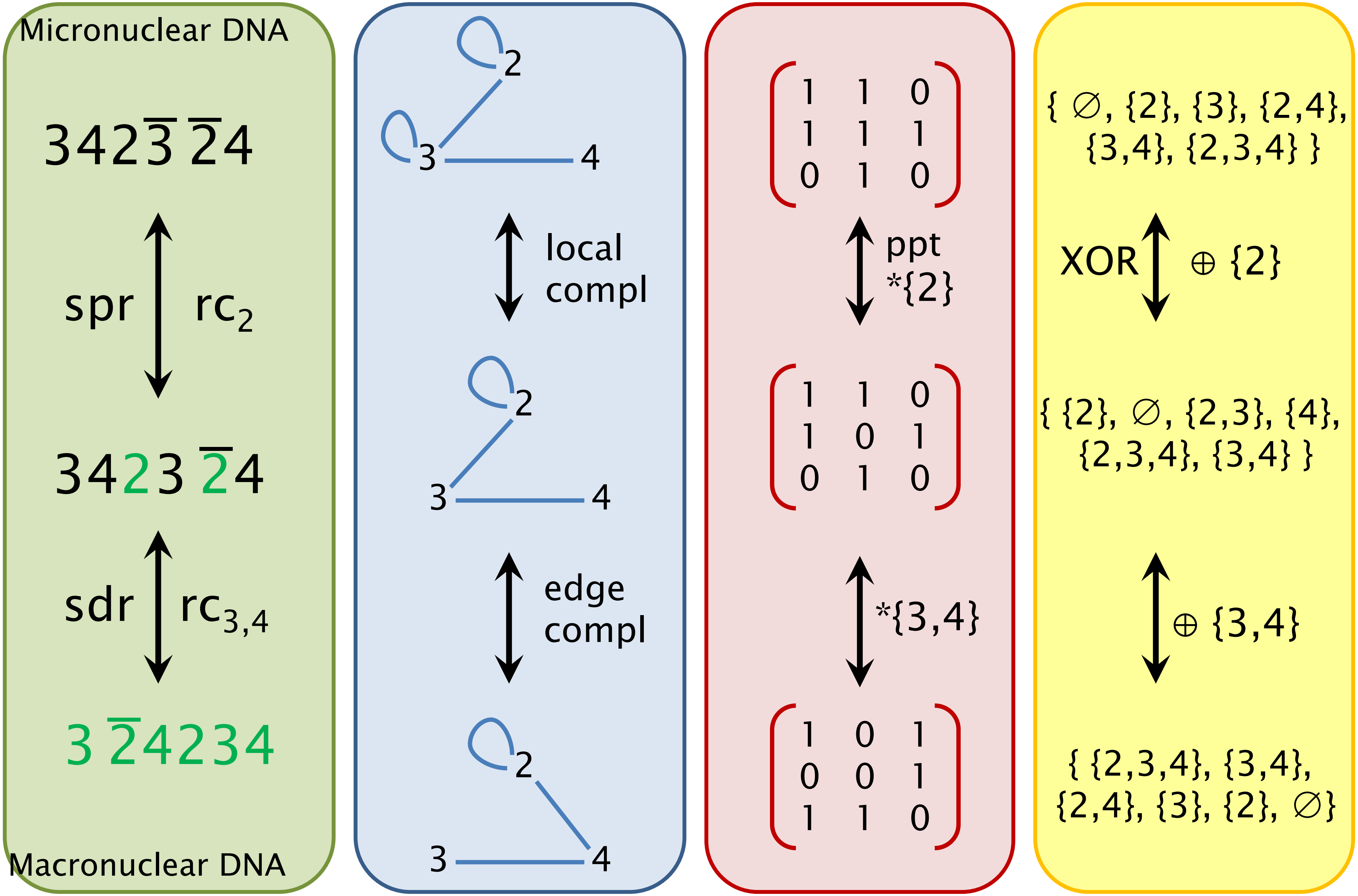
$$\begin{array}{c|ccc} & 2 & 3 & 4 \\ \hline 2 & 0 & 1 & 1 \\ 3 & 1 & 1 & 1 \\ 4 & 1 & 1 & 1 \end{array} \quad \longleftrightarrow \quad \begin{array}{l} V = \{2,3,4\} \\ D' = \{\, \{3\}, \{2,3\}, \emptyset, \{2,3,4\}, \{4\}, \{2,4\} \,\} \end{array}$$

applicability (!)

XOR {4} is defined, while rc_4 is not

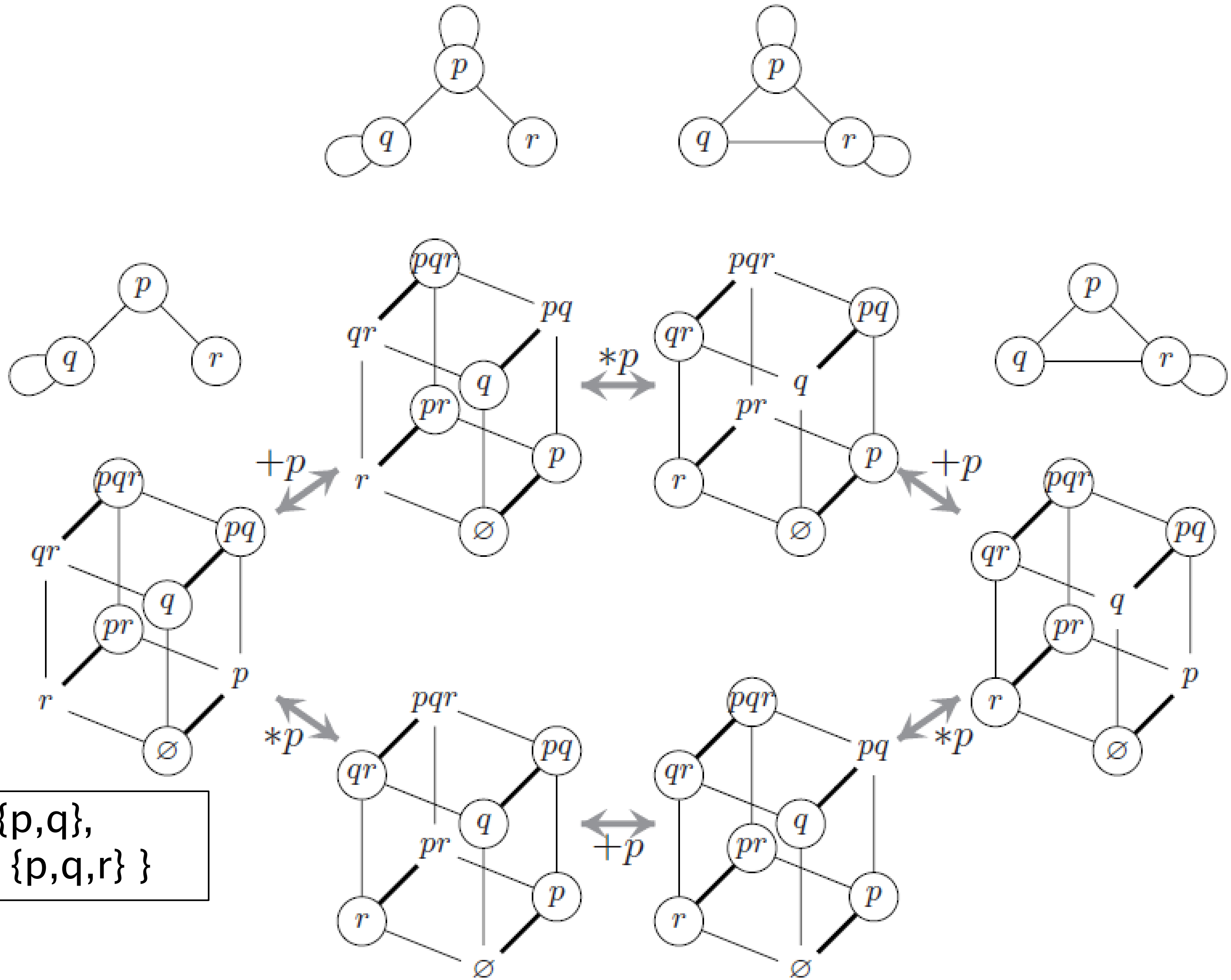
nb. {4} not in D

four worlds



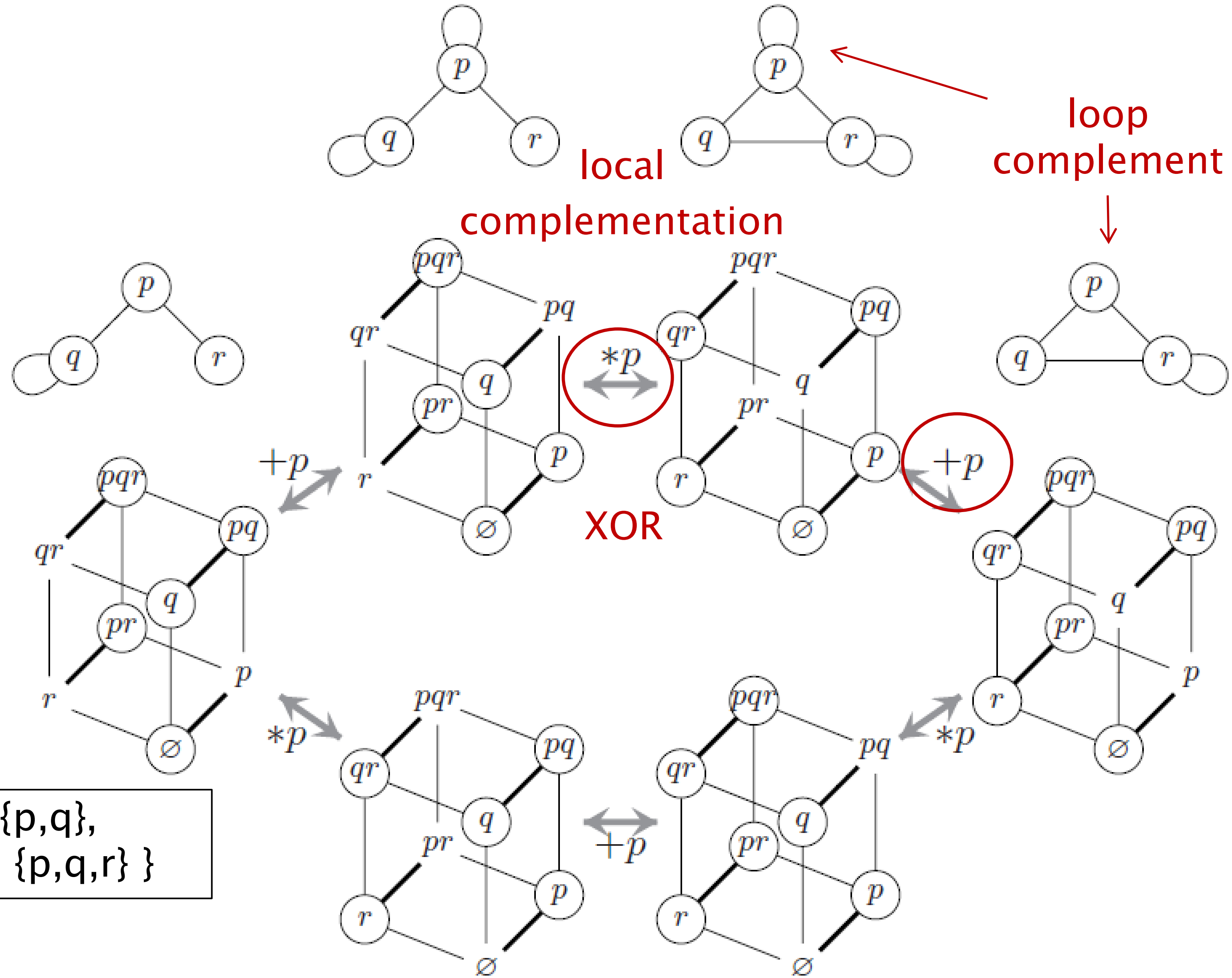
Micronuclear DNA
$342\overline{3}\,\overline{2}4$
spr
rc_2
$3423\overline{2}4$
sdr
$rc_{3,4}$
$3\overline{2}4234$
Macronuclear DNA
2
3
4
local
compl
2
3
4
edge
compl
2
3
4
1 1 0
1 1 1
0 1 0
ppt
*{2}
1 1 0
1 0 1
0 1 0
*{3,4}
1 0 1
0 0 1
1 1 0
{ ∅, {2}, {3}, {2,4}, {3,4}, {2,3,4} }
XOR
⊕ {2}
{ {2}, ∅, {2,3}, {4}, {2,3,4}, {3,4} }
⊕ {3,4}
{ {2,3,4}, {3,4}, {2,4}, {3}, {2}, ∅}

algebra of set systems



{ ∅, {q}, {p,q},
{p,r}, {p,q,r} }

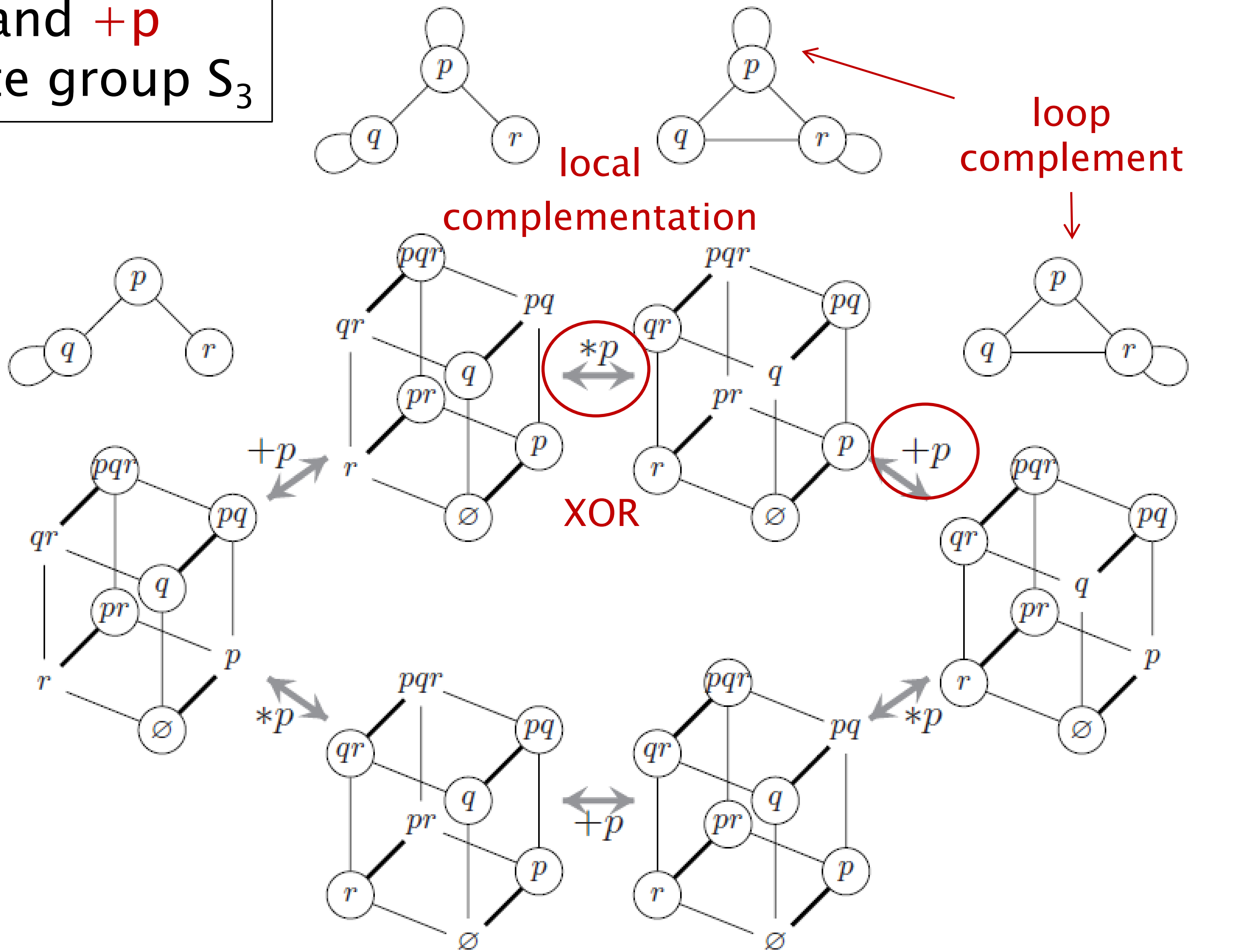
algebra of set systems



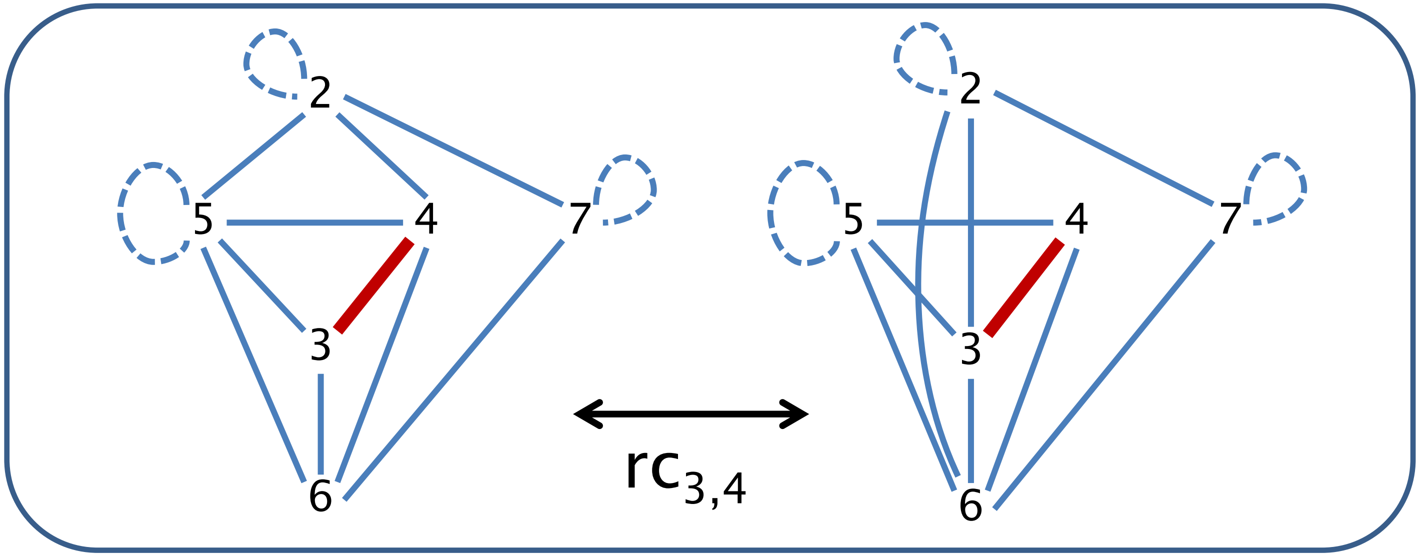
{ ∅, {q}, {p,q},
{p,r}, {p,q,r} }

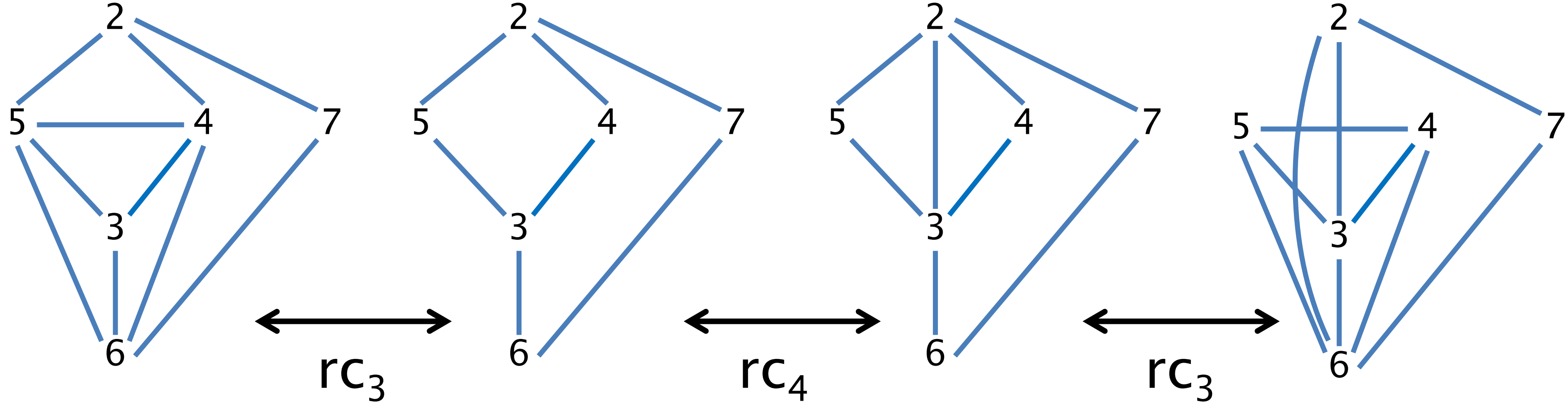
algebra of set systems

*p and +p generate group S_3



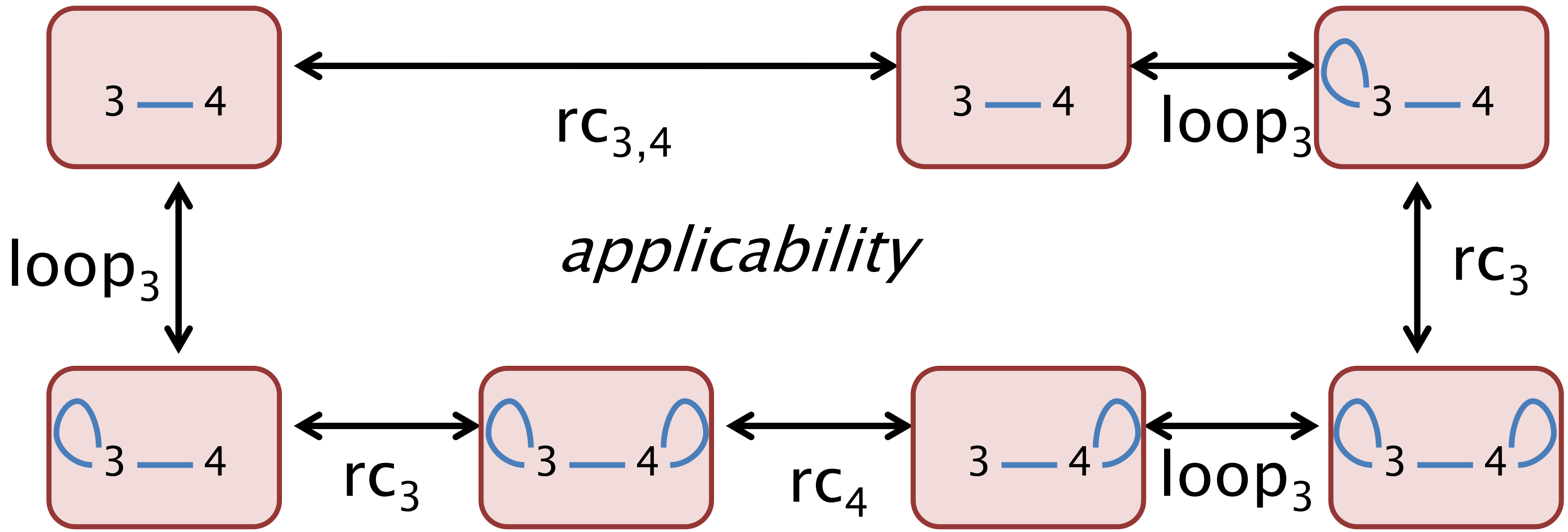
edge complement vs. local complement





ignoring loops

edge complement vs. local complement



basic algebra S_3

*3 *4 = *4 *3

*3 *3 = id = +3 +3

+3 *3 +3 = *3 +3 *3

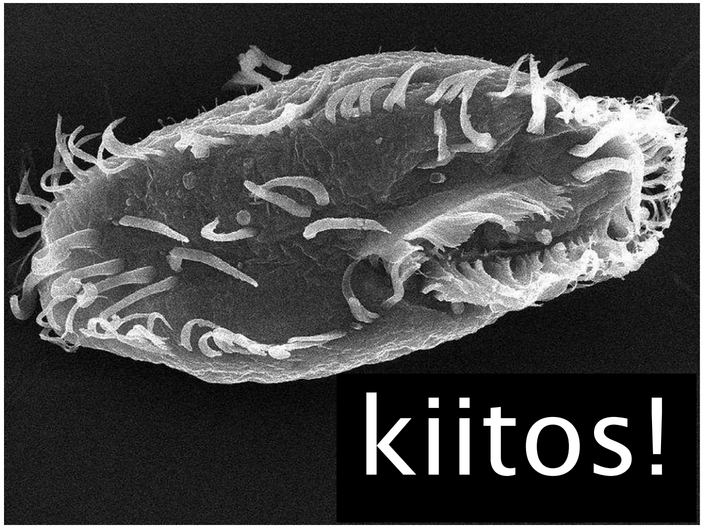
+3 *3 *4 +3 *3 +3 =
+3 *3 +3 *3 +3 *4 =
+3 *3 *3+3 *3 *4 =
+3 +3 *3 *4 =
*3 *4 =
*{3,4}

conclusion (updated)

- by careful modeling we find that gene assembly is *actually* principal pivot transform (ppt) and XOR
- we can use results about ppt (on matrices) and XOR (on set systems) to know more about gene assembly
- but also inspiration the other way around …

however …

- parallellism
- ‘simple’ operations



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(*this one you know, of course*)