Démonstration 11/Ift3290

Calcul Moléculaire

Ordinateur à ADN

Le 12 Avril 2003

Calcul moléculaire

- Le lien entre l’informatique et la biologie moléculaire est la similitude du langage utilisé pour former des mots
- La présentation de l’information au lieu qu’elle soit binaire 0 et 1, correspondant aux impulsions du courant, sera de quatre symboles de l’ADN (A,C,G,T ou U pour l’ARN), donc au lieu d’avoir A = 10000001 en binaire pourrait devenir AGTCTGCT tours sur 8 bits (4^8).
- La différence est aussi physique, les transistors sont remplacés par des éprouvettes d’ADN, vu que les instructions vont changer.
- L’information doit être fournie, d’ou plusieurs opérations sont nécessaires. Les opérations équivalentes aux opérateurs logiques sont assumées par des enzymes qui coupent, copient, réparent ou collent des segments.

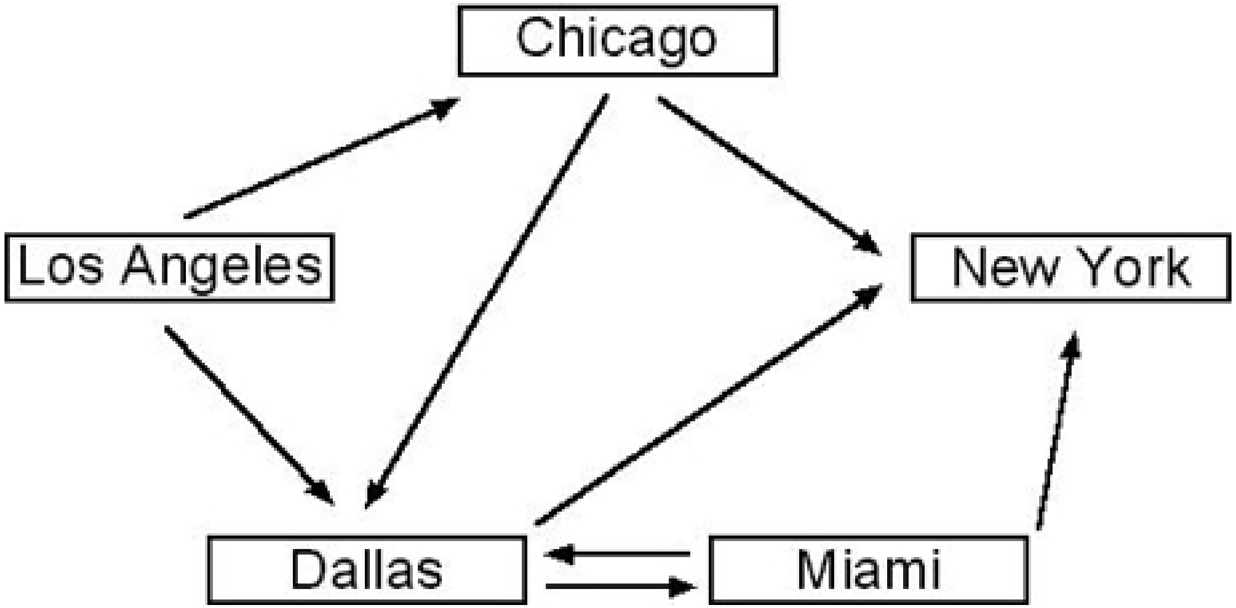
ADN vs Silicium

- ADN structure de donnée en soi
- Plusieurs ops en paralléle
- PC basés sur les transistors séquentiel.

Résolution Pb Hamilton silicium vs ADN

- Méthode naive:arbre de recherche, et parcours chaque branche séquentiellement.
- Amélioration, coupé l'arbre.
- Génération de tous les chemins impossible trop long. Liste des routes avec 20 villes (18!)

Expérience de Adleman



Algorithme

- Genérer tous les chemins possibles.
- Sélectionner les chemins avec début ville origine et fin ville finale.
- Choisir le chemin avec le bon nombre de villes.
- Sélectionner les itinéraires qui ne contiennet qu’une seule ville.

Génération de tous les chemins possibles.

- Los Angeles GCTACG
- Chicago CTAGTA
- Dallas TCGTAC
- Miami CTACGG
- New York ATGCCG

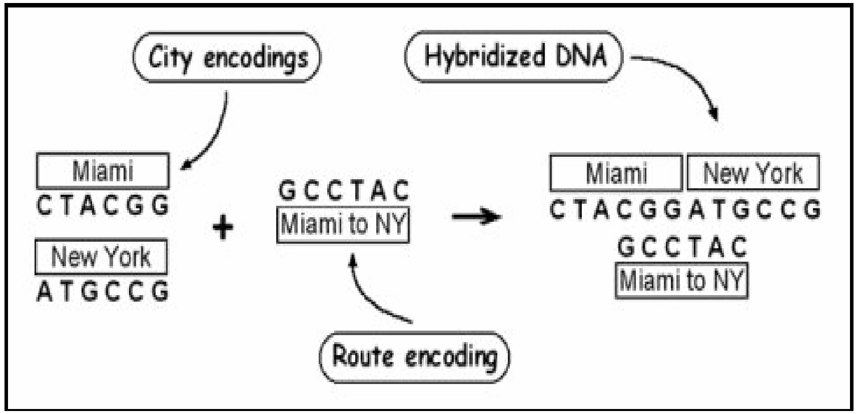
LA > Chicago > Dallas > Miami > NY

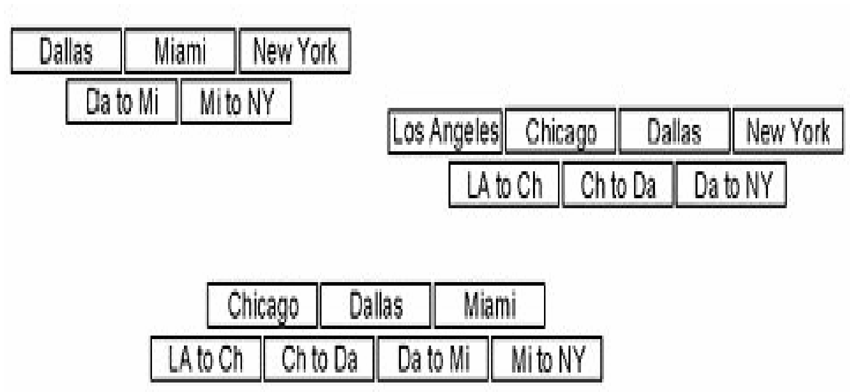
GCTACGCTAGTATCGTACCTACGGATGCCG

Comment générer ? : les synthétiseur d'ADN

Av : complémentarité : exemple R(Miami(CTACGG) et NY(ATGCCG)) Miami (CGG) et NY (ATG)

Connection des brins ADN avec enzyme (ligase)

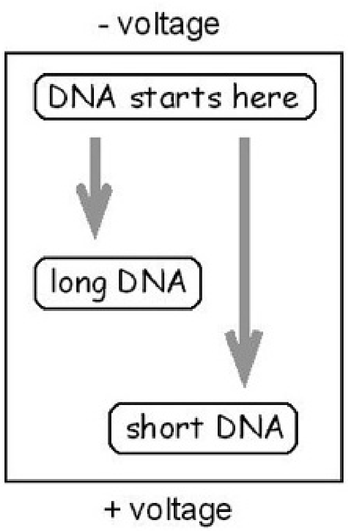


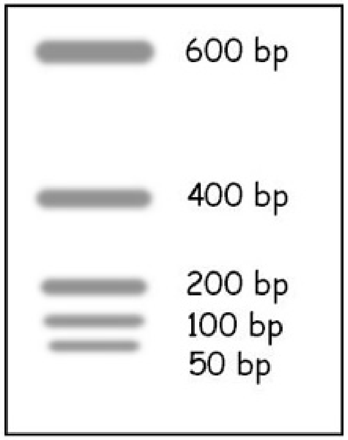


Sélection des itinéraires

- Statégie: copier et amplifier l’ADN qui débute avec LA et fini par NY (technique PCR).
- On se retrouve avec un tube plein dÀDN double brin de longueurs variables

Dernière Étape



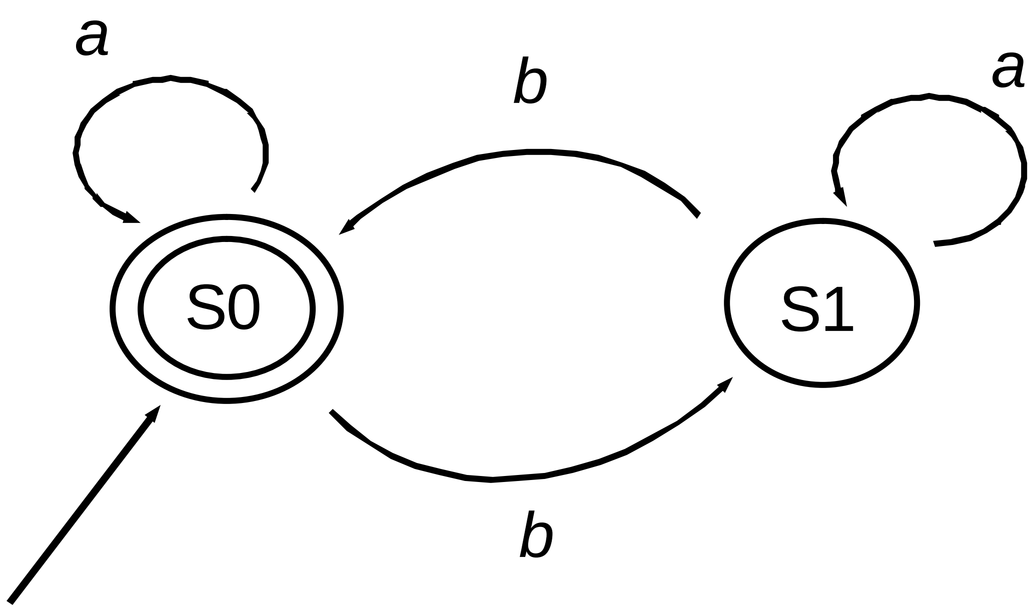


- Sélectionner les itinéraires qui contiennent le nombre correct de villes.
- Classer par longueur et sélectionner l'ADN avec 5 comme longueur.

Exemple de séquenceur d'ADN fait par une compagnie canadienne (visgen.com)

- Une bonne façon de transformer une information en une autre selon un certain processus consistera à utiliser un automate.
- Les caractéristiques qui permettent de modéliser le processus de transformation de la molécule d'ADN, qui sont la combinaison de l'information codante et les capacités de reconnaissance de l'ADN et la machinerie enzymatique.
- Avec un automate à état fini, comprenant l'ADN et les enzymes, les problèmes computationnels peuvent se résoudre de façon autonome. Le matériel consistera en les enzymes de restriction nucléase et ligase, le double brin d'ADN comme paramètres d'entrée, et un peu de programmation pour sélectionner les molécules qu'il faut.

Automaton *A1* accepting inputs with an even number of *b* 's

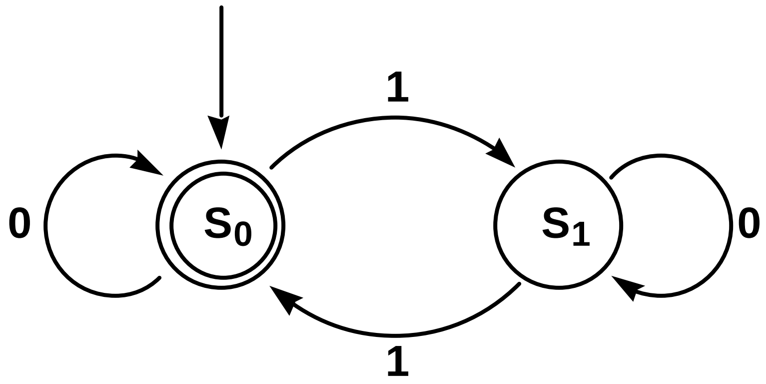


A1: even number of *b*'s

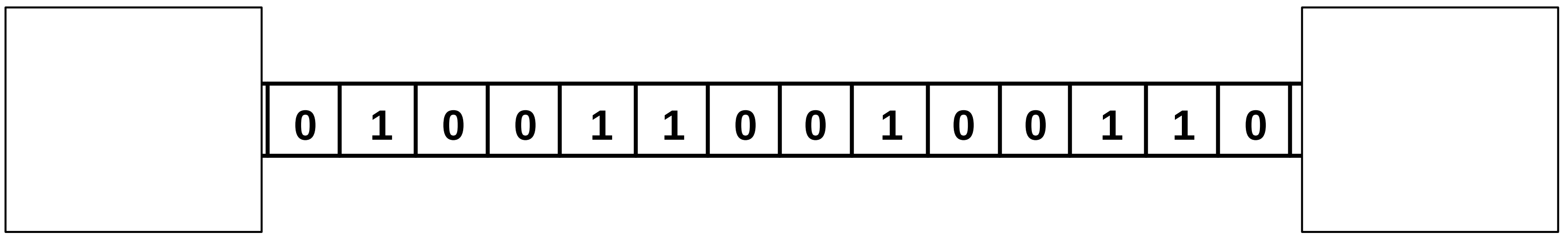
Turing Machine and Finite Automaton

$S_0,0 \Rightarrow S_0$
$S_1,0 \Rightarrow S_1$
$S_0,1 \Rightarrow S_1$
$S_1,1 \Rightarrow S_0$

State transition rules



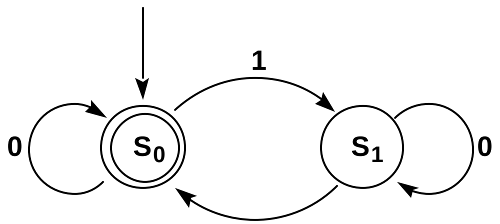
State transition diagram



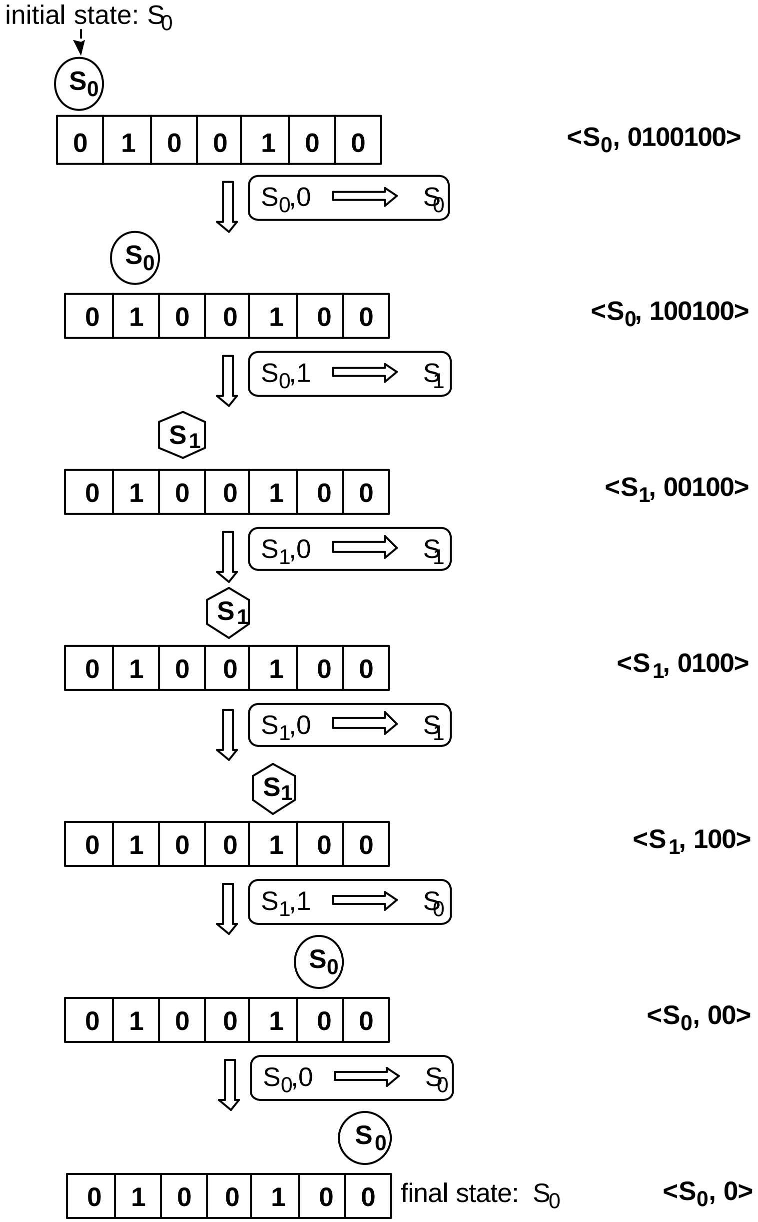
Example Computation

$S_0,0 \Longrightarrow S_0$
$S_1,0 \Longrightarrow S_1$
$S_0,1 \Longrightarrow S_1$
$S_1,1 \Longrightarrow S_0$

State transition rules



State transition diagram



An example computation over *abaaba*

S0-abaaba $(S0\ ?\overset{a}{?}?\ S0)$

S0-baaba $(S0\ ?\overset{b}{?}?\ S1)$

S1-aaba $(S1\ ?\overset{a}{?}?\ S1)$

S1-aba $(S1\ ?\overset{a}{?}?\ S1)$

S1-ba $(S1\ ?\overset{b}{?}?\ S0)$

S0-a $(S0\ ?\overset{a}{?}?\ S0)$

S0 (final state)

The input is accepted

A list of all 8 possible transition rules

T1: $S0 \xrightarrow{a} S0$

T2: $S0 \xrightarrow{a} S1$

T3: $S0 \xrightarrow{b} S0$

T4: $S0 \xrightarrow{b} S1$

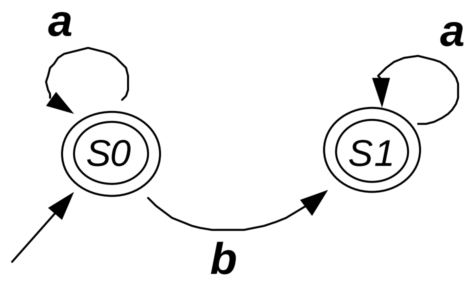
T5: $S1 \xrightarrow{a} S0$

T6: $S1 \xrightarrow{a} S1$

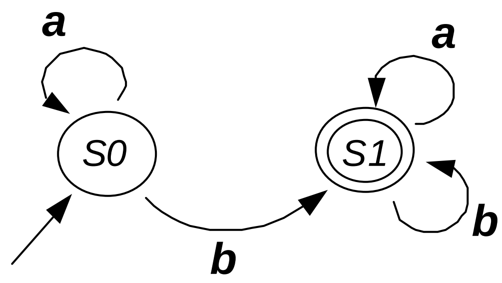
T7: $S1 \xrightarrow{b} S0$

T8: $S1 \xrightarrow{b} S1$

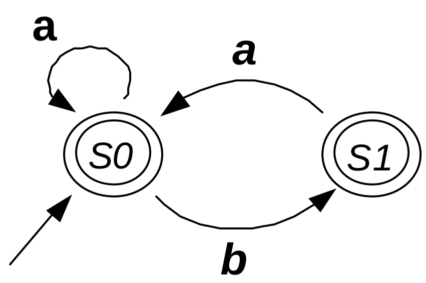
Automata programs used to test the molecular implementation



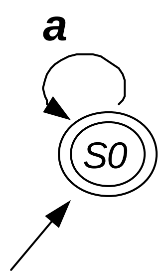
_A2_: at most one



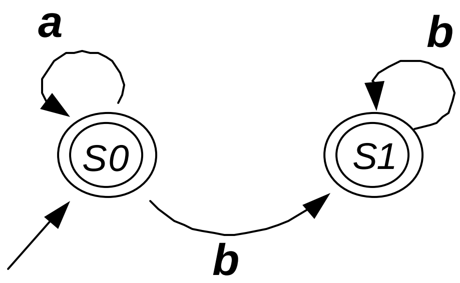
_A3_: at least one _b_



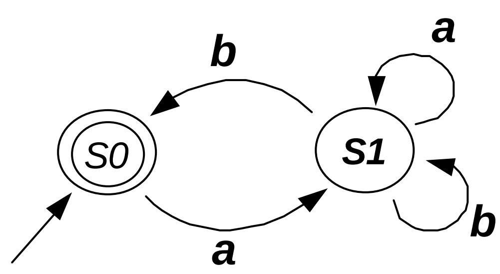
_A4_: no two consecutive _b_’s



_A5_: only _a_’s



_A6_: no _a_ after _b_

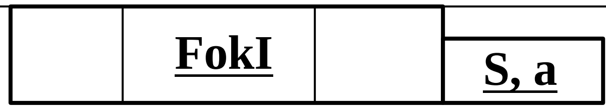


_A7_: starts with _a_ and ends with _b_

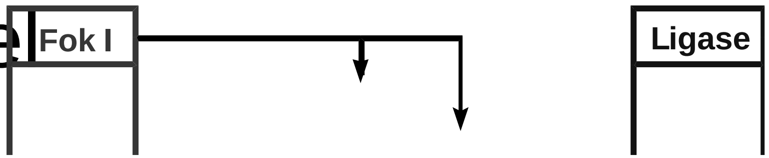
Molecular realization of Finite Automata

- Input: DNA

- Software: DNA

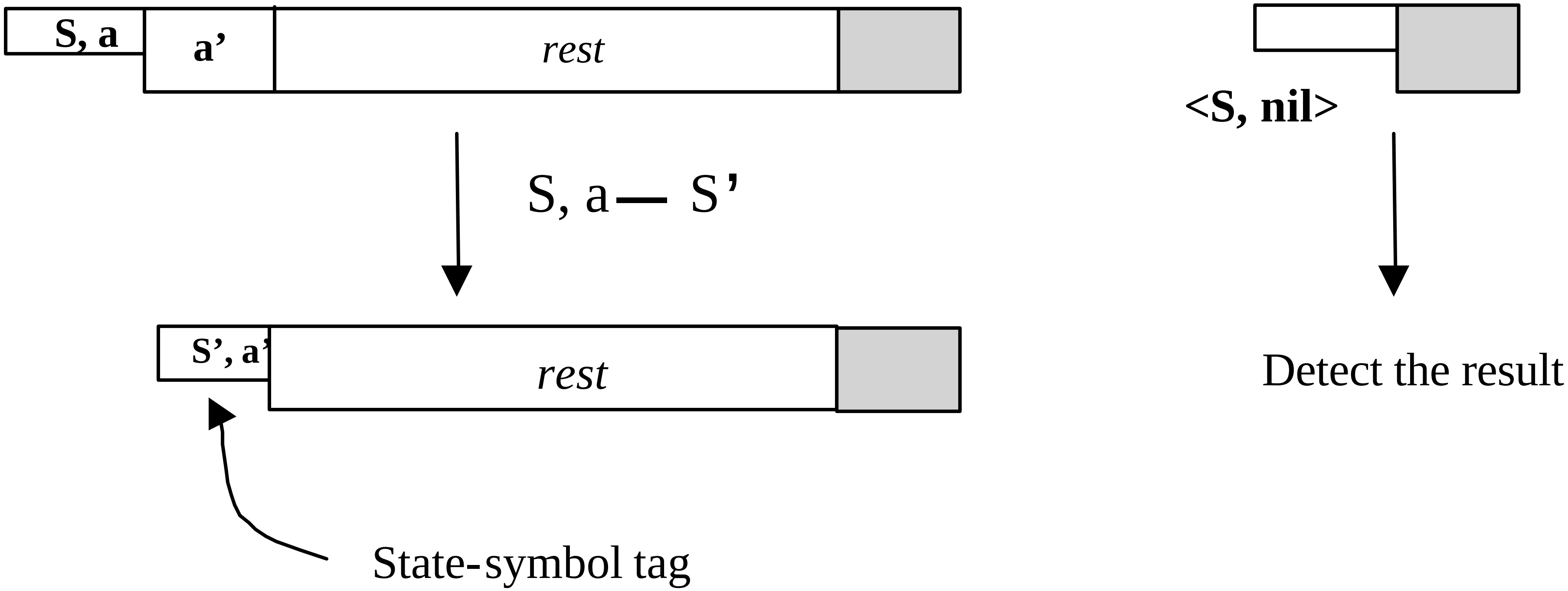


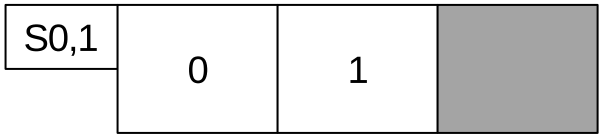
- Hardware: Class-II restriction enzyme FokI, DNA Ligase, ATP as fuel

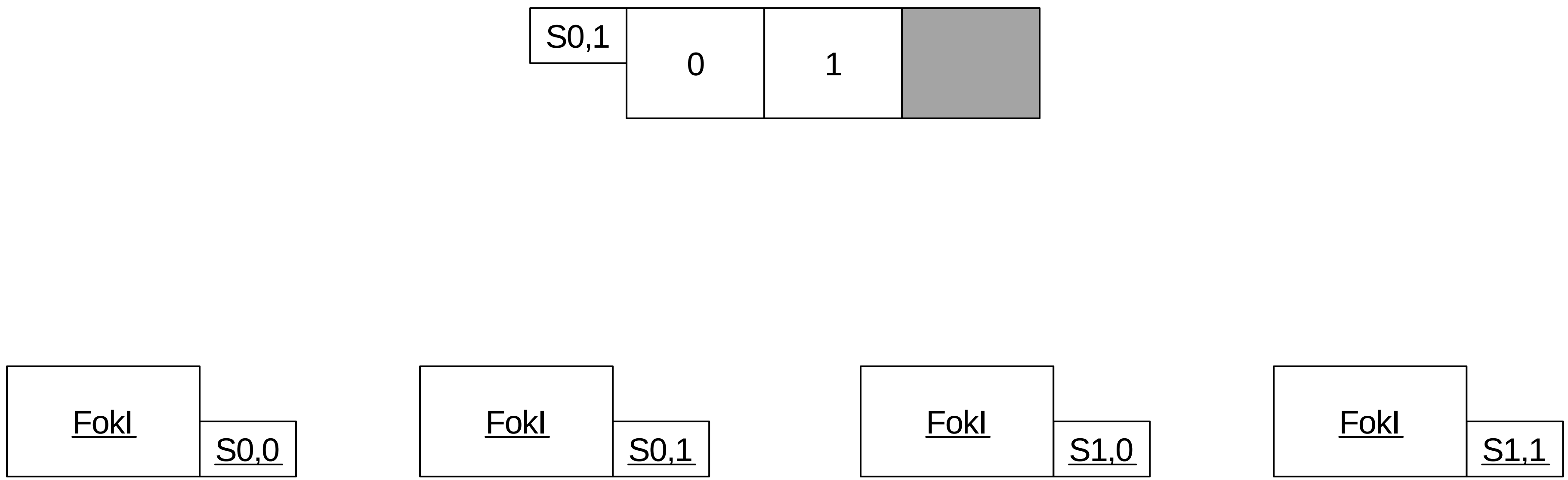


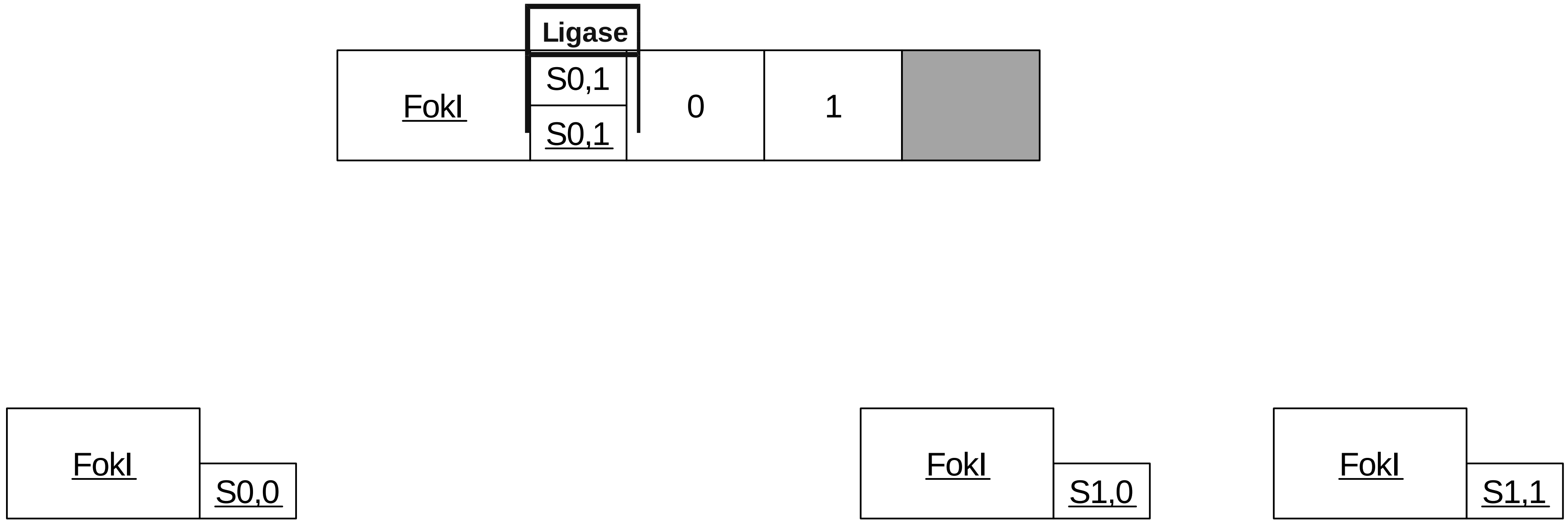
Basic cycle of automaton

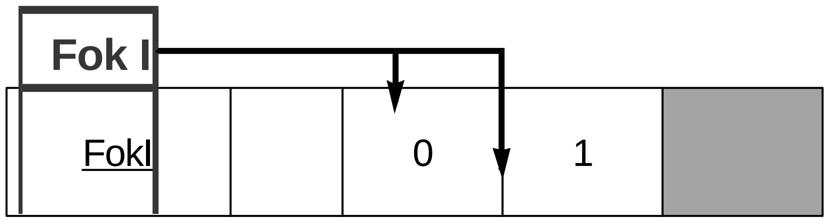
Iterative processing of input until the end is reached



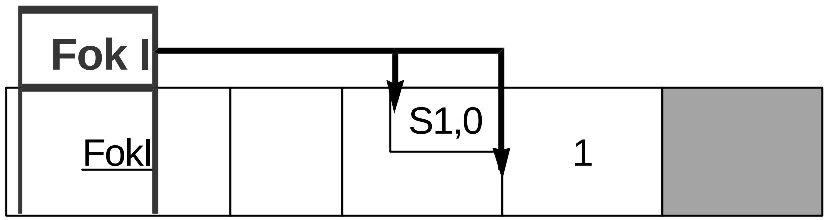

S0,1
0
1

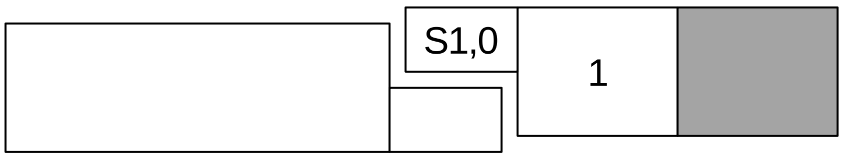

S0,1
0
1
FokI
S0,0
FokI
S0,1
FokI
S1,0
FokI
S1,1

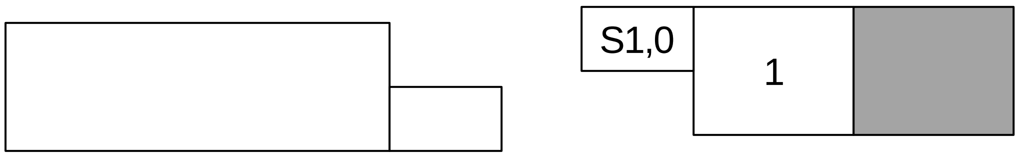

Ligase
FokI
S0,1
S0,1
0
1
FokI
S0,0
FokI
S1,0
FokI
S1,1



Fok I
FokI
0
1


Fok I
FokI
S1,0
1


S1,0
1


S1,0
1

Molecular realization of FA

***Alphabet*:**

{0 = 5’- CTGGCT,
1 = 5’- CGCAGC}

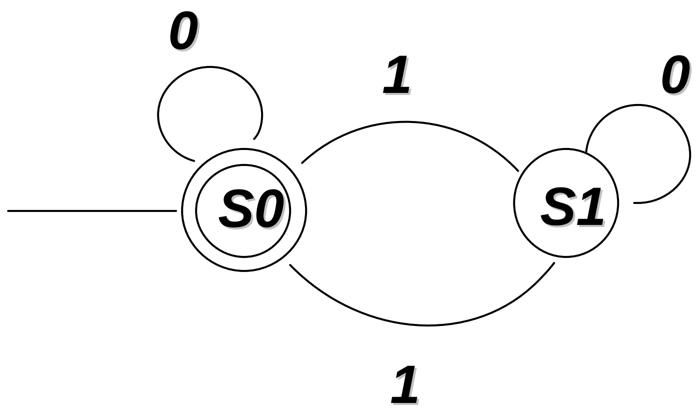
***States*:**

{S0,S1}

FA

***Transition Table*:**

S0, 0 ✍ S0
S0, 1 ✍ S1
S1, 0 ✍ S1
S1, 1 ✍ S0



The encoding for *a*, *b*, and *terminator* and the <*state, symbol*> sticky ends

symbol	*a*	*b*	*terminator (t)*
encodings & <state, symbol> sticky ends	<*S1*, *a*> CTGGCT <*S0*, *a*>	<*S1*, *b*> CGCAGC <*S0*, *b*>	<*S1*, *t*> TGTCGC <*S0*, *t*>

Transition molecules

Fok I (9/13) recognition site

GGATG NNNN
CCTAC

S0, 0 ✍ S0	*3 bp*	CCGA
S0, 1 ✍ S1	*5 bp*	GTCG
S1, 0 ✍ S1	*3 bp*	GACC
S1, 1 ✍ S0	*1 bp*	GCGT

Structure of the transition molecules

*Fok*I recognition site

p $\boxed{22}$ GGATGTAC
GGT CCTACATGCCGAp

T1: S0 ? ?a? S0

p $\boxed{22}$ GGATGACGAC
GGT CCTACTGCTGCCGAp

T2: S0 ? ?a? S1

p $\boxed{28}$ GGATG ACG
GGT CCTAC TGC GTCG p

T3: S0 ? ?b? S0

p $\boxed{15}$ GGATG ACGAC
GGT CCTAC TGCTGGTCG p

T4: S0 ? ?b? S1

p $\boxed{28}$ GGATGA
GGT CCTACTGACCp

T5: S1 ? ?a? S0

p $\boxed{15}$ GGATGACG
GGT CCTACTGCGACCp

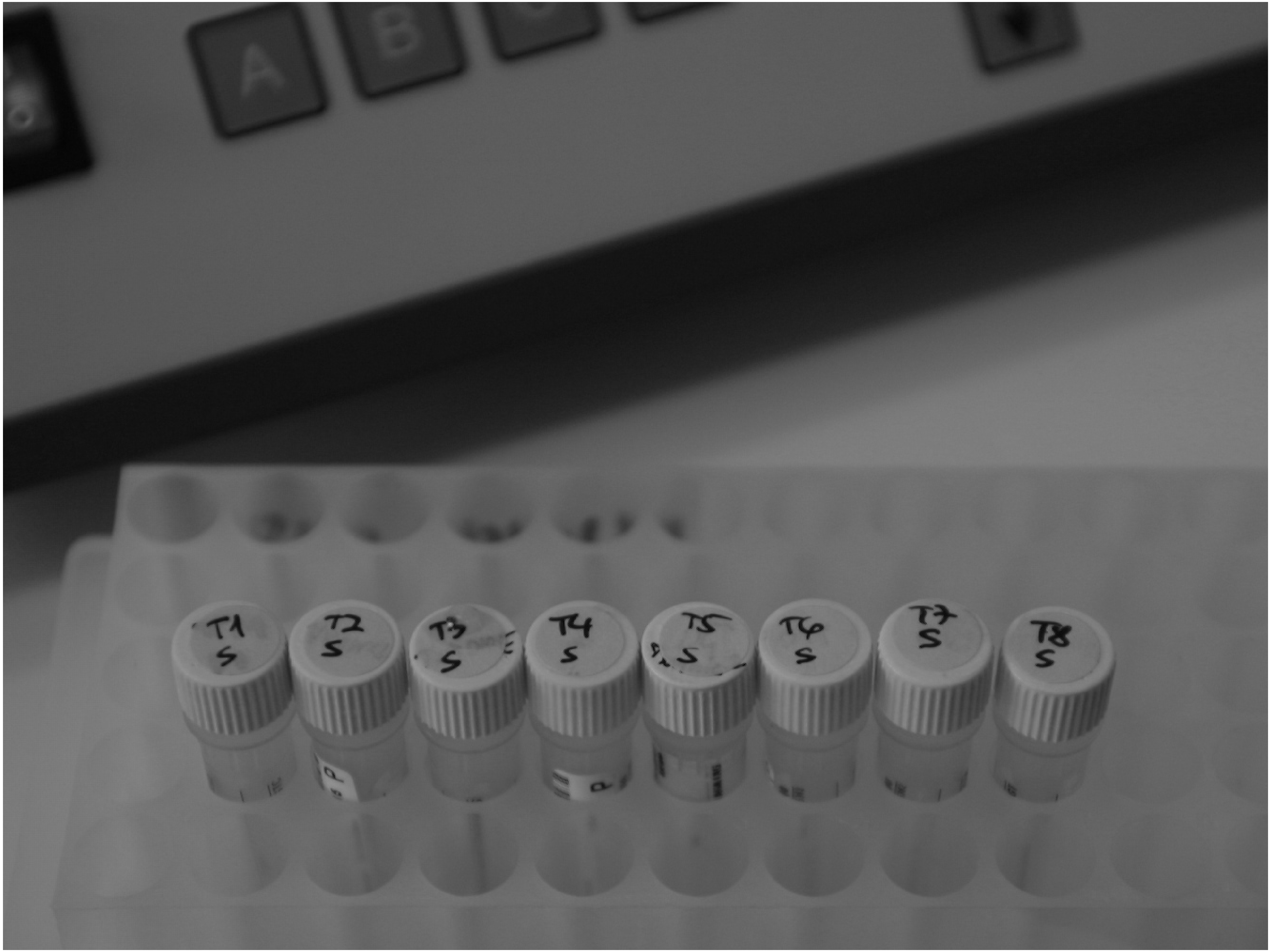
T6: S1 ? ?a? S1

p $\boxed{21}$ GGATG G
GGT CCTAC CGCGT p

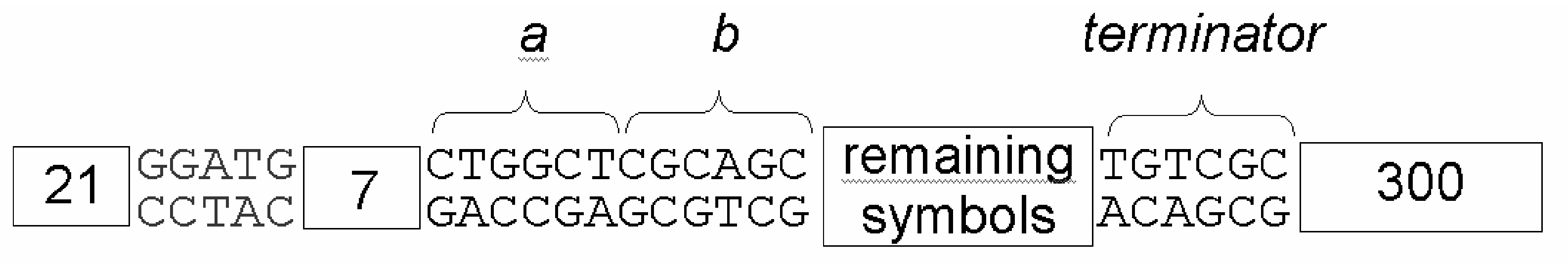
T7: S1 ? ?b? S0

p $\boxed{30}$ GGATG ACG
GGT CCTAC TGC GCGT p

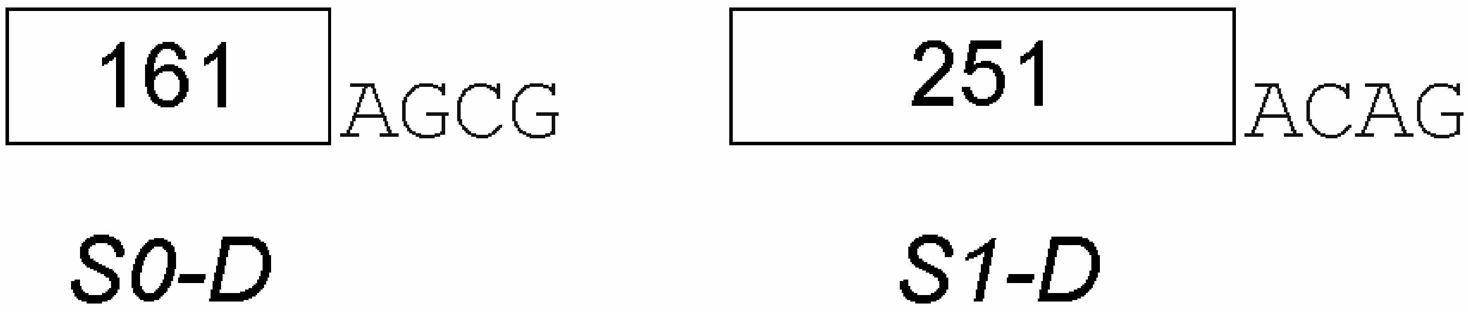
T8: S1 ? ?b? S1


A
B
T1
S
T2
S
T3
S
T4
S
T5
S
T6
S
T7
S
T8
S

Structure of an input molecule



Structure of the output-detection molecules

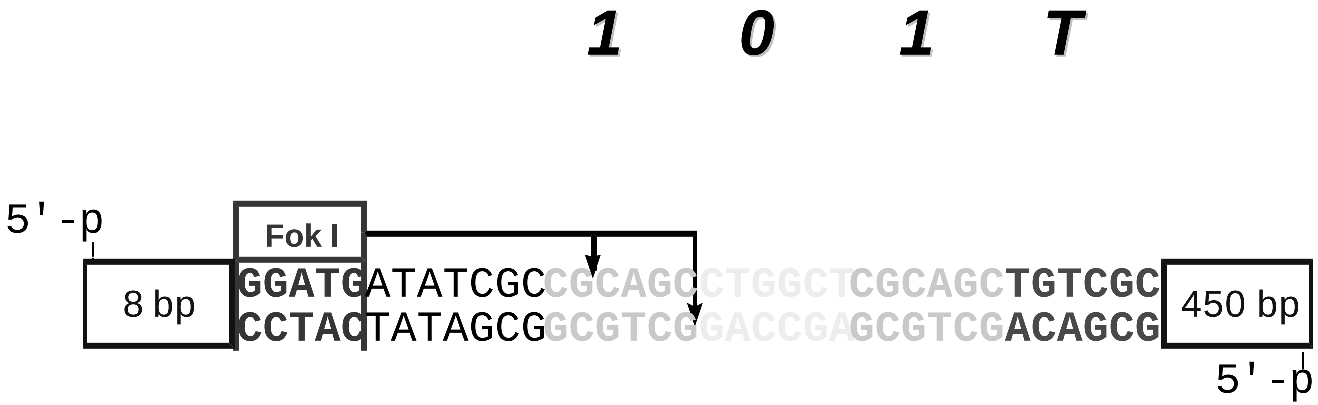


Animation of experiment

$S_0,0 \Longrightarrow S_0$
$S_1,0 \Longrightarrow S_1$
$S_0,1 \Longrightarrow S_1$
$S_1,1 \Longrightarrow S_0$

State transition rules

$<S_0>$ = "cut inside"
$<S_1>$ = "cut outside"



$S_0,0 \Longrightarrow S_0$
$S_1,0 \Longrightarrow S_1$
$S_0,1 \Longrightarrow S_1$
$S_1,1 \Longrightarrow S_0$

State transition rules

$\langle S_0 \rangle$ = "cut inside"

$\langle S_1 \rangle$ = "cut outside"

1 0 1 T

$S_0,0 \Longrightarrow S_0$
$S_1,0 \Longrightarrow S_1$
$S_0,1 \Longrightarrow S_1$
$S_1,1 \Longrightarrow S_0$

State transition rules

$\langle S_0 \rangle$ = "cut inside"
$\langle S_1 \rangle$ = "cut outside"

1 0 1 T

```
5'-p                                 5'-p
[8 bp] GGATGATATCGCCG    CAGCCTGGCTCGCAGCTGTCGC [450 bp]
       CCTACTATAGCGGCGTCG    GACCGAGCGTCGACAGCG
                     5'-p                        5'-p
```

$S_0,0 \Longrightarrow S_0$
$S_1,0 \Longrightarrow S_1$
$S_0,1 \Longrightarrow S_1$
$S_1,1 \Longrightarrow S_0$

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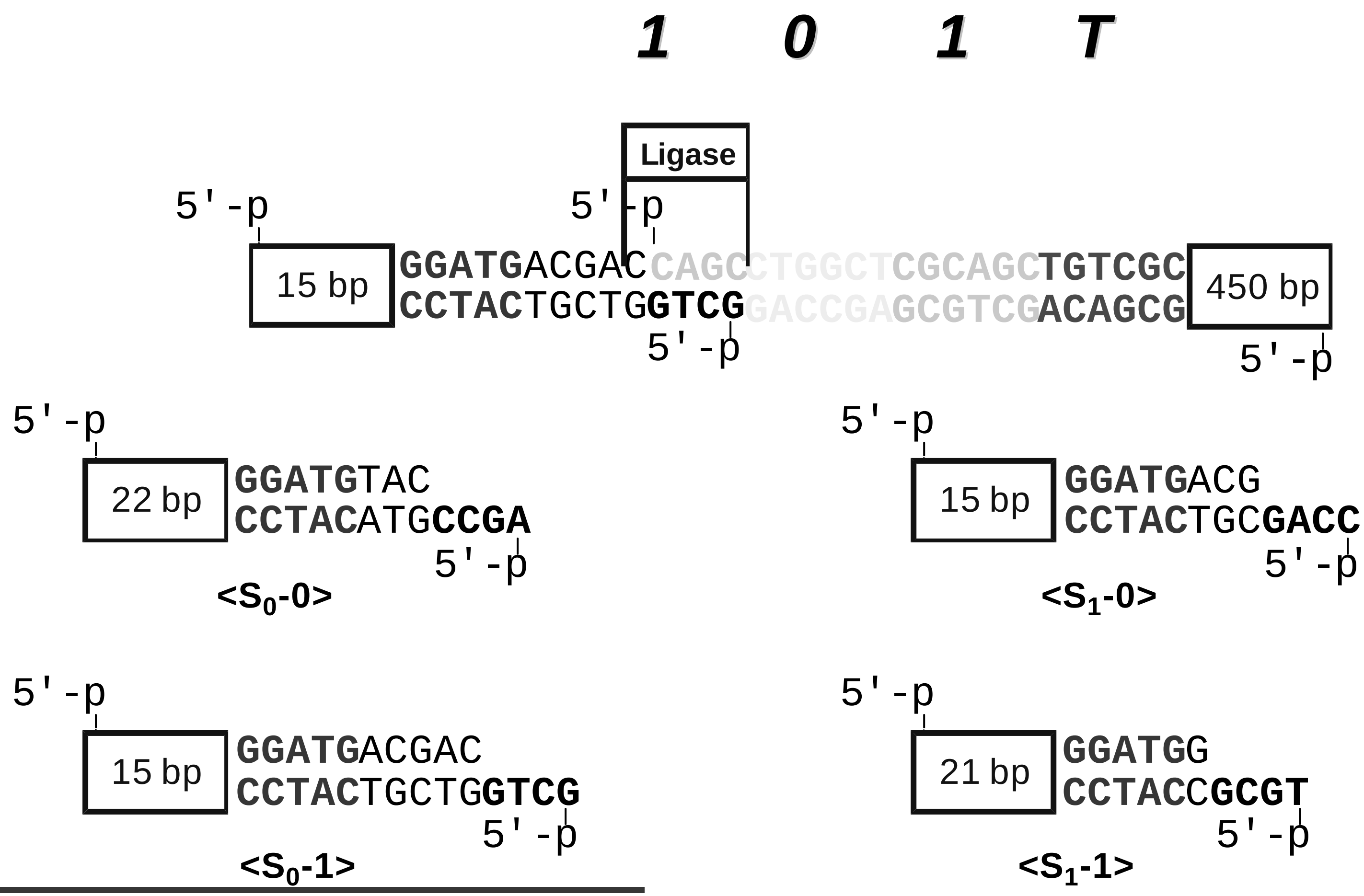
```
5'-p                                            5'-p
 [ 8 bp ] GGATGATATCGCCG                          CAGCCTGGCTCGCAGCTGTCGC [ 450 bp ]
          CCTACTATAGCGGCGTCG                            GACCGAGCGTCGACAGCG
                          5'-p                                         5'-p
```

$S_0, 0 \Longrightarrow S_0$
$S_1, 0 \Longrightarrow S_1$
$S_0, 1 \Longrightarrow S_1$
$S_1, 1 \Longrightarrow S_0$

State transition rules

<S_0> = "cut inside"
<S_1> = "cut outside"



$S_0,0 \Longrightarrow S_0$
$S_1,0 \Longrightarrow S_1$
$S_0,1 \Longrightarrow S_1$
$S_1,1 \Longrightarrow S_0$

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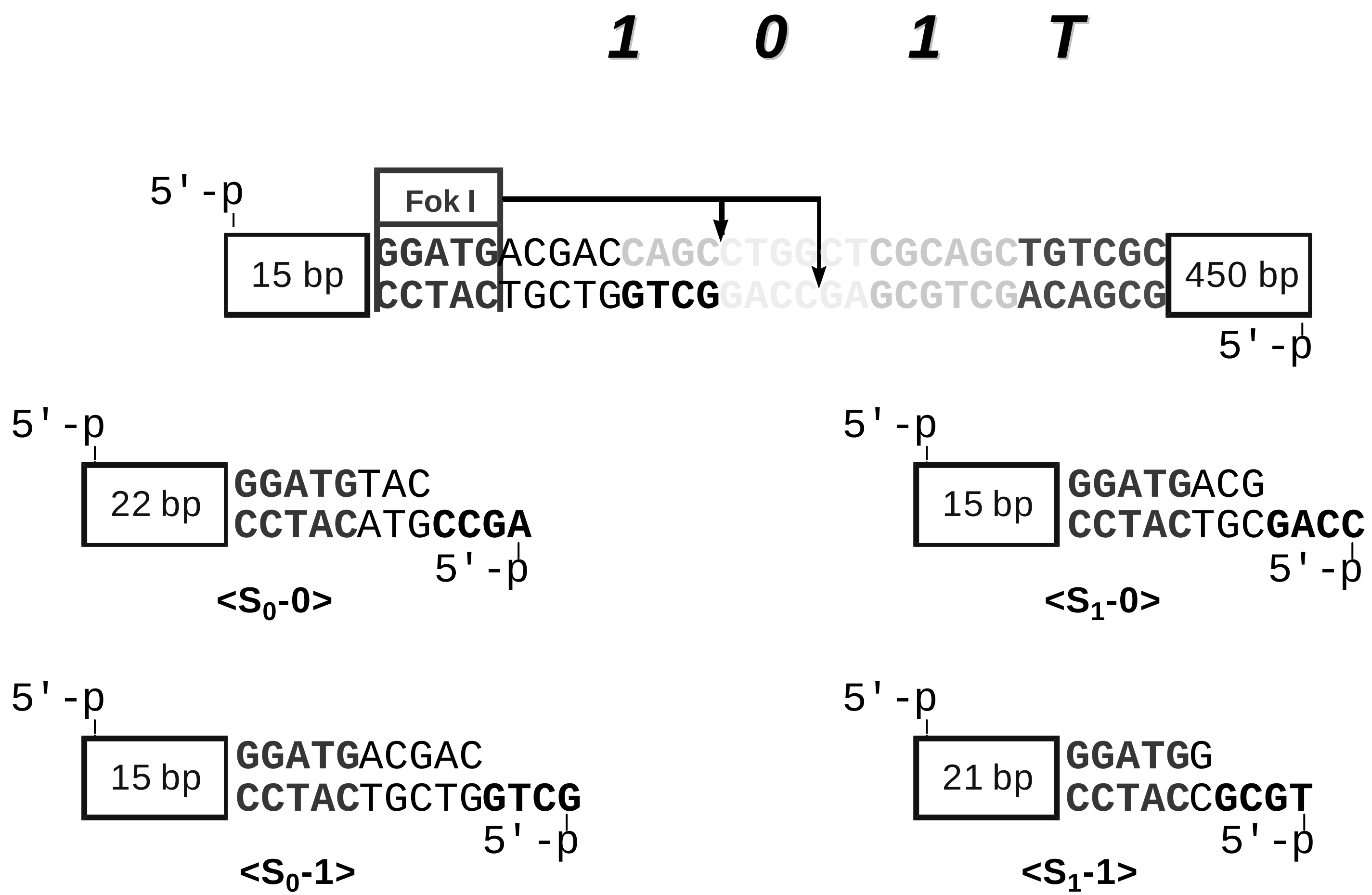

$S_0,0 \Longrightarrow S_0$
$S_1,0 \Longrightarrow S_1$
$S_0,1 \Longrightarrow S_1$
$S_1,1 \Longrightarrow S_0$

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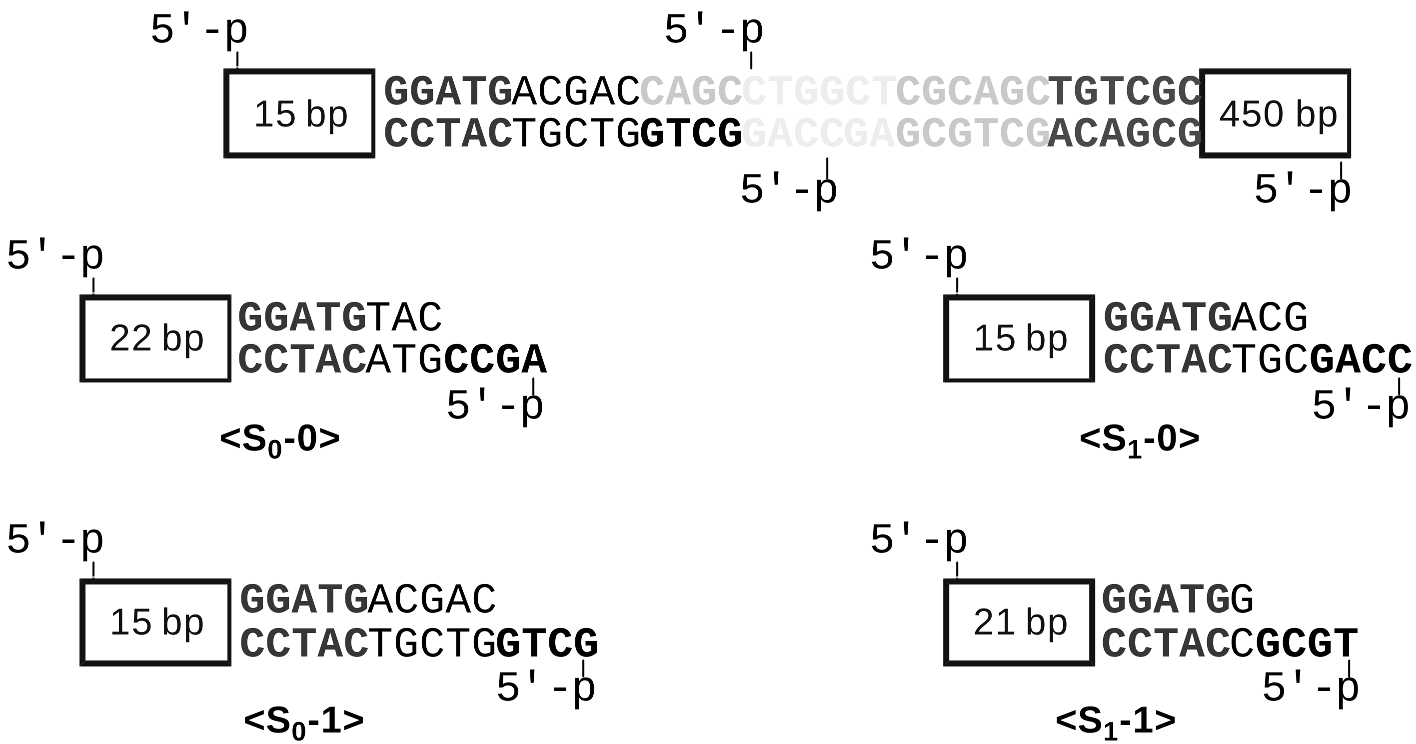

$S_0,0 \Longrightarrow S_0$
$S_1,0 \Longrightarrow S_1$
$S_0,1 \Longrightarrow S_1$
$S_1,1 \Longrightarrow S_0$

State transition rules

<S_0> = "cut inside"
<S_1> = "cut outside"

1 0 1 T

5'-p 5'-p
15 bp GGATGACGACCAGC CTGGCTCGCAGCTGTCGC 450 bp
CCTACTGCTGGTCGGACC GAGCGTCGACAGCG
5'-p 5'-p

5'-p
22 bp GGATGTAC
CCTACATGCCGA
5'-p
<S_0-0>

5'-p
15 bp GGATGACG
CCTACTGCGACC
5'-p
<S_1-0>

5'-p
15 bp GGATGACGAC
CCTACTGCTGGTCG
5'-p
<S_0-1>

5'-p
21 bp GGATGG
CCTACCGCGT
5'-p
<S_1-1>

$S_0,0 \Longrightarrow S_0$
$S_1,0 \Longrightarrow S_1$
$S_0,1 \Longrightarrow S_1$
$S_1,1 \Longrightarrow S_0$

State transition rules

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1 0 1 T

5'-p
15 bp GGATGACGACCAGC
CCTACTGCTGGTCGGACC
5'-p

5'-p
CTGGCTCGCAGCTGTCGC 450 bp
GAGCGTCGACAGCG
5'-p

5'-p
22 bp GGATGTAC
CCTACATGCCGA
5'-p
<S_0-0>

5'-p
15 bp GGATGACG
CCTACTGCGACC
5'-p
<S_1-0>

5'-p
15 bp GGATGACGAC
CCTACTGCTGGTCG
5'-p
<S_0-1>

5'-p
21 bp GGATGG
CCTACCGCGT
5'-p
<S_1-1>

$S_0,0 \Longrightarrow S_0$
$S_1,0 \Longrightarrow S_1$
$S_0,1 \Longrightarrow S_1$
$S_1,1 \Longrightarrow S_0$

State transition rules

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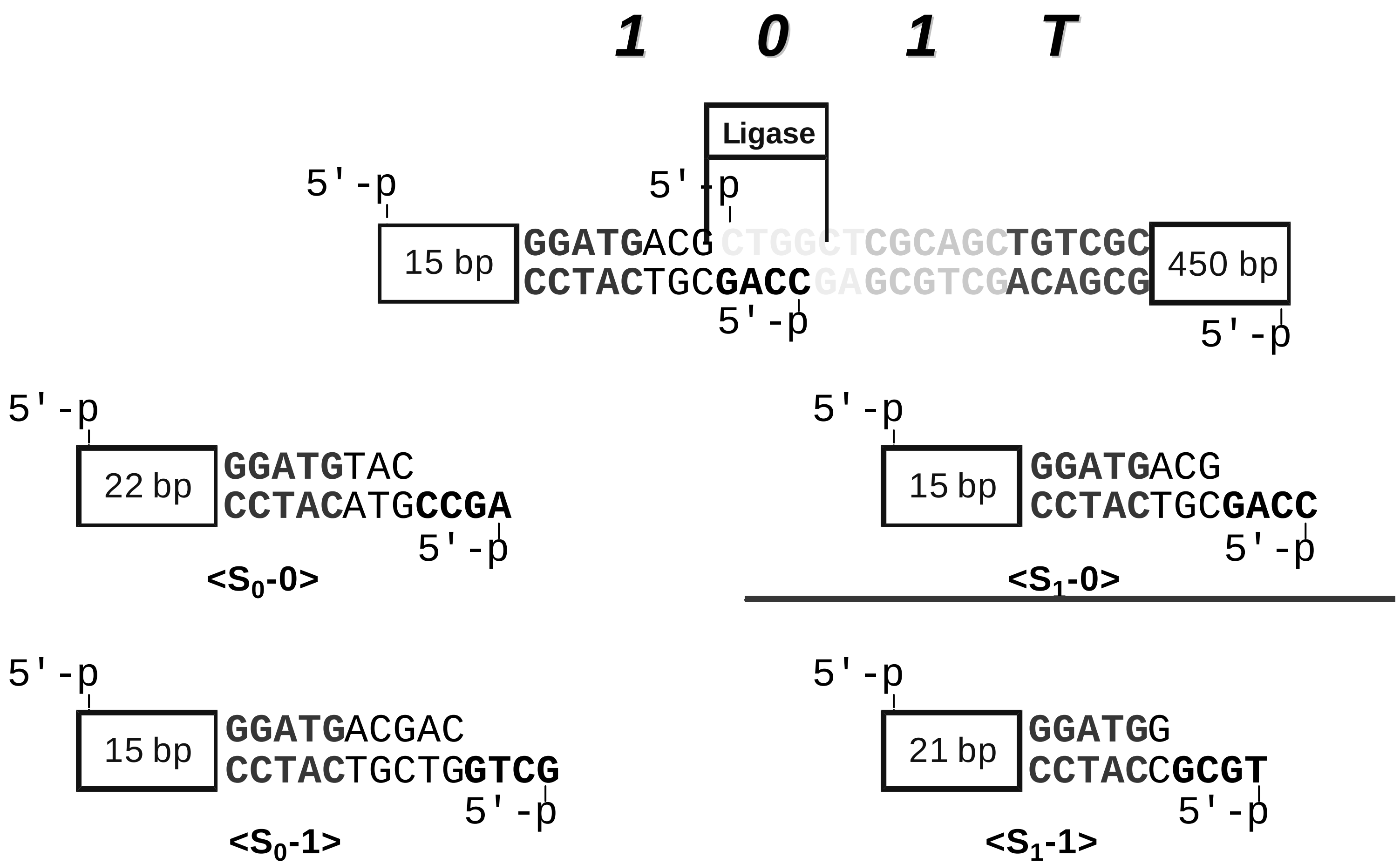

$S_0,0 \Longrightarrow S_0$
$S_1,0 \Longrightarrow S_1$
$S_0,1 \Longrightarrow S_1$
$S_1,1 \Longrightarrow S_0$

State transition rules

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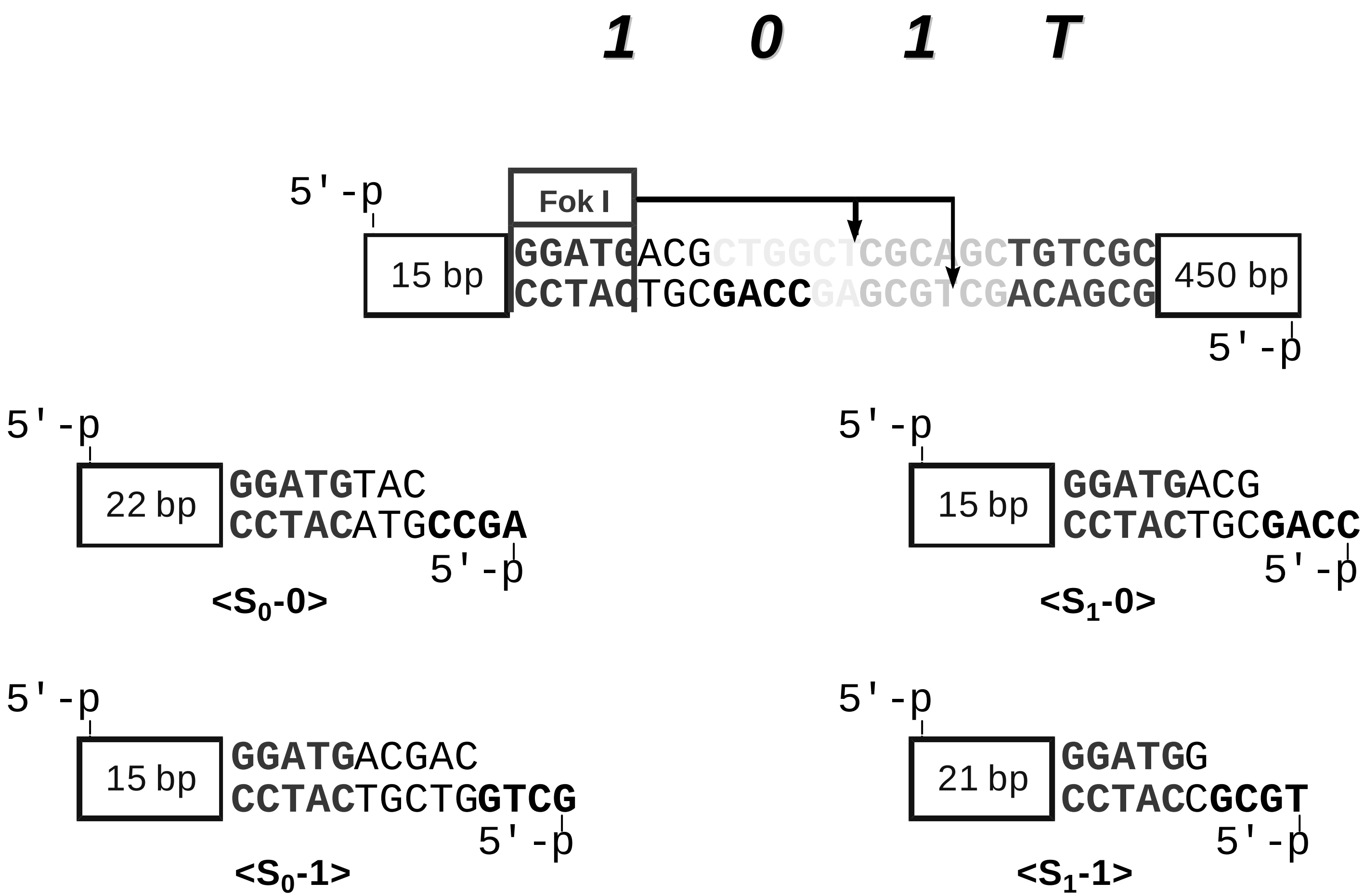

$S_0,0 \Longrightarrow S_0$
$S_1,0 \Longrightarrow S_1$
$S_0,1 \Longrightarrow S_1$
$S_1,1 \Longrightarrow S_0$

State transition rules

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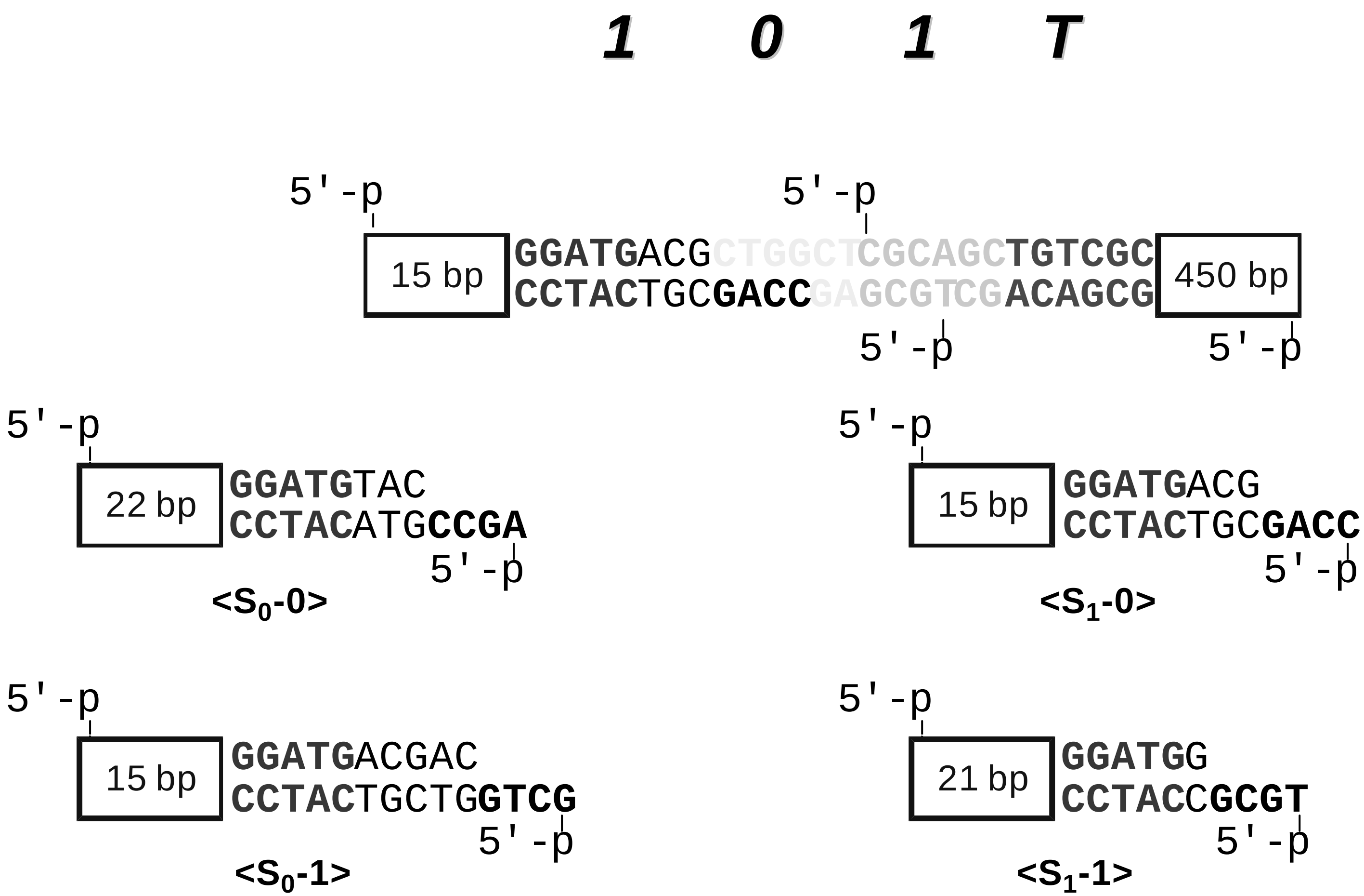
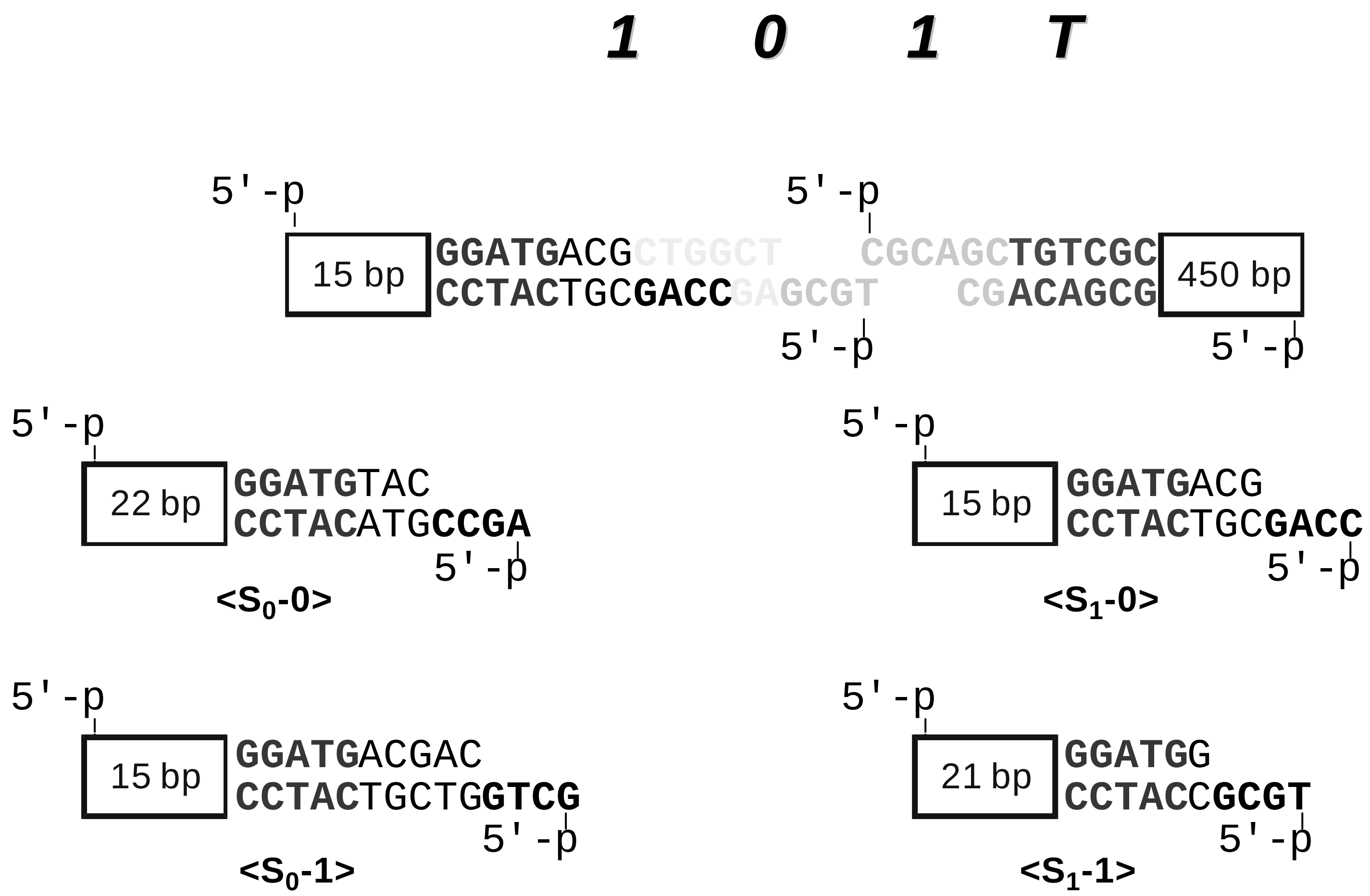


$S_0,0 \Longrightarrow S_0$
$S_1,0 \Longrightarrow S_1$
$S_0,1 \Longrightarrow S_1$
$S_1,1 \Longrightarrow S_0$

State transition rules

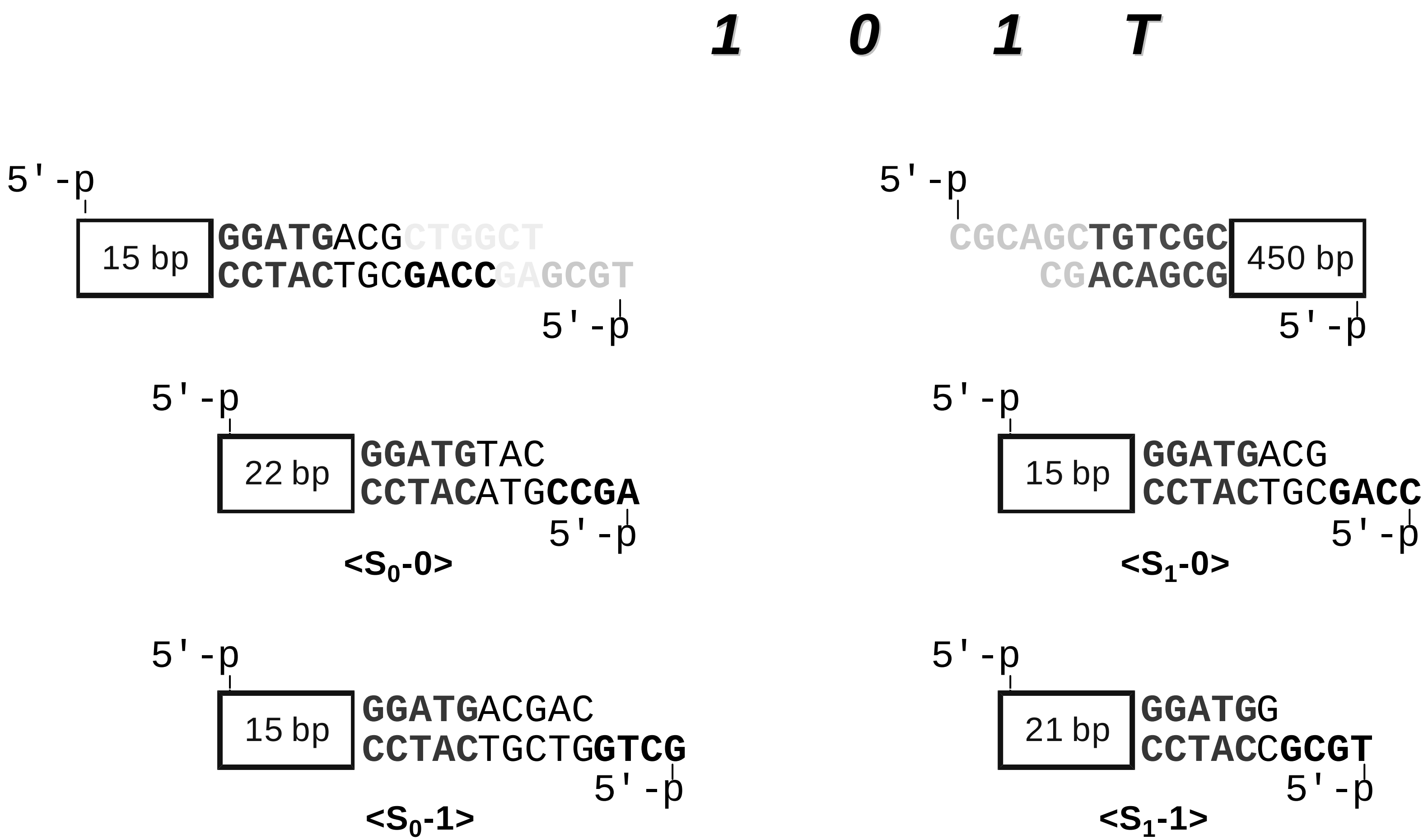
$\langle S_0 \rangle$ = **"cut inside"**
$\langle S_1 \rangle$ = **"cut outside"**



$S_0,0 \Longrightarrow S_0$
$S_1,0 \Longrightarrow S_1$
$S_0,1 \Longrightarrow S_1$
$S_1,1 \Longrightarrow S_0$

State transition rules

<S_0> = "cut inside"
<S_1> = "cut outside"

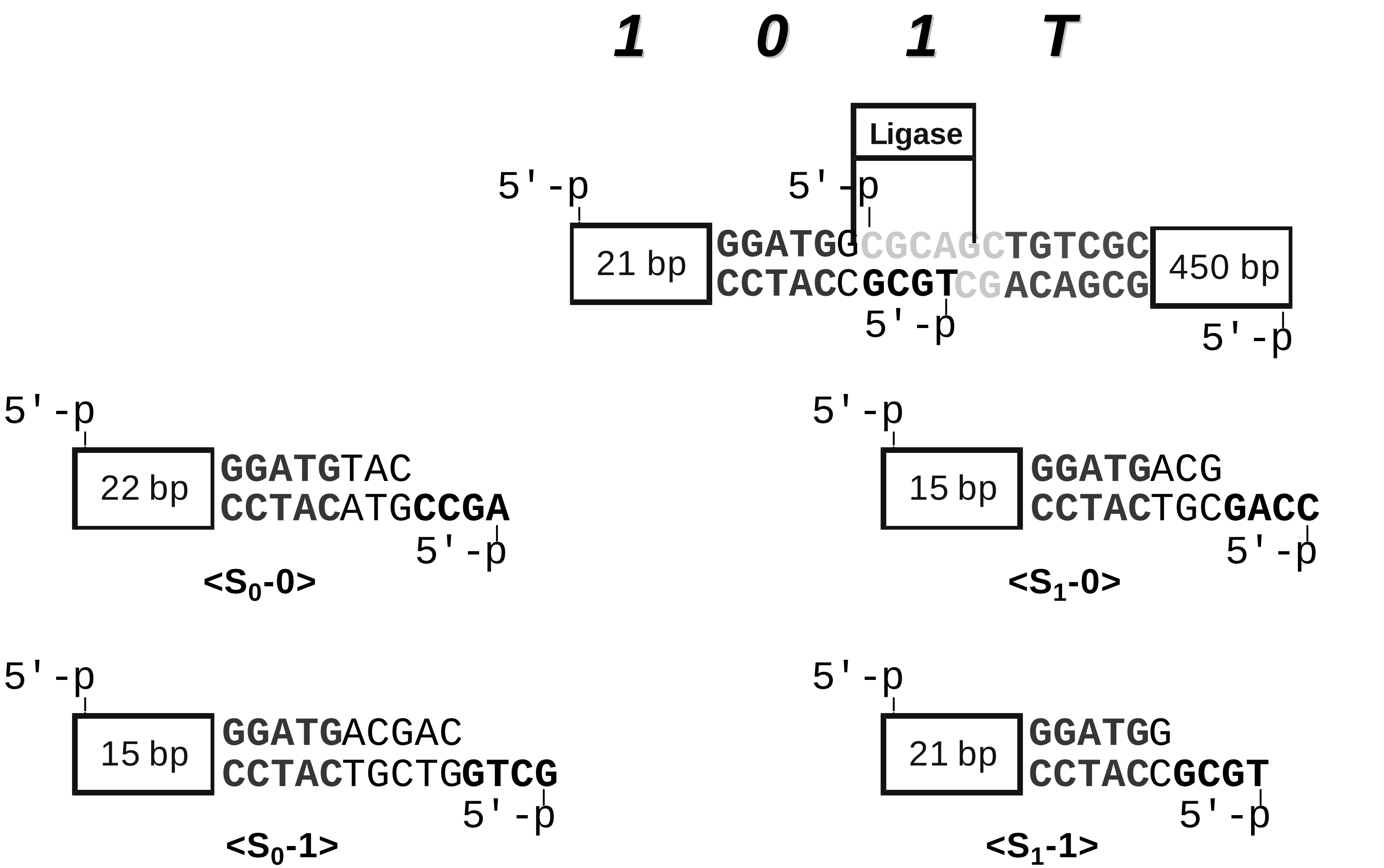


$S_0,0 \Longrightarrow S_0$
$S_1,0 \Longrightarrow S_1$
$S_0,1 \Longrightarrow S_1$
$S_1,1 \Longrightarrow S_0$

State transition rules

<S_0> = "cut inside"

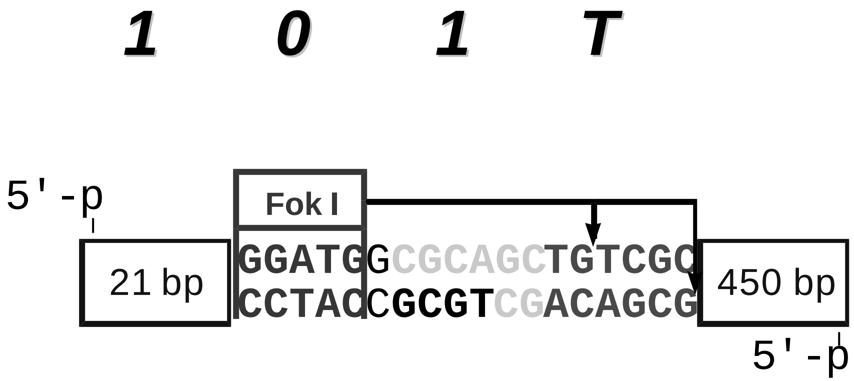
<S_1> = "cut outside"



$S_0,0 \Longrightarrow S_0$
$S_1,0 \Longrightarrow S_1$
$S_0,1 \Longrightarrow S_1$
$S_1,1 \Longrightarrow S_0$

State transition rules

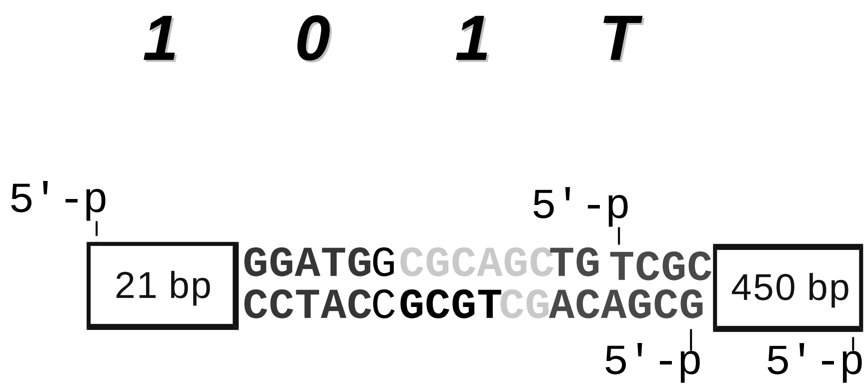
$\langle S_0 \rangle$ = "cut inside"
$\langle S_1 \rangle$ = "cut outside"



$S_0, 0 \Longrightarrow S_0$
$S_1, 0 \Longrightarrow S_1$
$S_0, 1 \Longrightarrow S_1$
$S_1, 1 \Longrightarrow S_0$

State transition rules

$<S_0>$ = "cut inside"
$<S_1>$ = "cut outside"

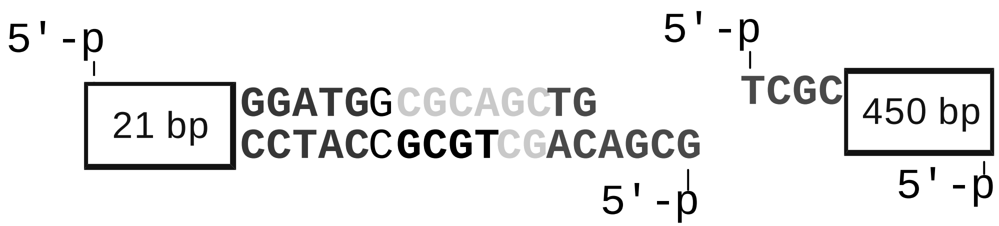


$S_0,0 \Longrightarrow S_0$
$S_1,0 \Longrightarrow S_1$
$S_0,1 \Longrightarrow S_1$
$S_1,1 \Longrightarrow S_0$

State transition rules

$<S_0>$ = "cut inside"
$<S_1>$ = "cut outside"

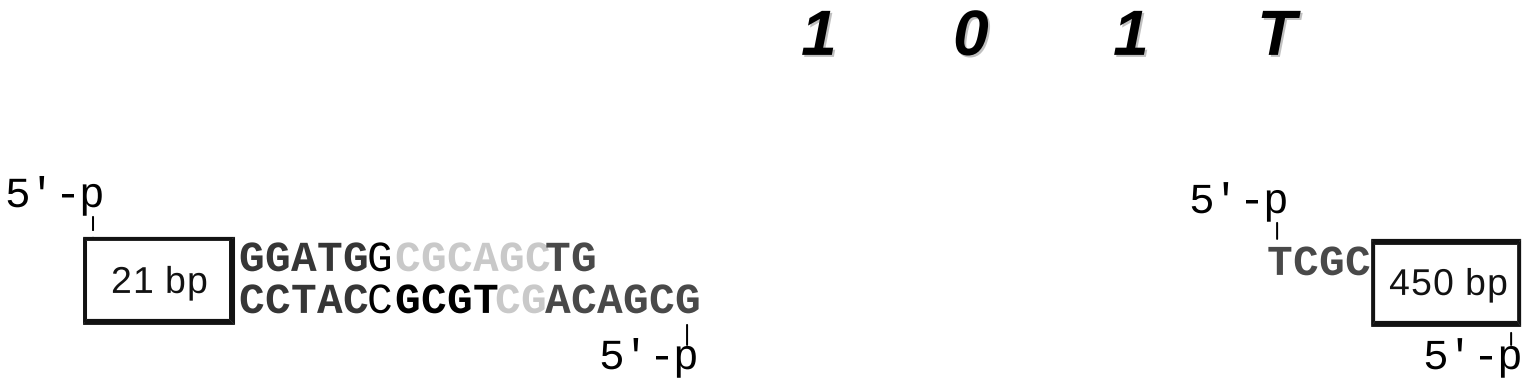
1 0 1 T



$S_0,0 \Longrightarrow S_0$
$S_1,0 \Longrightarrow S_1$
$S_0,1 \Longrightarrow S_1$
$S_1,1 \Longrightarrow S_0$

State transition rules

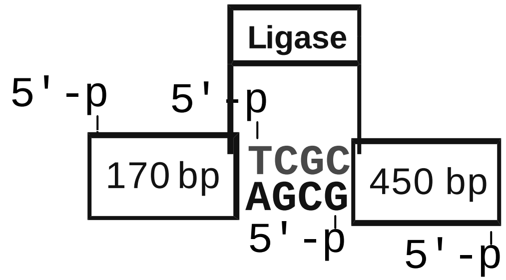
<S_0> = "cut inside"
<S_1> = "cut outside"

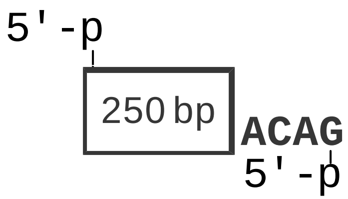


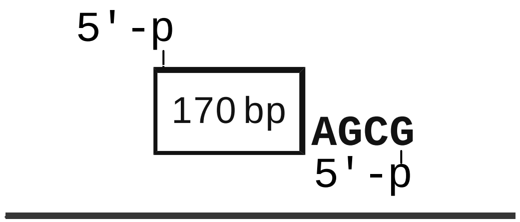
$S_0,0 \Longrightarrow S_0$
$S_1,0 \Longrightarrow S_1$
$S_0,1 \Longrightarrow S_1$
$S_1,1 \Longrightarrow S_0$

State transition rules

<S_0> = "cut inside"
<S_1> = "cut outside"







$S_0,0 \Longrightarrow S_0$
$S_1,0 \Longrightarrow S_1$
$S_0,1 \Longrightarrow S_1$
$S_1,1 \Longrightarrow S_0$

State transition rules

$\langle S_0 \rangle$ = "cut inside"
$\langle S_1 \rangle$ = "cut outside"