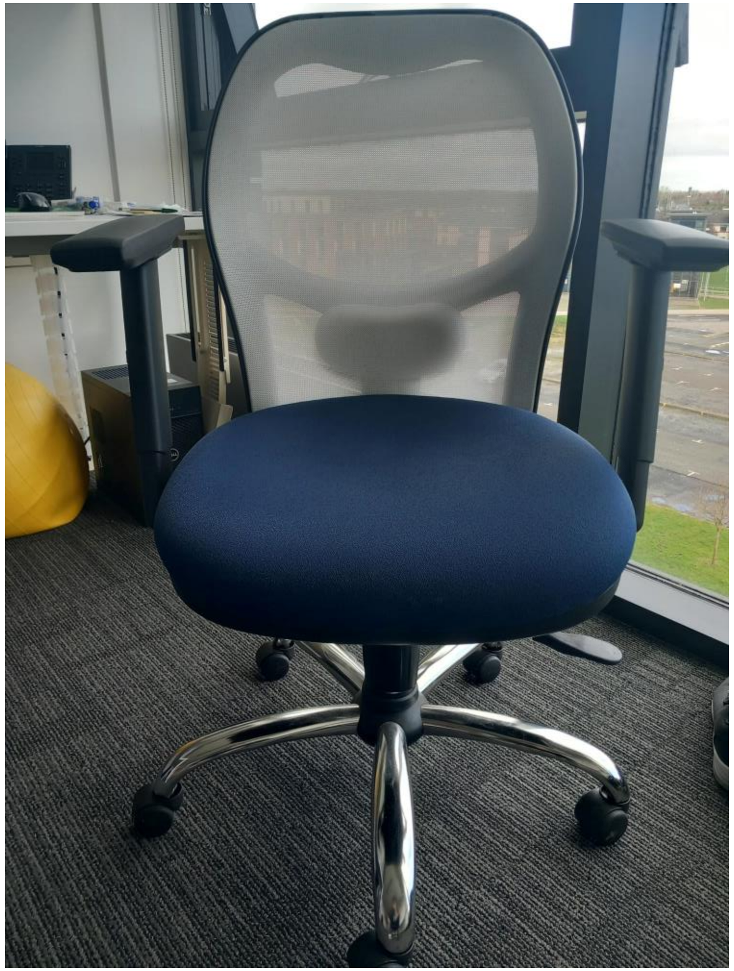
Just a quick, useless recap

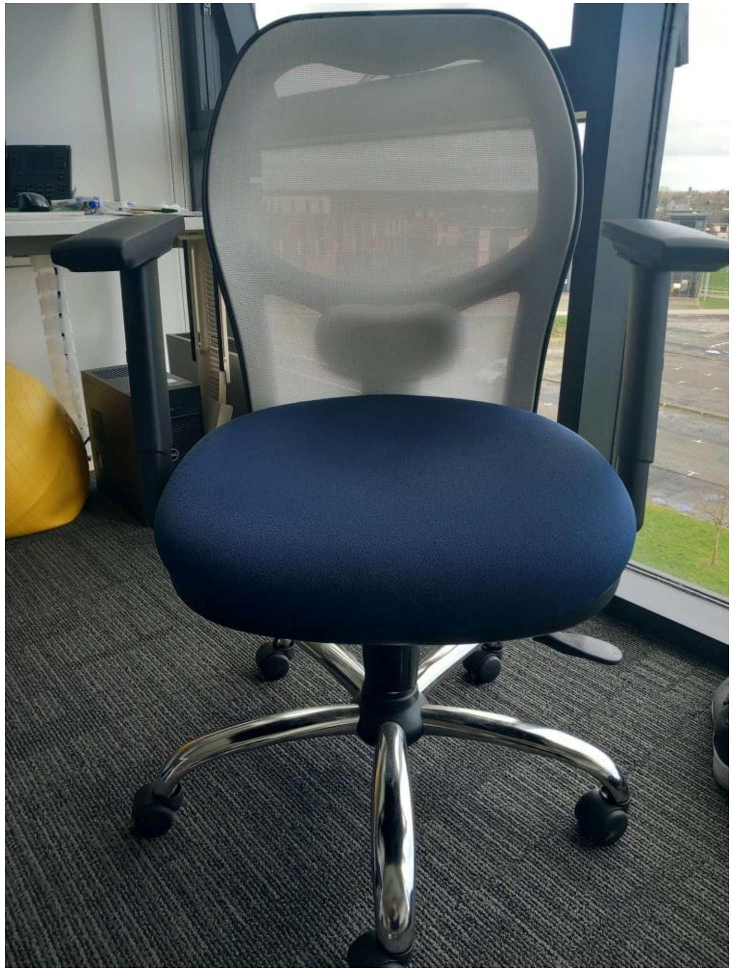
What happened last semester!

The Curse of Hamilton's Chairs

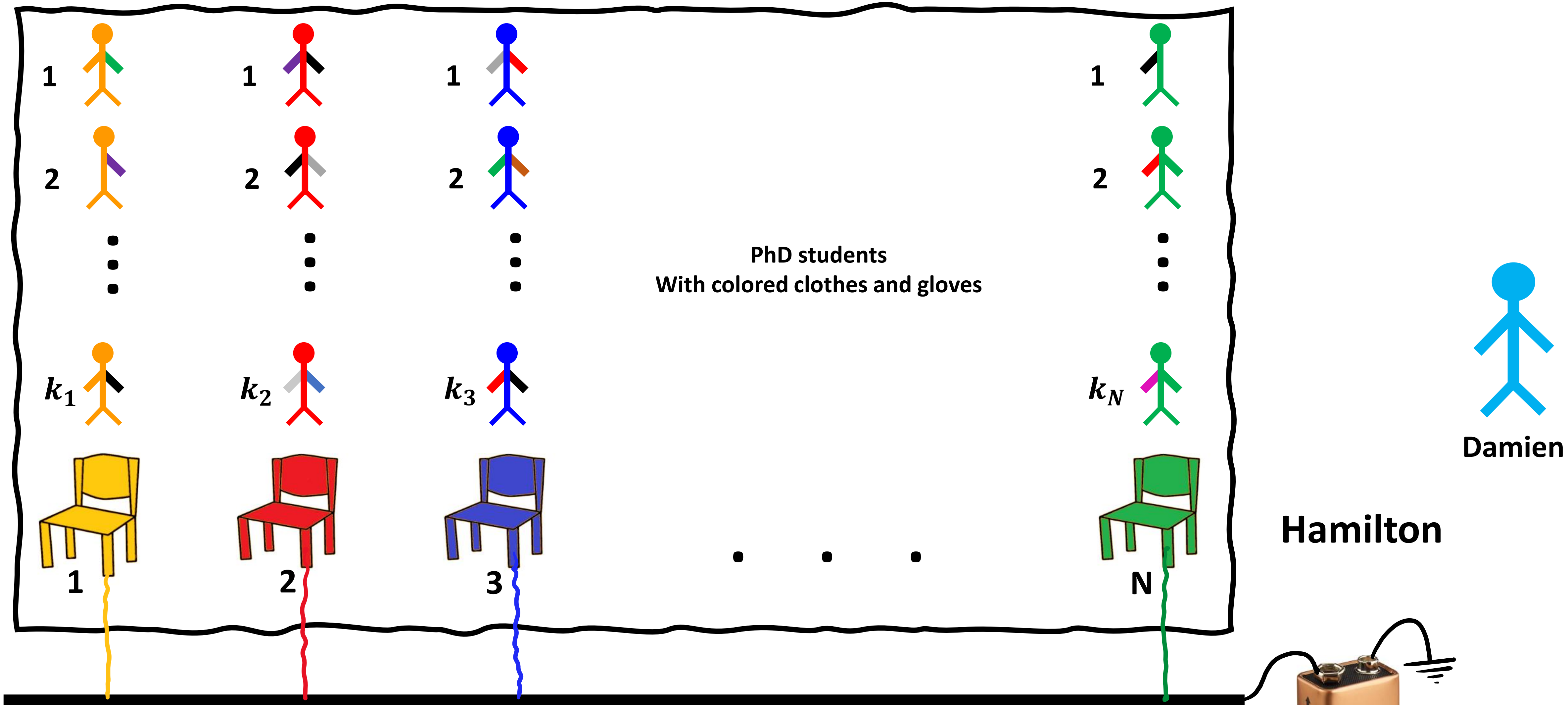
Ahmed Shalaby
2nd year PhD

Supervisor: Damien Woods





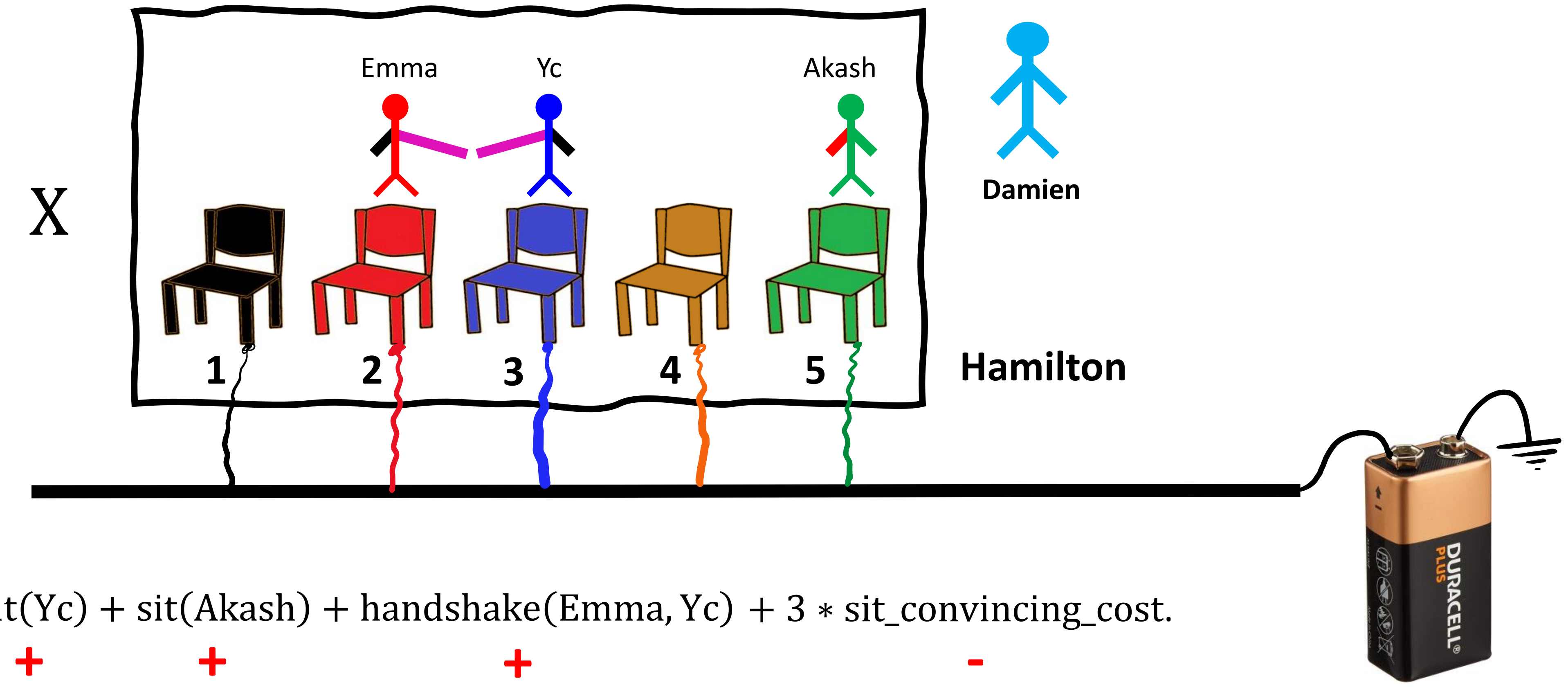
Let’s discover the rules of the game



- How many different configurations we will have ?

$$(K+1)^N$$

(Exponential in the # of chairs)



$$\mathrm{E}(\mathrm{X}) = \mathrm{sit}(\mathrm{Emma}) + \mathrm{sit}(\mathrm{Yc}) + \mathrm{sit}(\mathrm{Akash}) + \mathrm{handshake}(\mathrm{Emma}, \mathrm{Yc}) + 3 * \mathrm{sit\_convincing\_cost}.$$

\+ \+ \+ \+ -

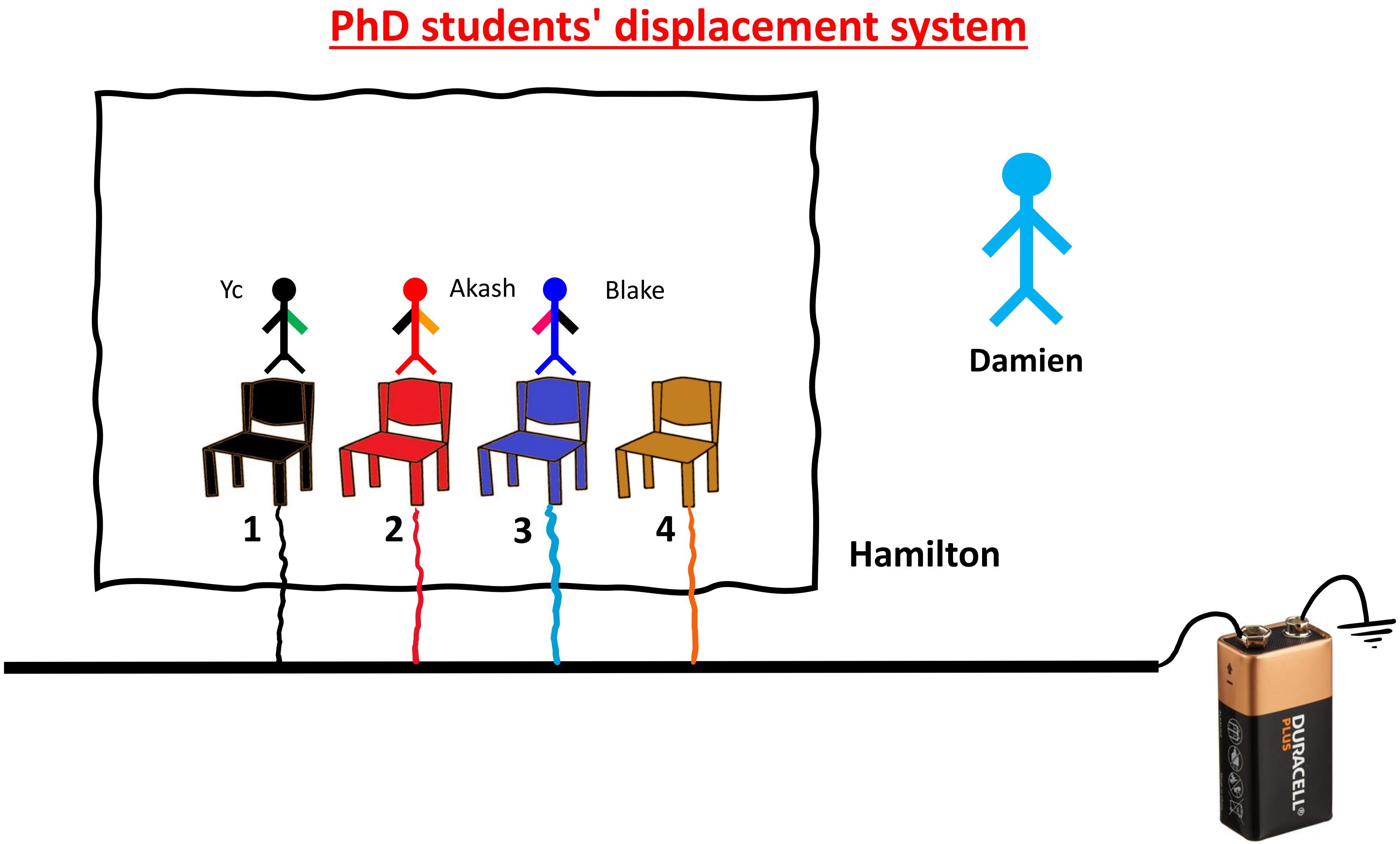
$$\mathrm{E}(X) = \sum_{p \in X} \mathrm{sit}(\mathrm{p}) + \sum_{p_i, p_{i+1} \in X} \mathrm{handshake}(p_i, p_{i+1}) + l * \mathrm{sit\_convincing\_cost}.$$

configuration X of size l PhD students

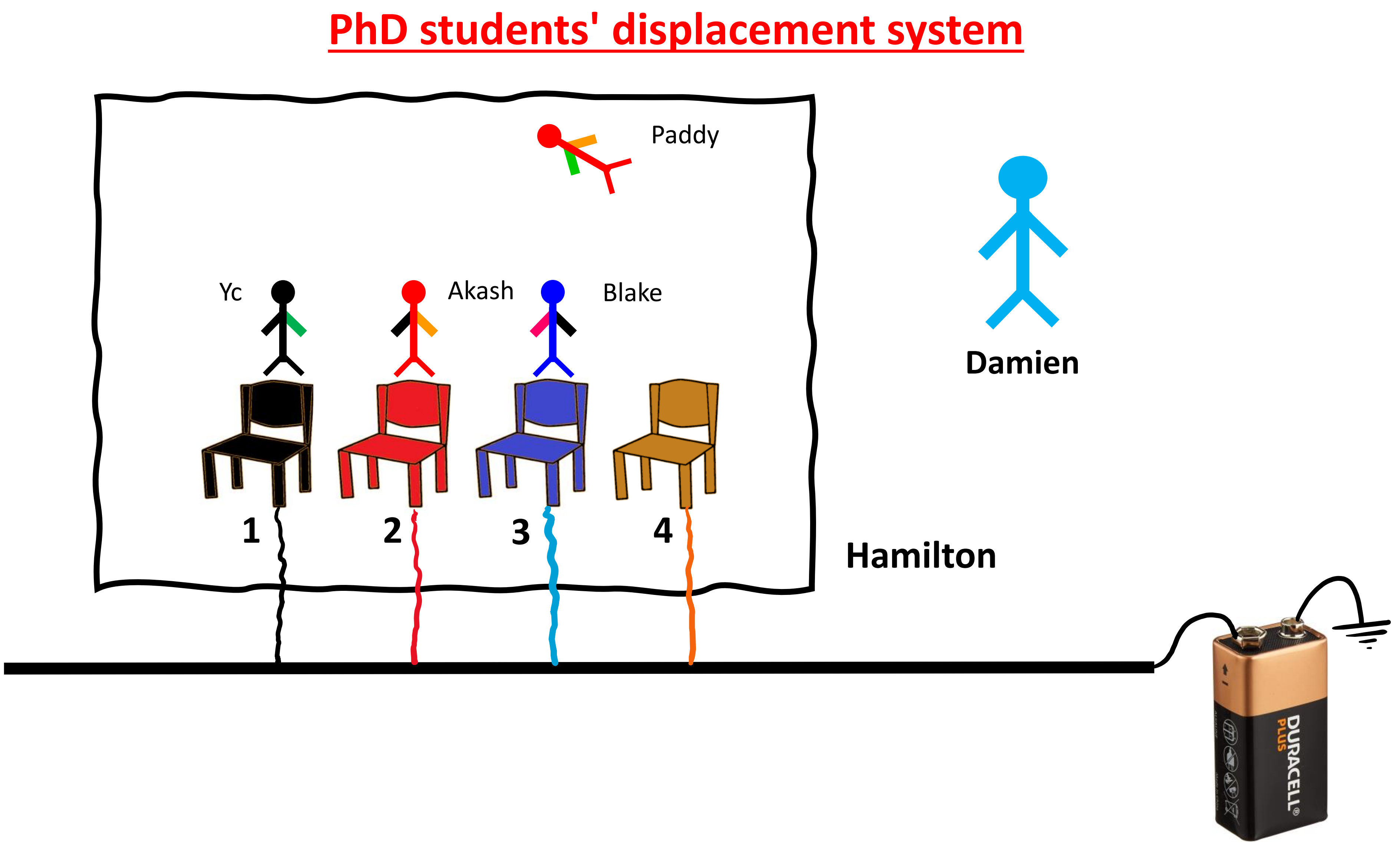
We further assume the following:

- $|\mathrm{sit}(p)| > |\mathrm{sit\_convincing\_cost}|$. (Damien always gains by convincing a PhD student to sit)

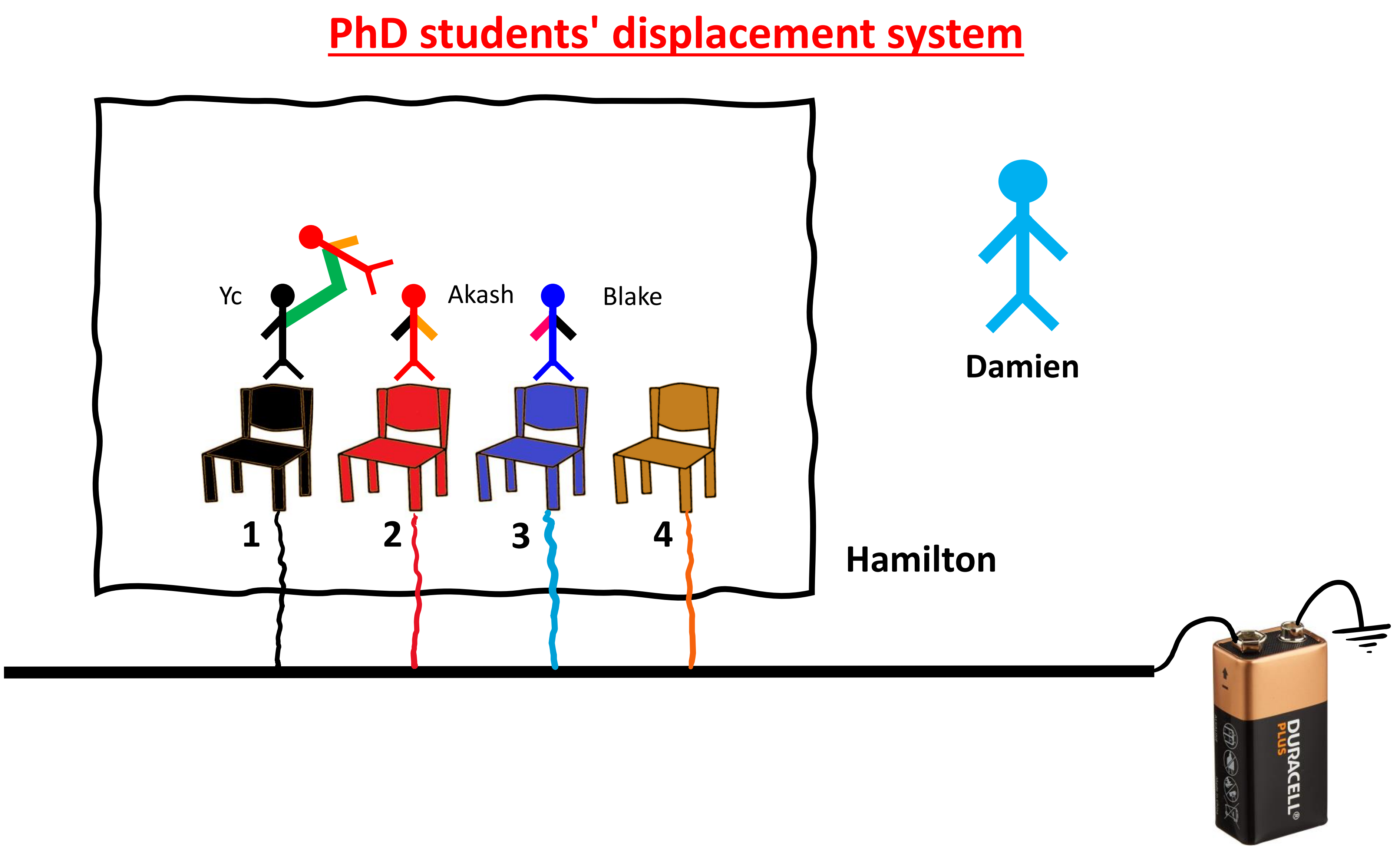
Built–in self improvement mechanism



Built–in self improvement mechanism

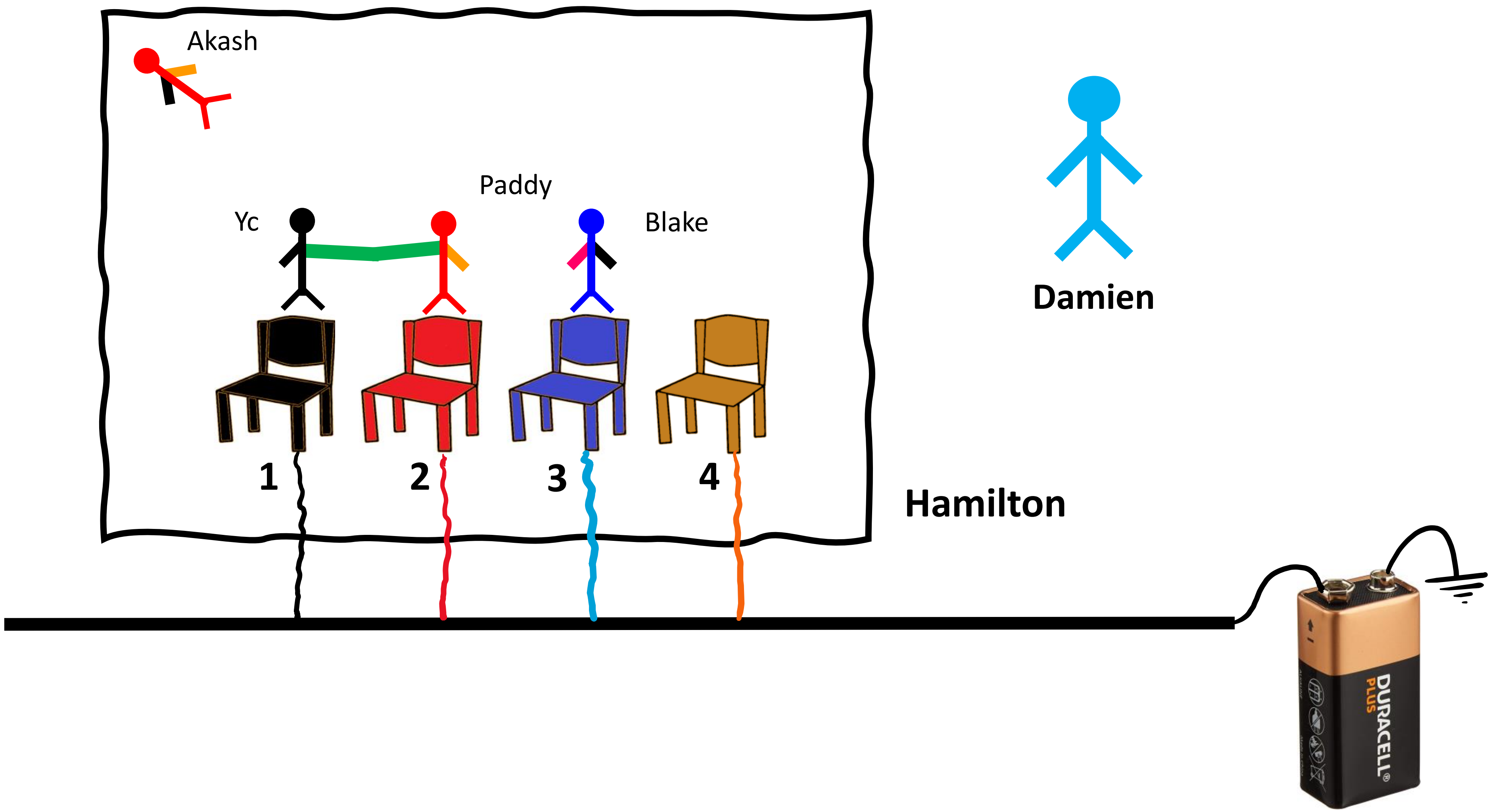


Built–in self improvement mechanism

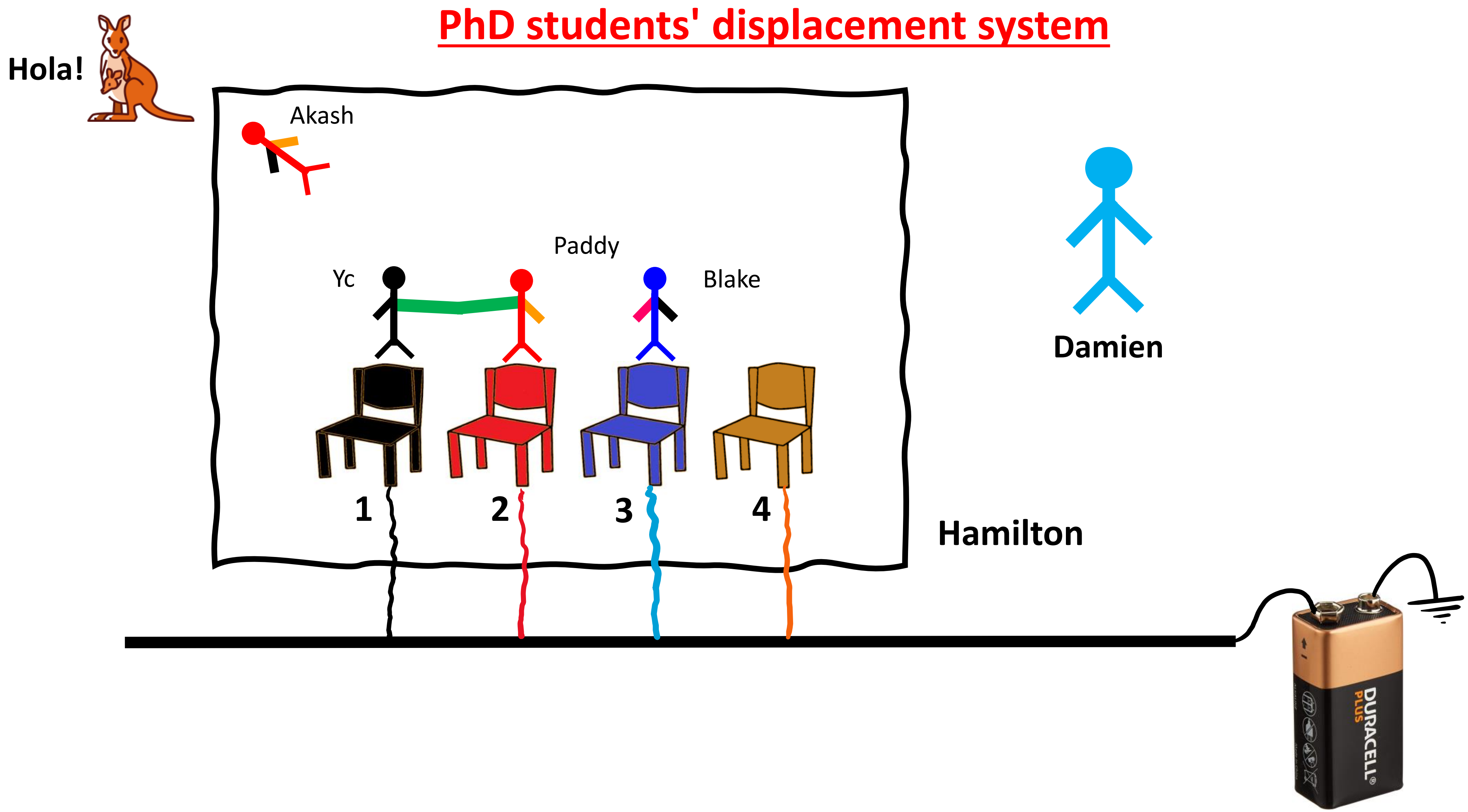


Built–in self improvement mechanism

PhD students' displacement system

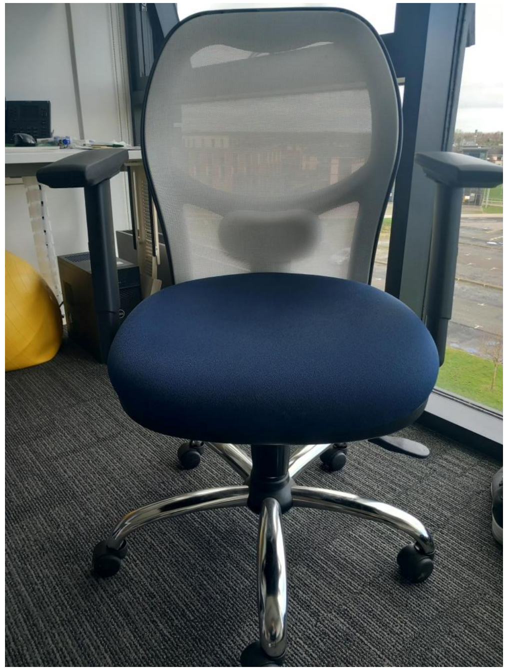


Built–in self improvement mechanism

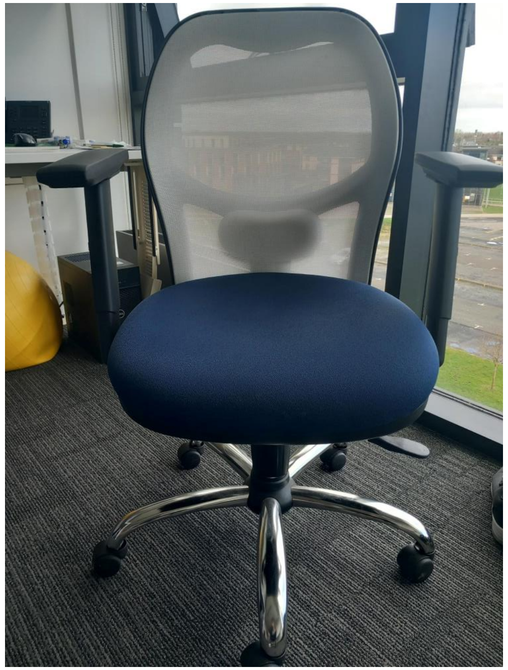


When you don't set your boundaries

When you don't set your boundaries



When you don’t set your boundaries



Hamilton Institute

Maynooth University
National University of Ireland Maynooth

The Curse of Hamilton’s Sofa

Ahmed Shalaby

2nd year PhD

Supervisor: Damien Woods

Fondúireacht Eolaíochta Éireann sfi Dá bhfuil romhainn

European Innovation Council

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How I discovered that my supervisor is actually a 

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How I discovered that my supervisor is actually a VAMPIRE

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The Curse of Hamilton's Sofa

How I discovered that my supervisor is actually a VAMPIRE

An efficient minimum free energy algorithm for interacting nucleic acid strands

Ahmed Shalaby

2nd year PhD

Supervisor: Damien Woods

Fondúireacht Eolaíochta Éireann sfi Dá bhfuil romhainn

European Innovation Council

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FIRE POINT

Let’s discover the rules of the game

In a perfect world

In a perfect world

- **Abstract Algebra**
- **Graph theory**
- **Algorithm analysis**
- **Number theory**

In a perfect world

- **Abstract Algebra**

- **Graph theory**

- **Algorithm analysis**

- **Number theory**

In a perfect world

- **Abstract Algebra**

DUNNES
STORES

- **Graph theory**

ALDI

- **Algorithm analysis**

- **Number theory**

In a perfect world

- Abstract Algebra

DUNNES STORES

- Graph theory

ALDI

- Algorithm analysis

TESCO

- Number theory

In a perfect world

- **Abstract Algebra**

DUNNES STORES

- **Graph theory**

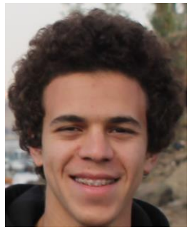
ALDI

- **Algorithm analysis**

TESCO

- **Number theory**

SuperValu



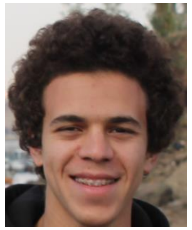
Ahmed’s goal

PI

?

?

?



Ahmed’s goal

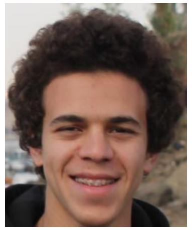
- What is his mindset?
- What he prefers?

PI

?

?

?



Ahmed’s goal

- What is his mindset?
- What he prefers?

Modelling

Computation

PI

?

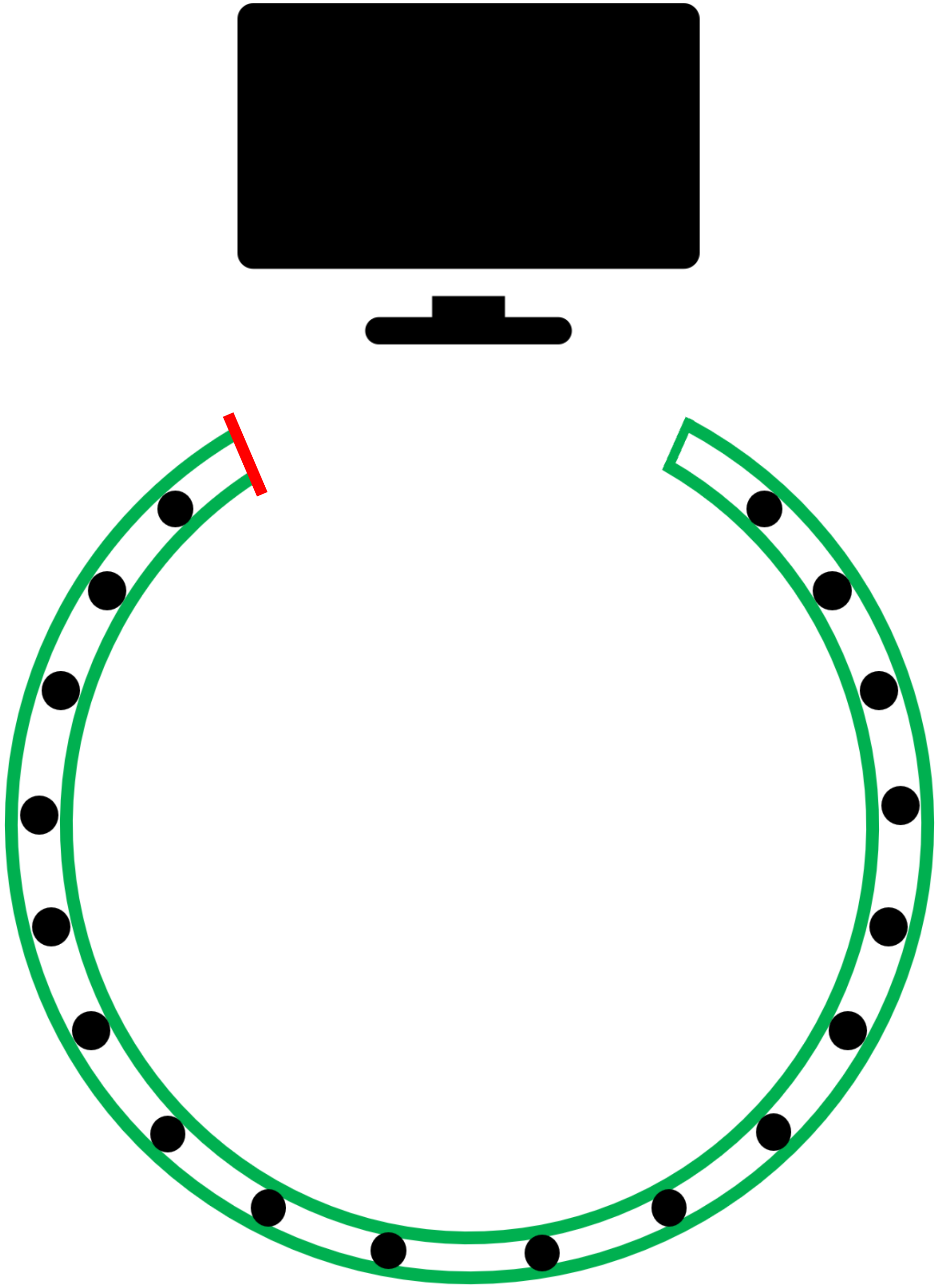
?

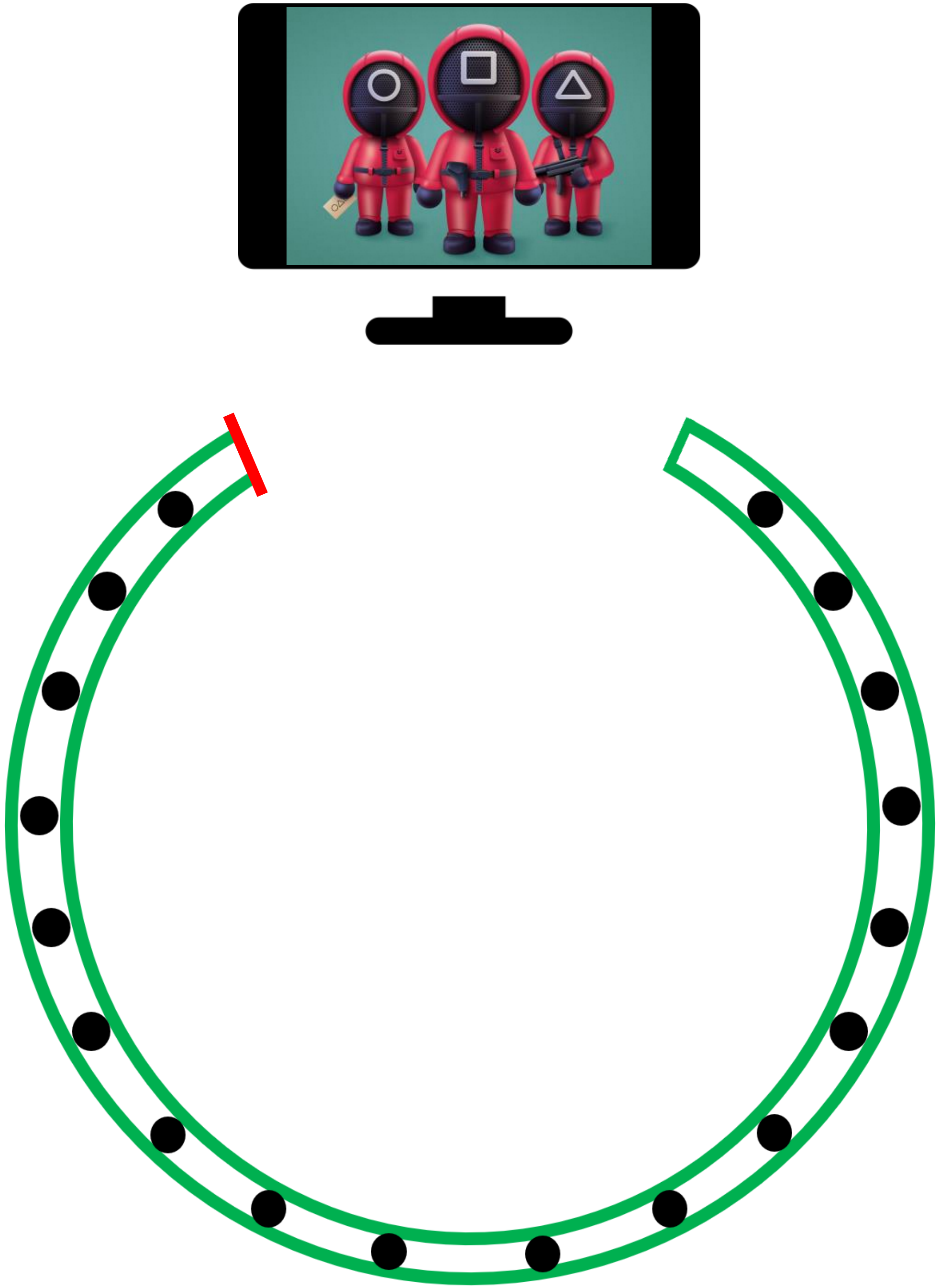
?

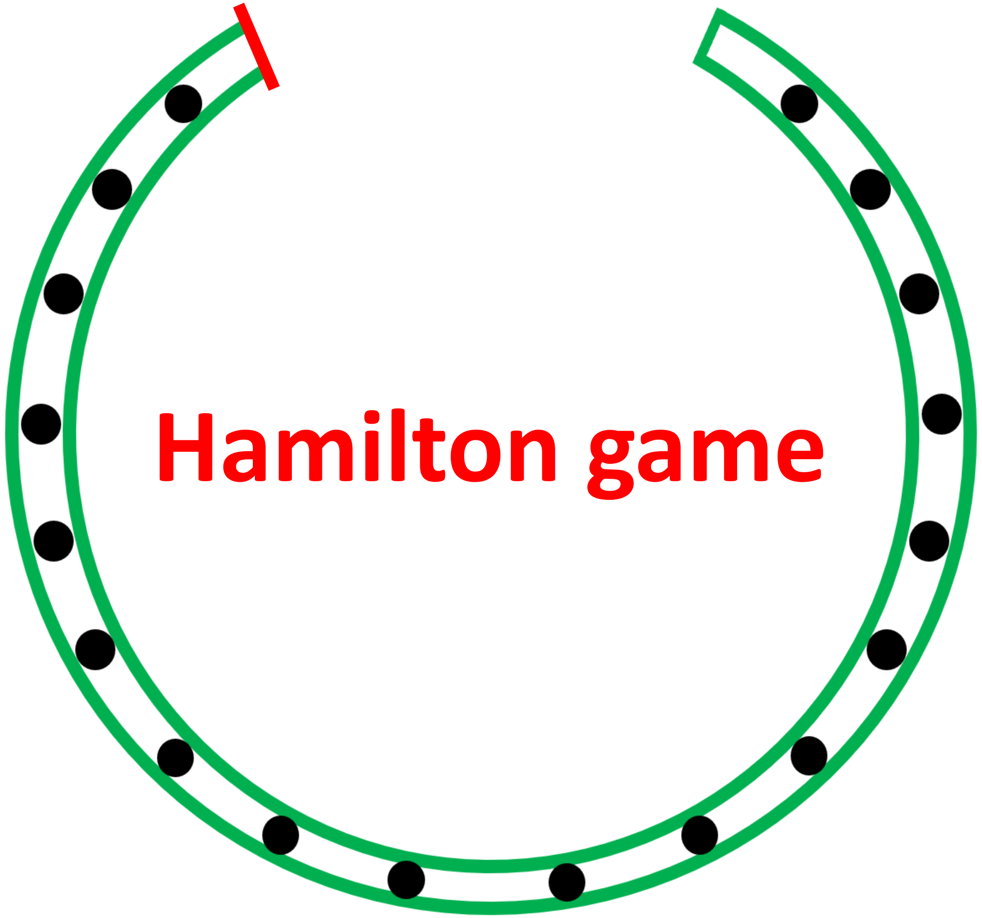
Once Upon a Time in Hamilton

Once Upon a Time in Hamilton

Email From Rosemary Kate







Hamilton game

Level 1

Hamilton game

Hamilton game

First year

Daniel
Augustina
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Second year

Ahmed
Andre
Paddy
Cormac
.
.

Third year

Dara
Solmaz
Oluwayomi
.
.
.

fourth year

Akash
Yc
Emma
Darshana
.
.

Hamilton game

First year

Daniel
Augustina
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fourth year

Akash
Yc
Emma
Darshana
.
.

Don’t trust our new lab

Hamilton game

First year	Second year	Third year	fourth year
Daniel Augustina . . .	Ahmed Andre Paddy Cormac . .	Dara Solmaz Oluwayomi . . .	Akash Yc Emma Darshana . .

Don’t trust our new lab

Akash Akash Akash Akash .	Dara Dara Dara Dara .	Darshana Darshana Darshana Darshana .	Fergal Fergal Fergal Fergal .	. . .	Ahmed

Hamilton game

First year	Second year	Third year	fourth year
Daniel Augustina . . .	Ahmed Andre Paddy Cormac . .	Dara Solmaz Oluwayomi . . .	Akash Yc Emma Darshana . .

Don’t trust our new lab

Akash Akash Akash Akash .	Dara Dara Dara Dara .	Darshana Darshana Darshana Darshana .	Fergal Fergal Fergal Fergal .	. . .	Ahmed

Hamilton game

First year	Second year	Third year	fourth year
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Don't trust our new lab

Akash Akash Akash Akash .	Dara Dara Dara Dara .	Darshana Darshana Darshana Darshana .	Fergal Fergal Fergal Fergal .	. . .	Ahmed

Hamilton game

First year

Daniel
Augustina
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Second year

Ahmed
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Third year

Dara
Solmaz
Oluwayomi
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fourth year

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Yc
Emma
Darshana
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Don't trust our new lab

Akash
Akash
Akash
Akash
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Dara
Dara
Dara
Dara
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Darshana
Darshana
Darshana
Darshana
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Fergal
Fergal
Fergal
Fergal
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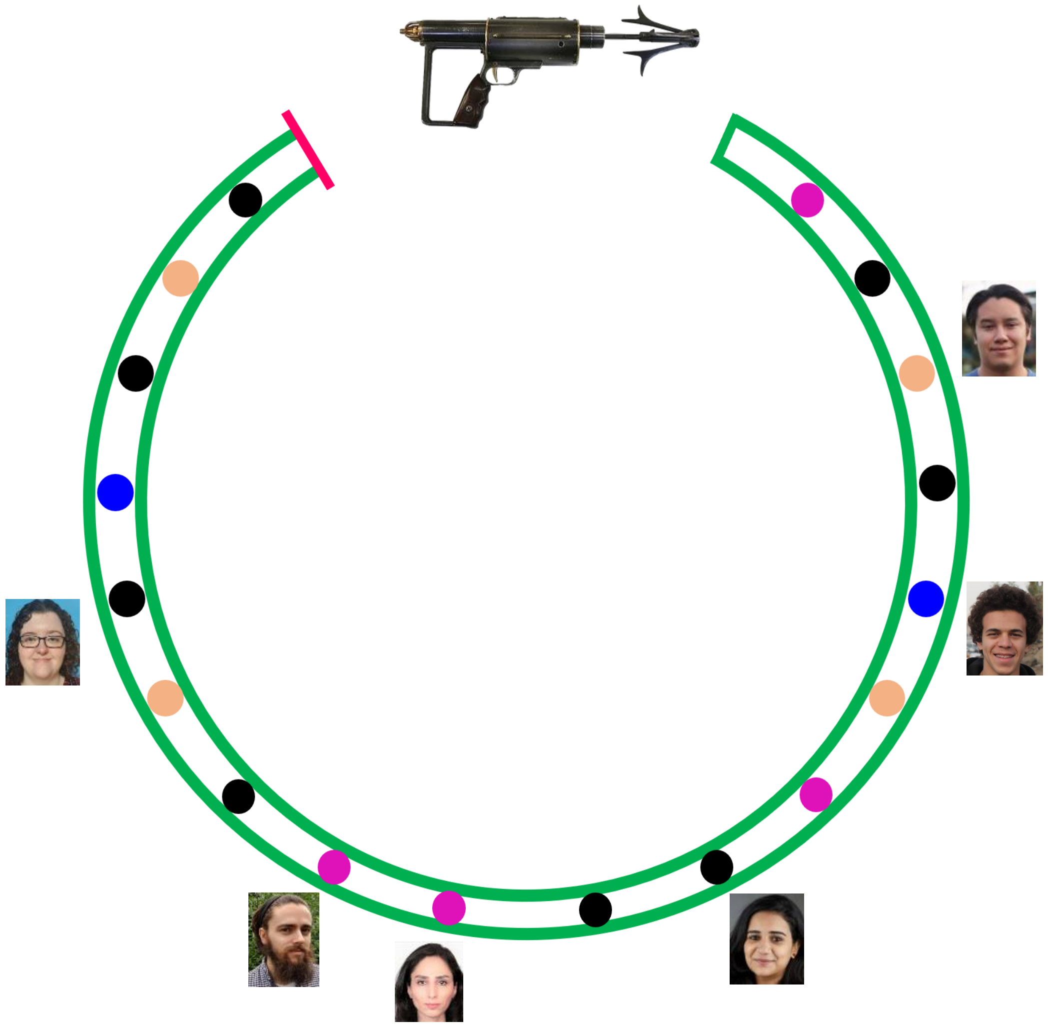
. . .

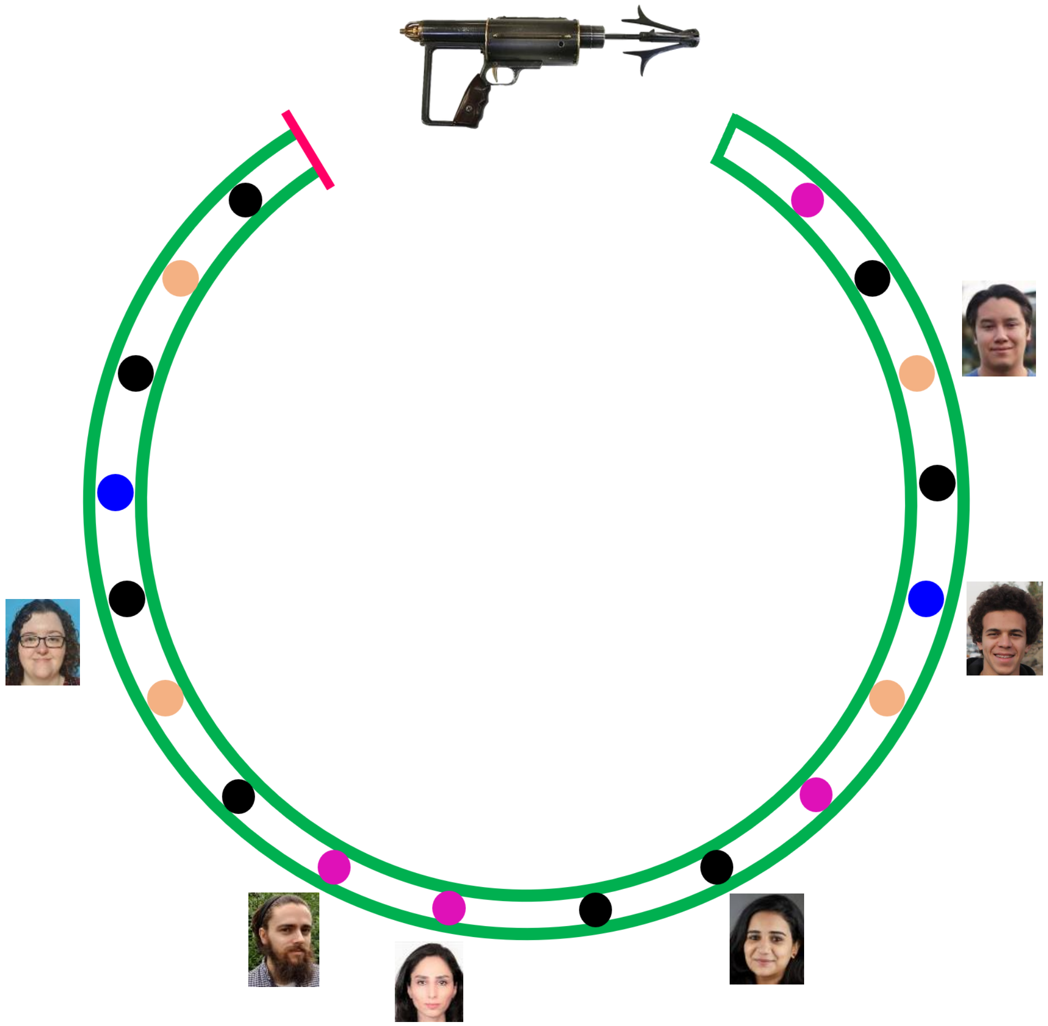
Ahmed

Rules of Hamilton game



Rules of Hamilton game

- If you kill, you are safe



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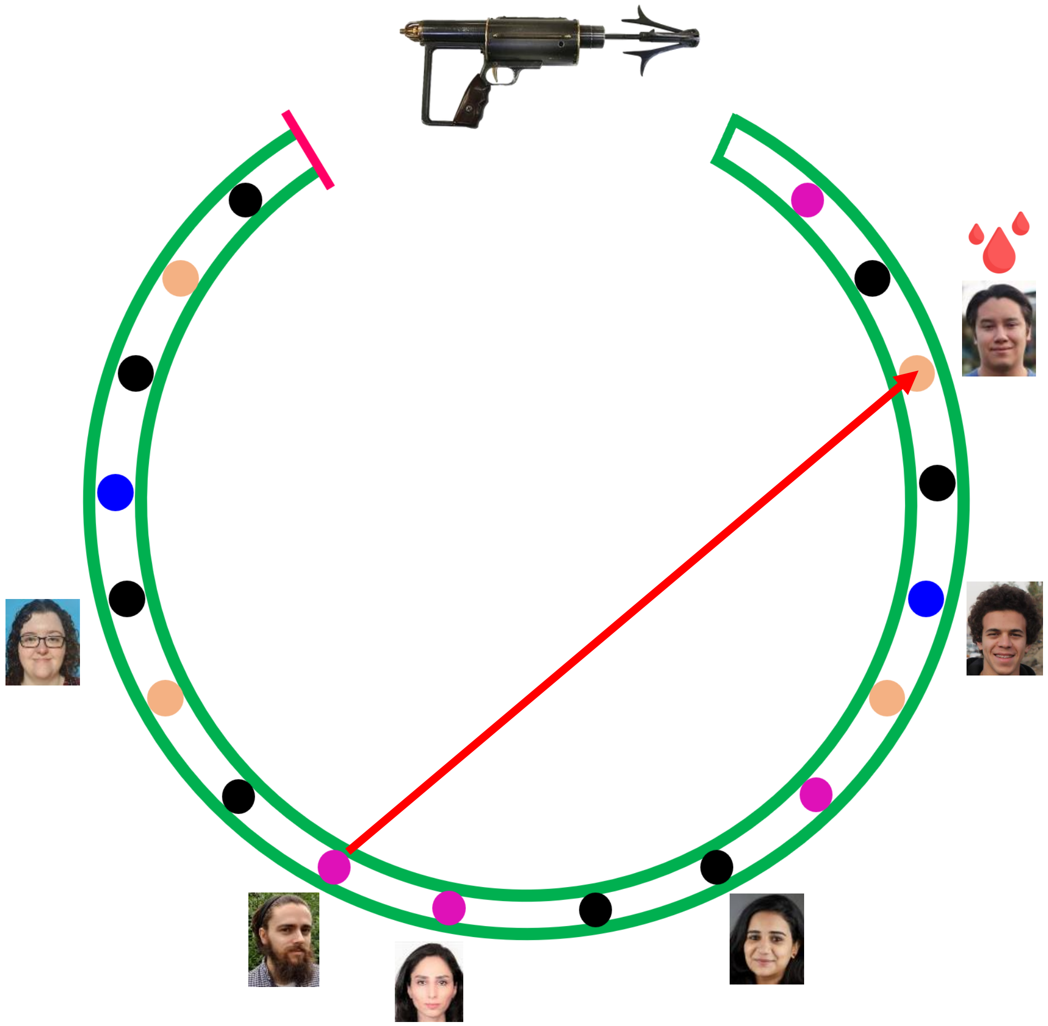

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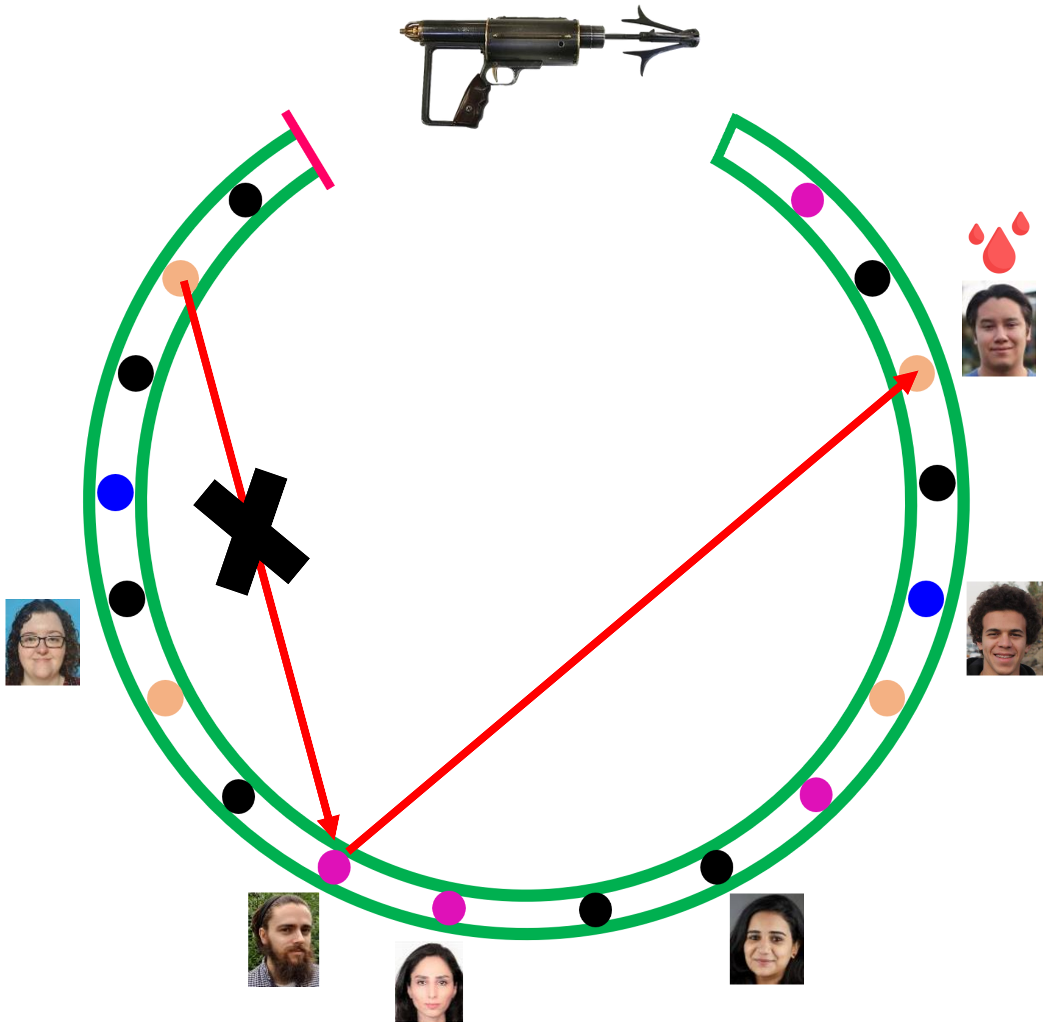
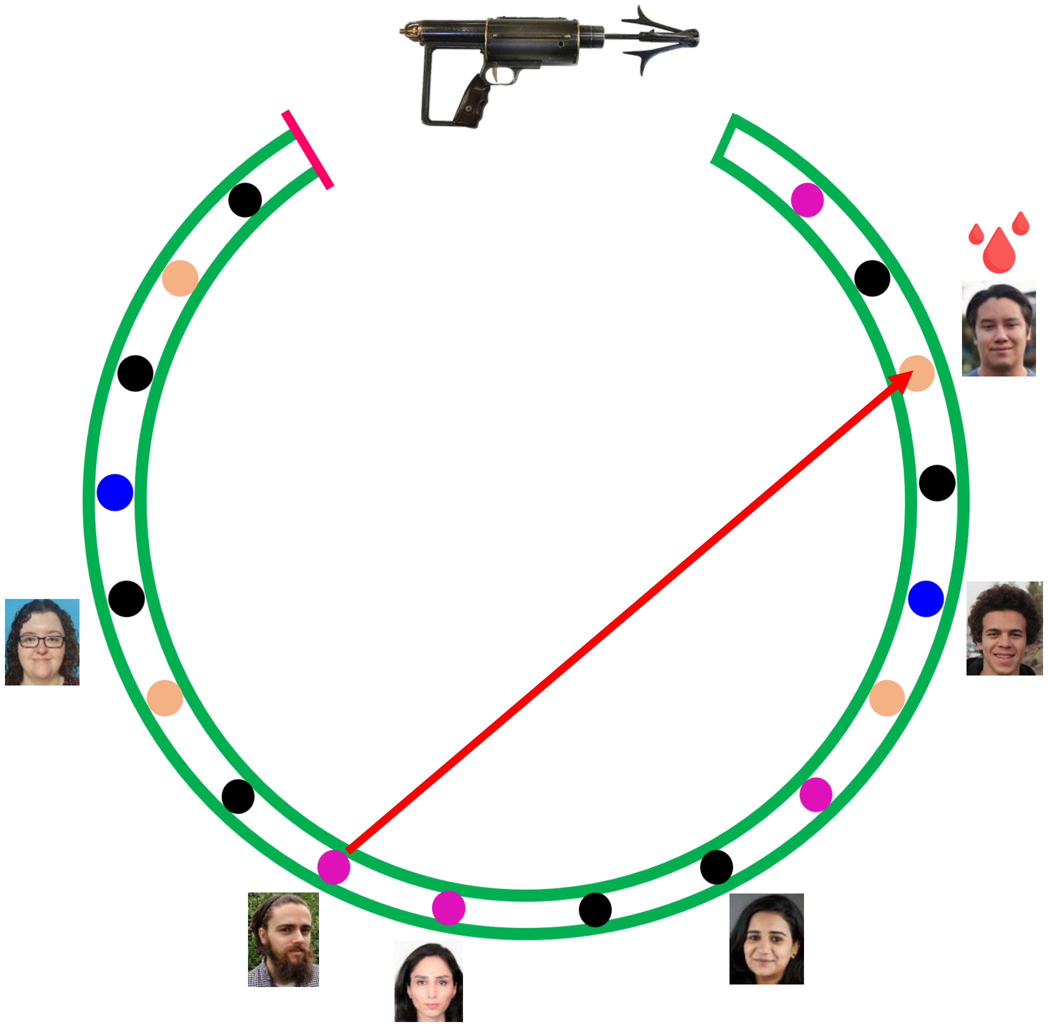


Rules of Hamilton game

- If you kill, you are safe
- You can only kill one student, you have only one bullet



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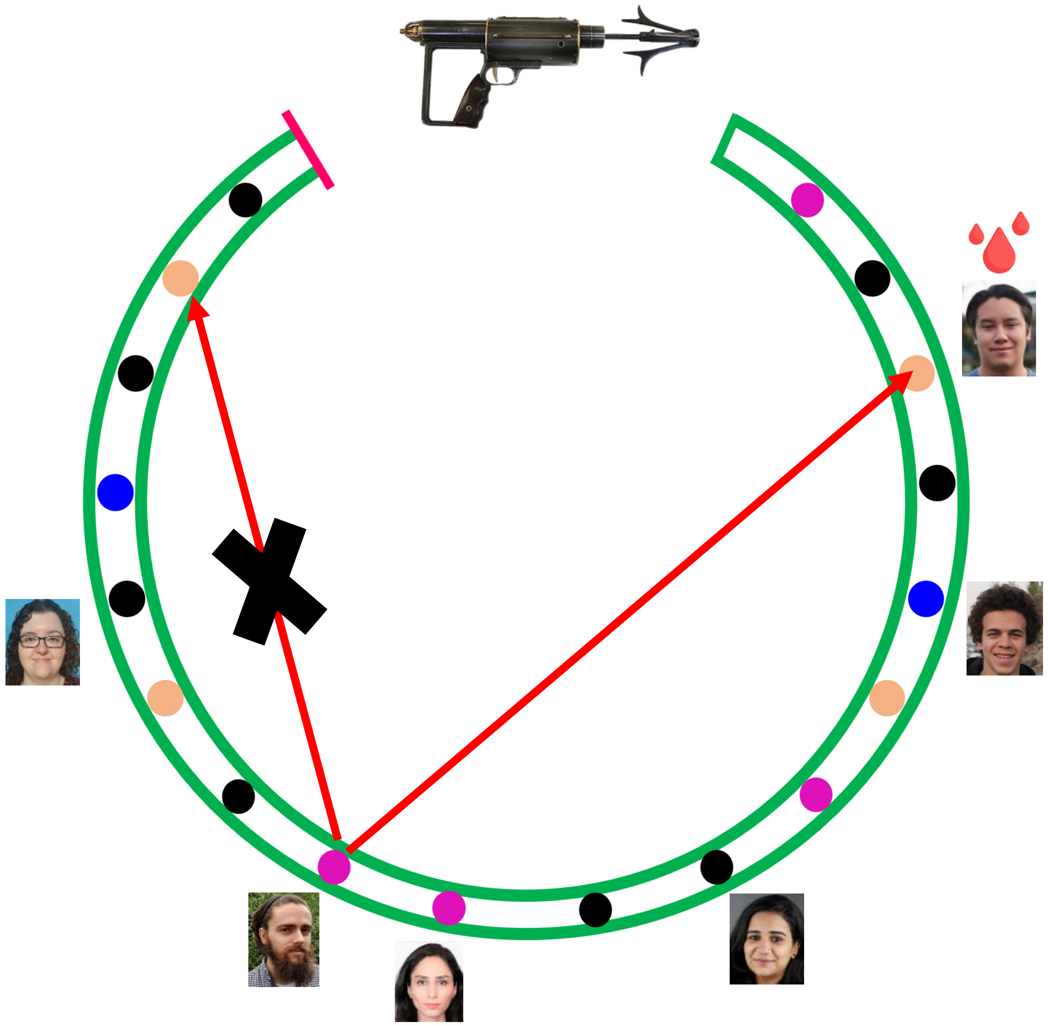

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- You can only kill one student, you have only one bullet
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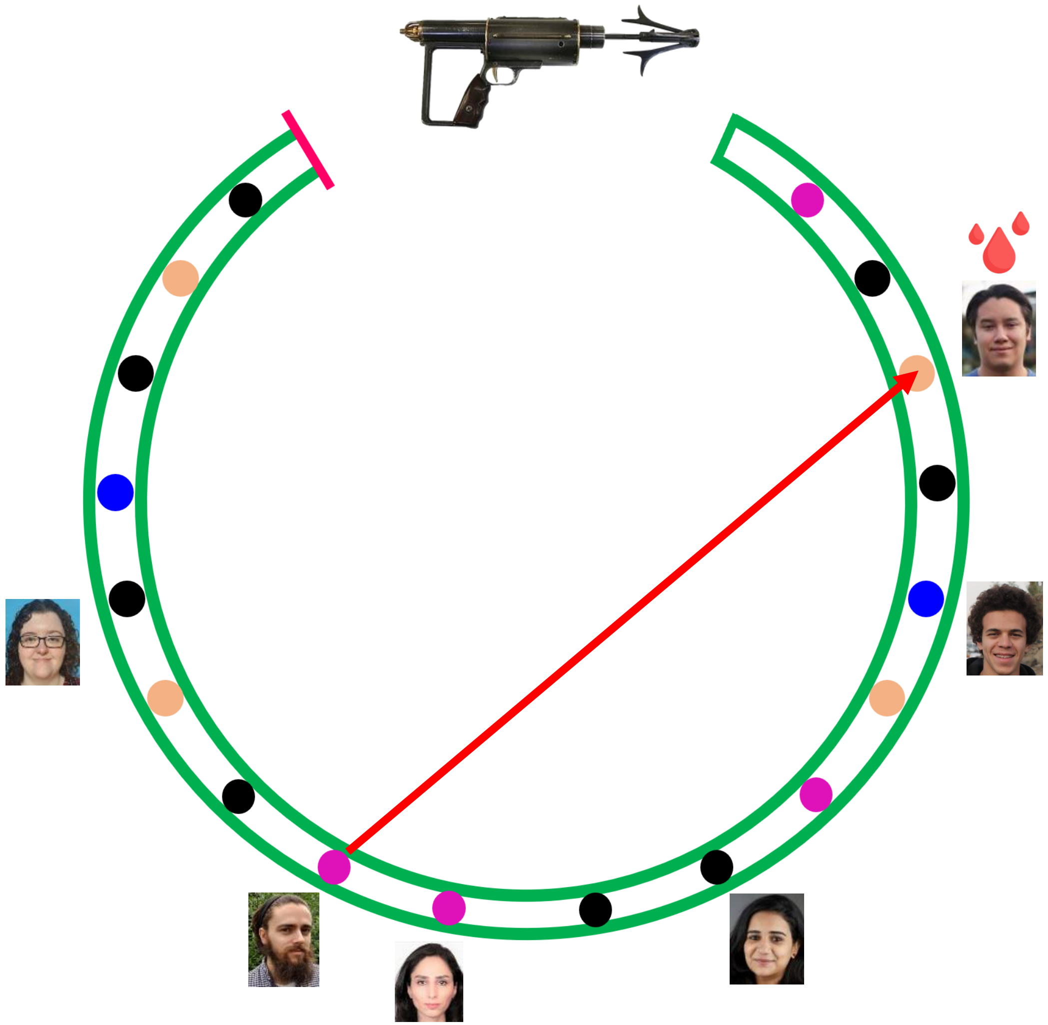

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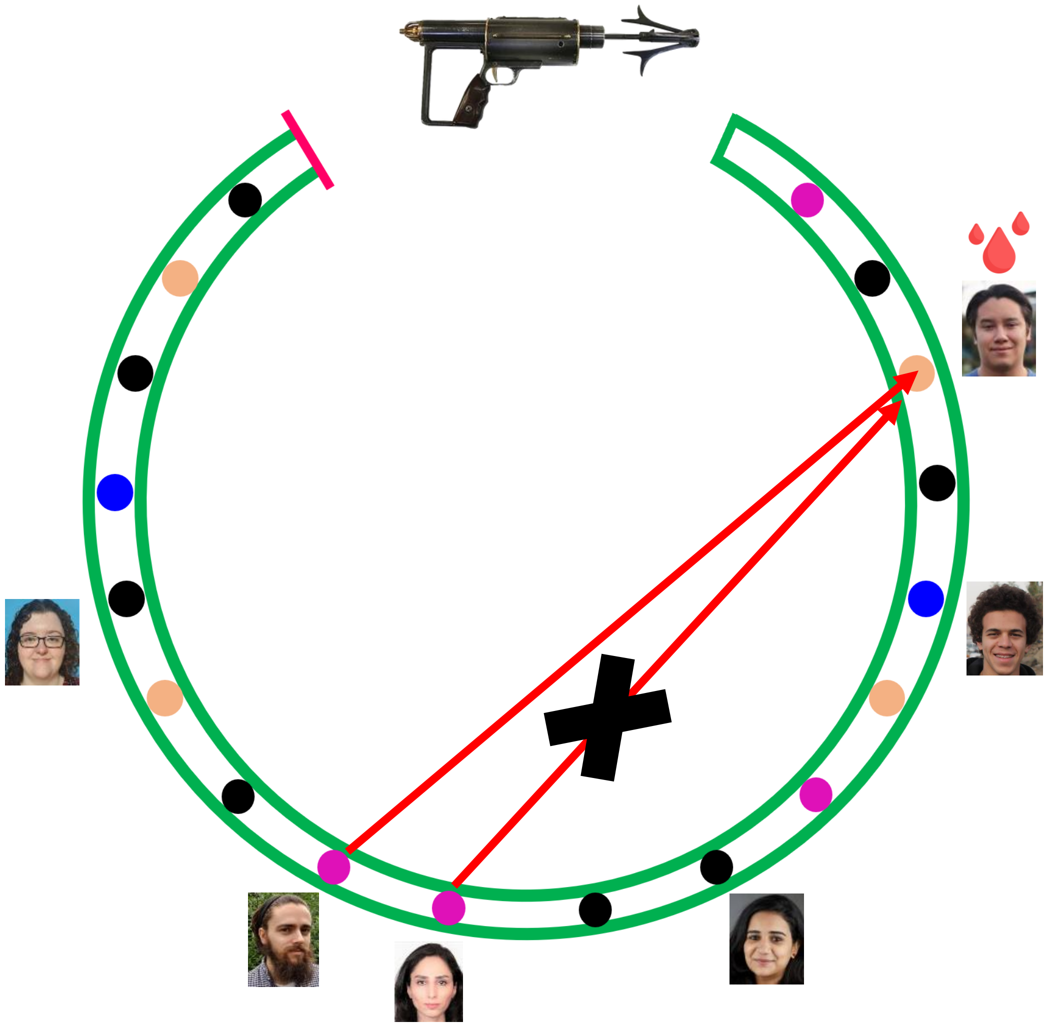
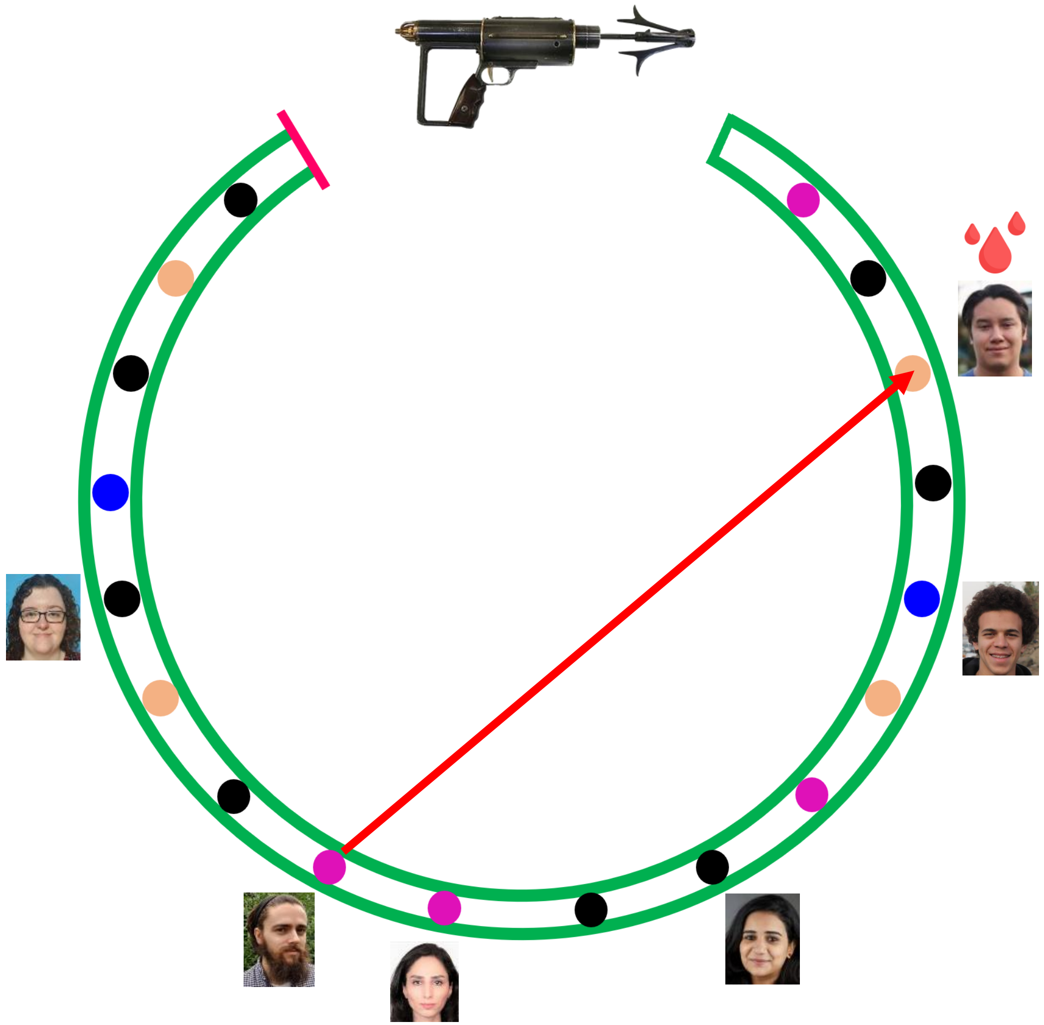


Rules of Hamilton game

- If you kill, you are safe
- You can only kill one student, you have only one bullet
- You can be killed once
- You must respect other killers, you can't cross their killing lines



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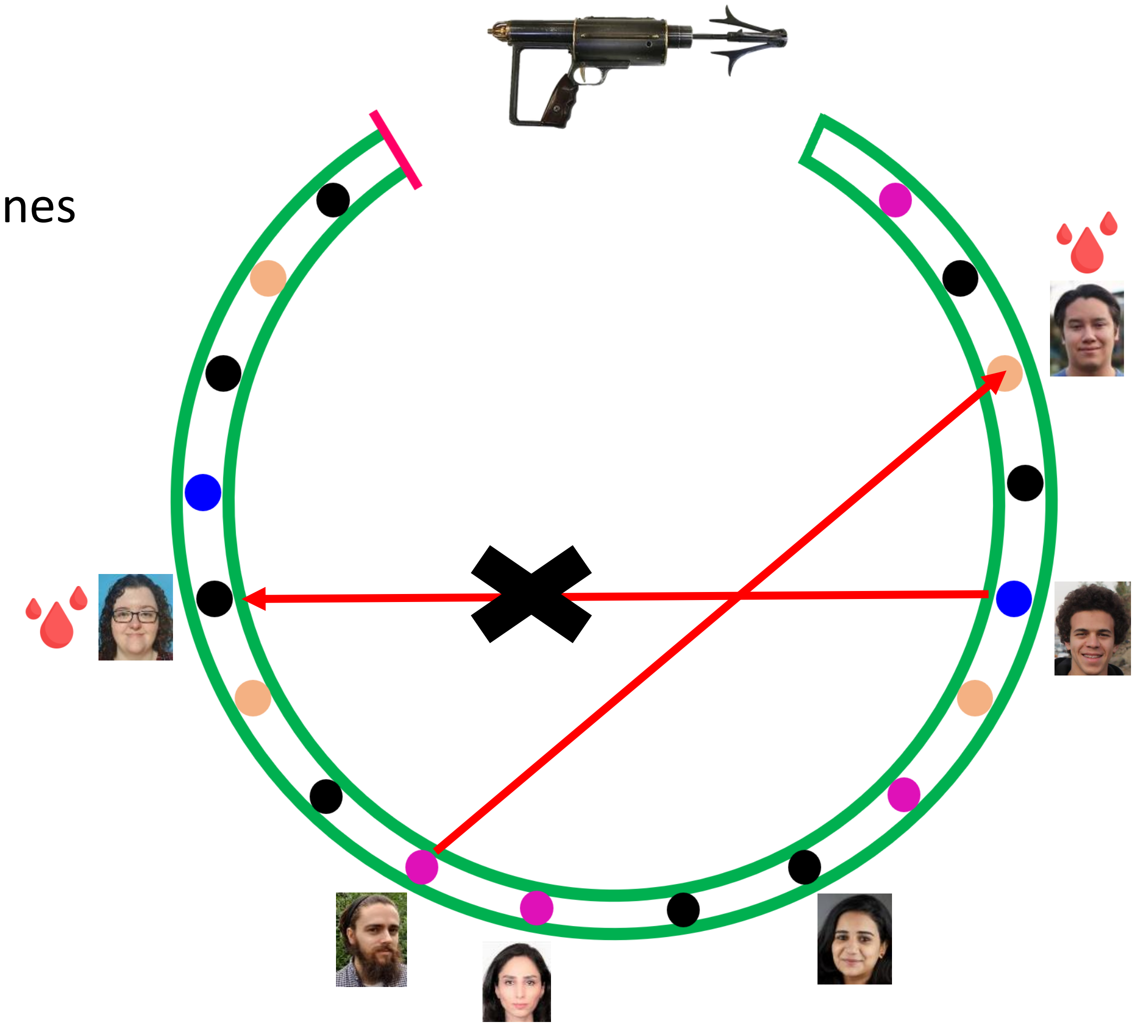

Rules of Hamilton game

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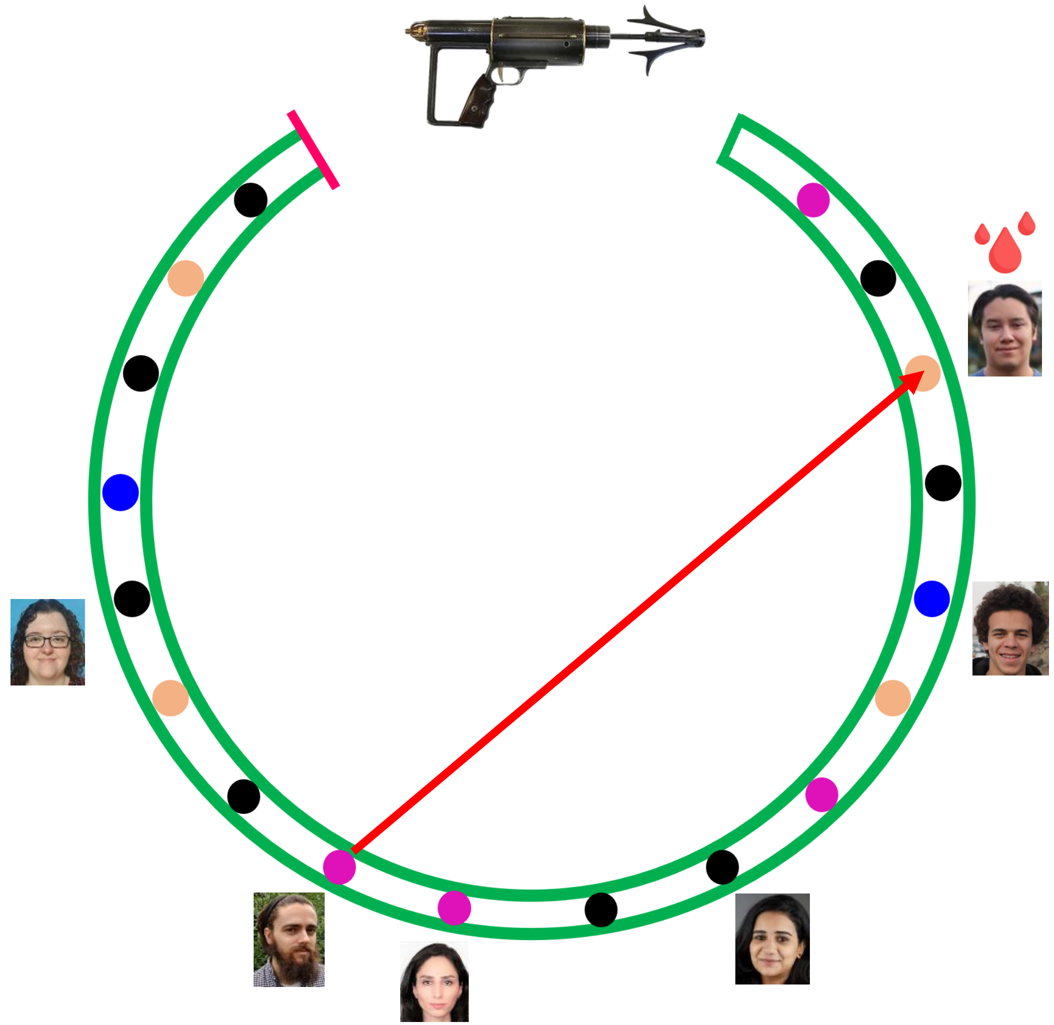
- Ahmed can only kill, he's an immortal man



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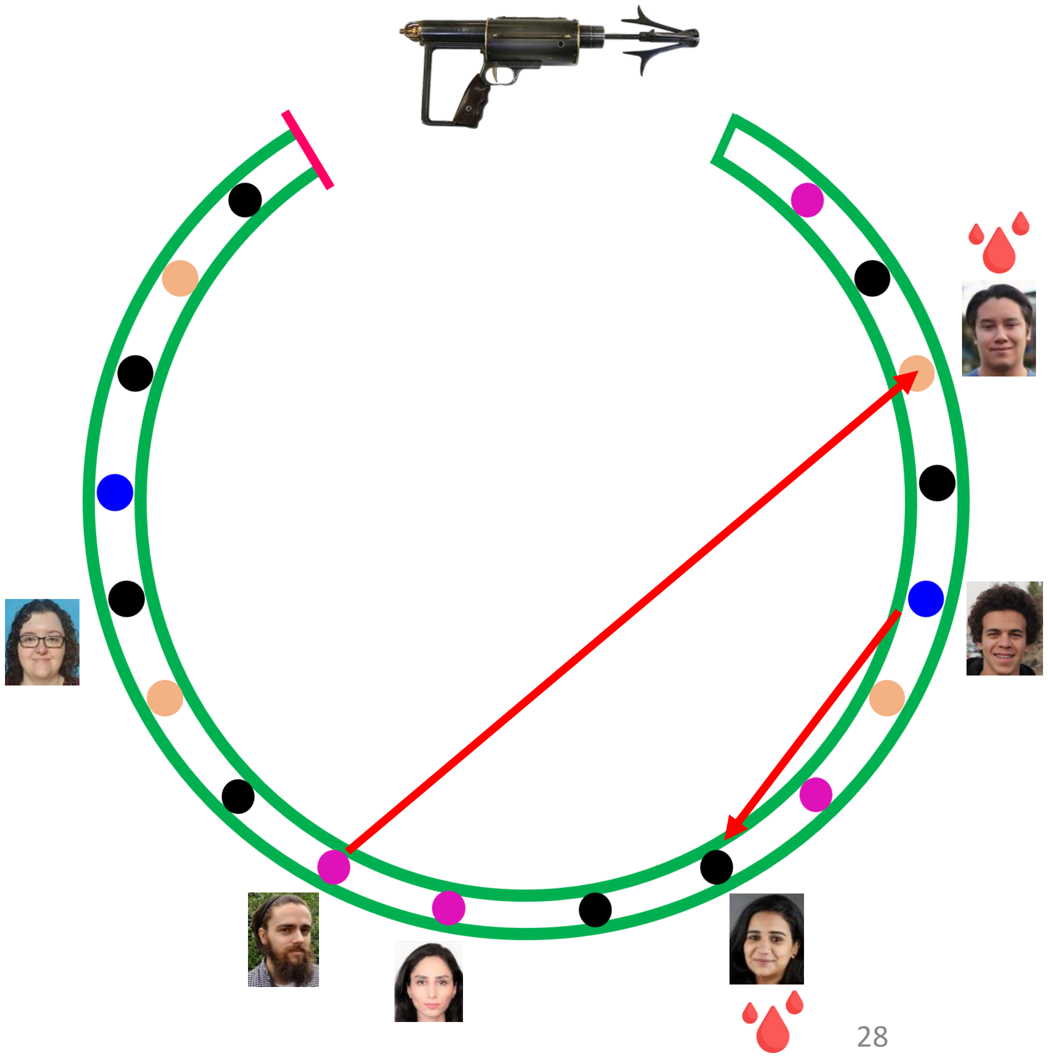
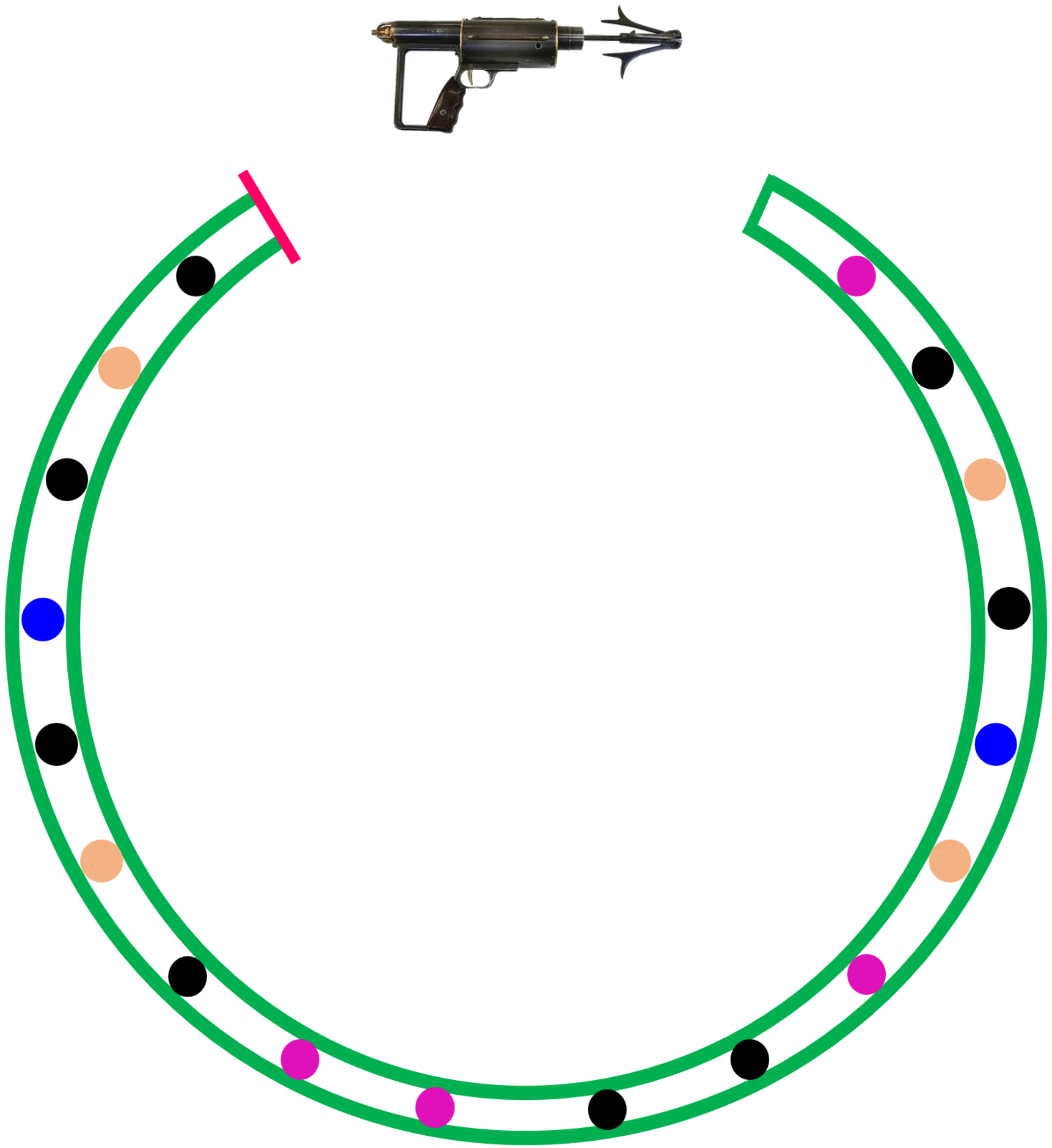
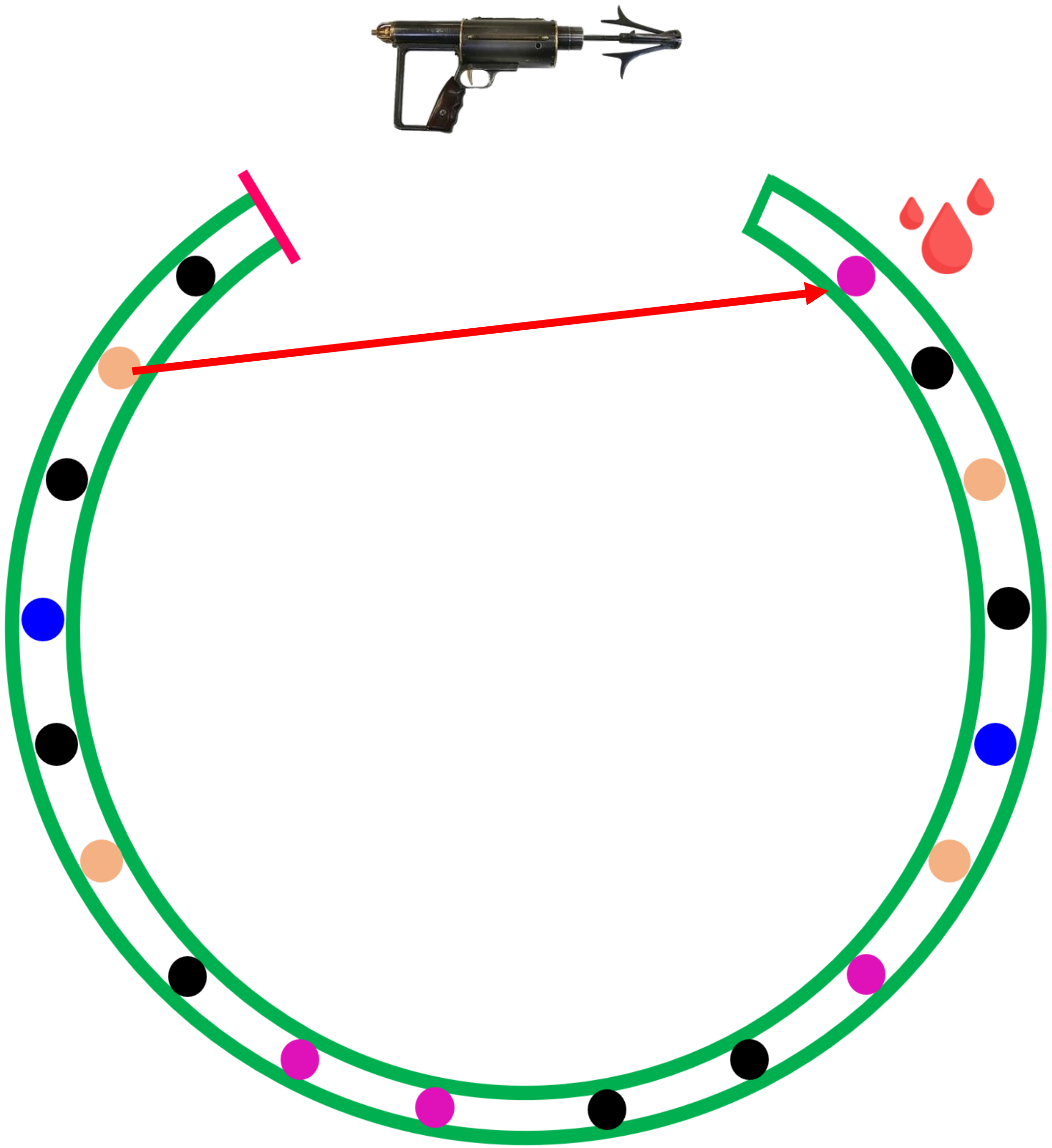
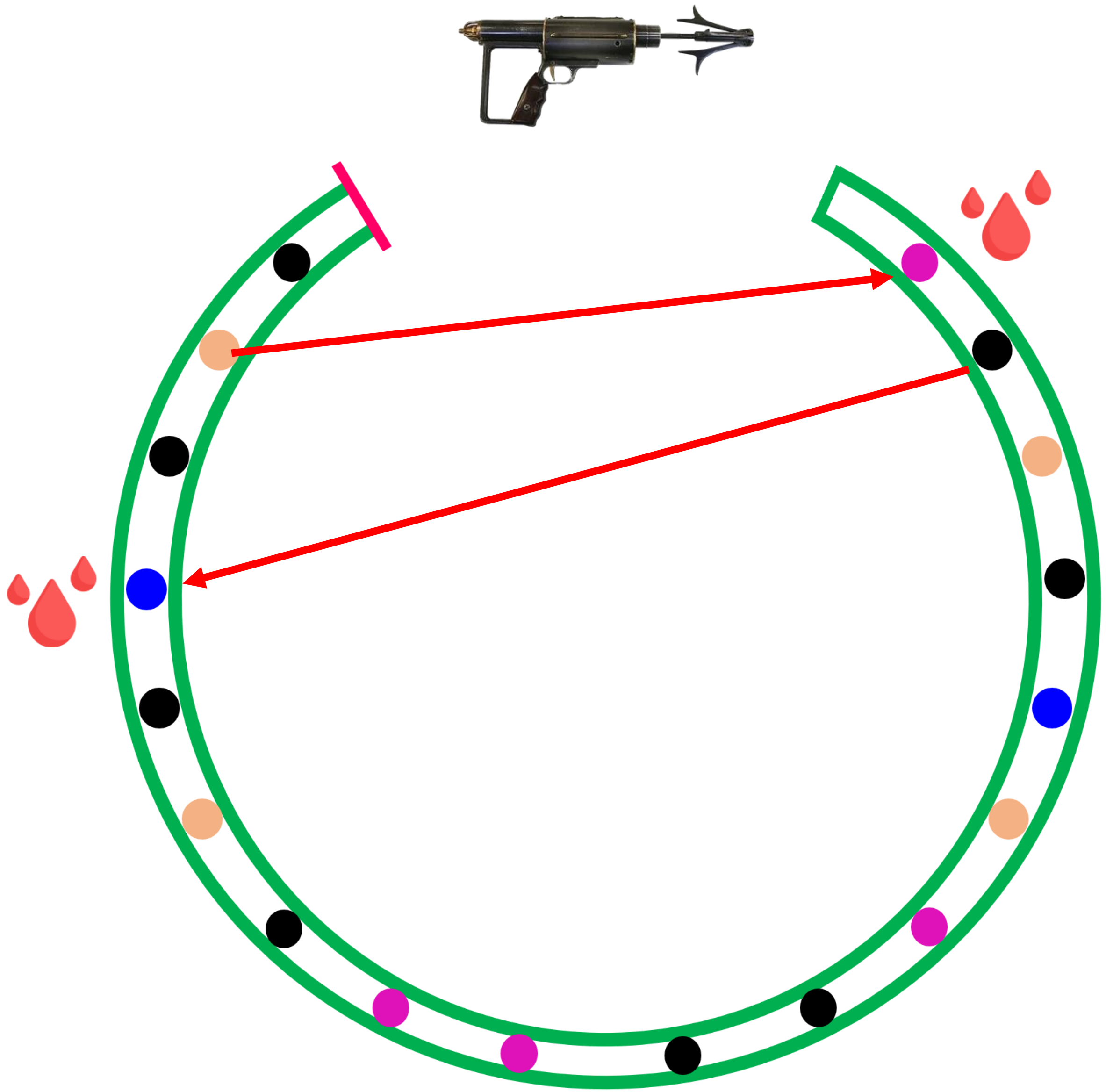
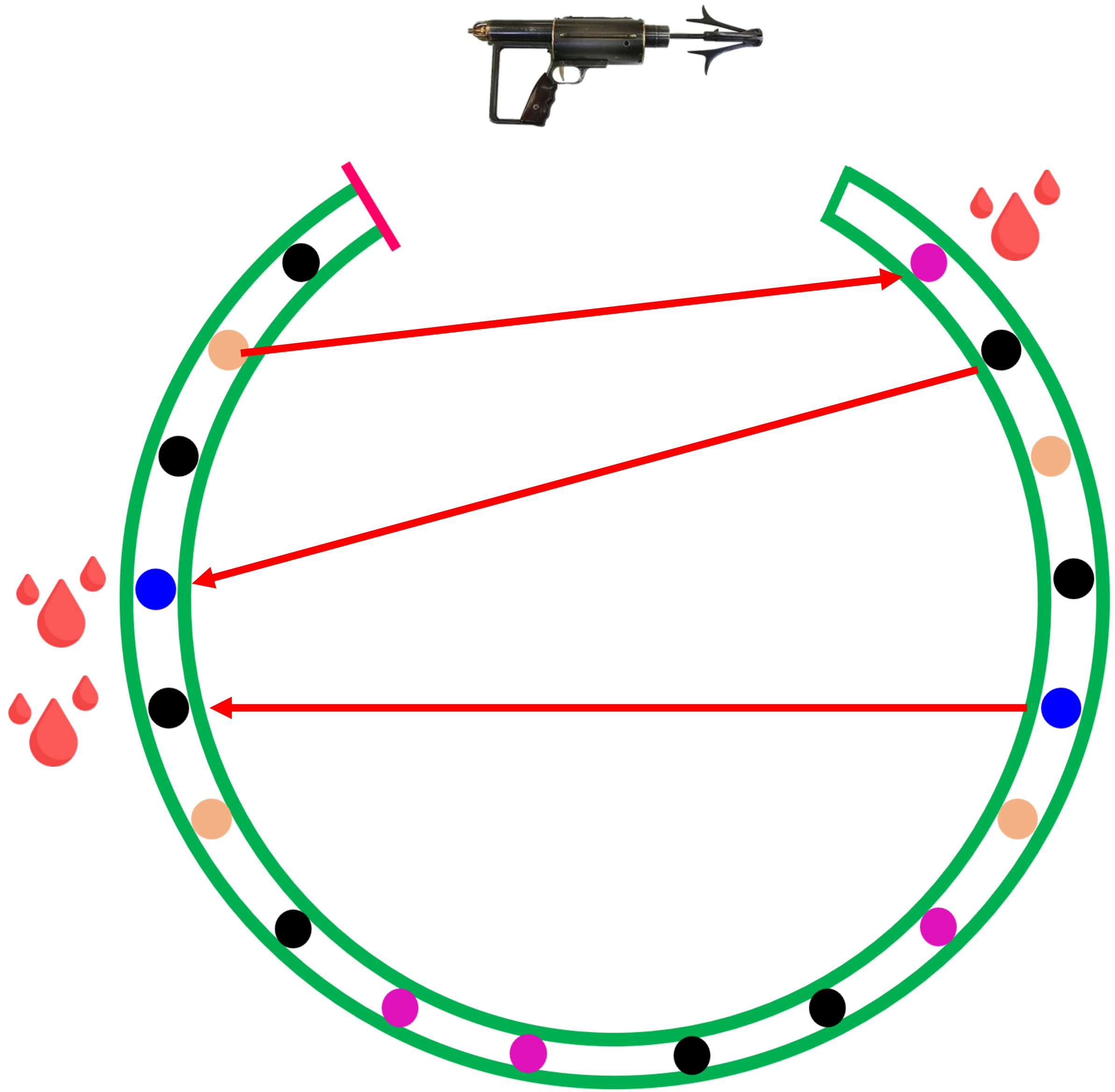
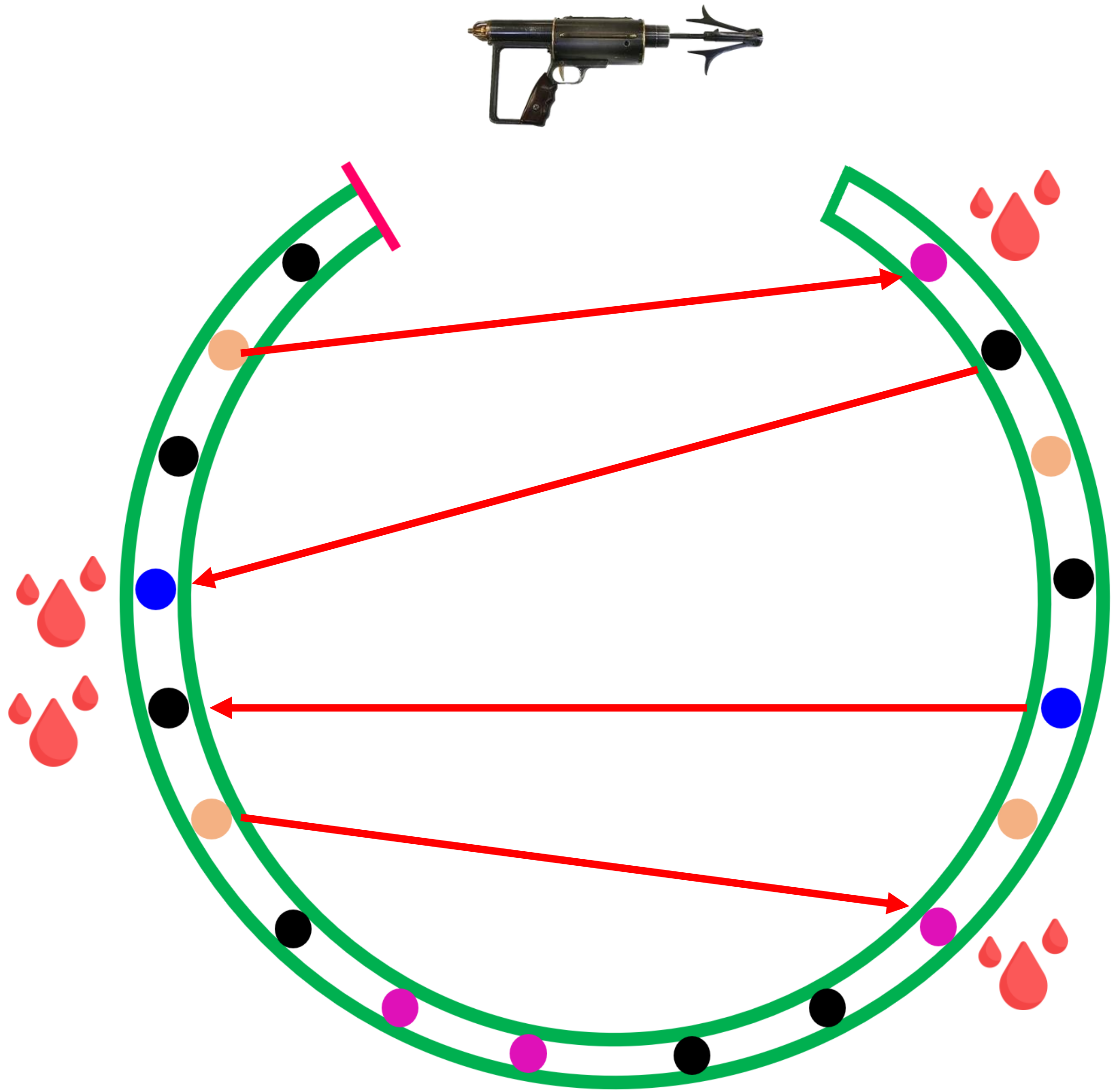


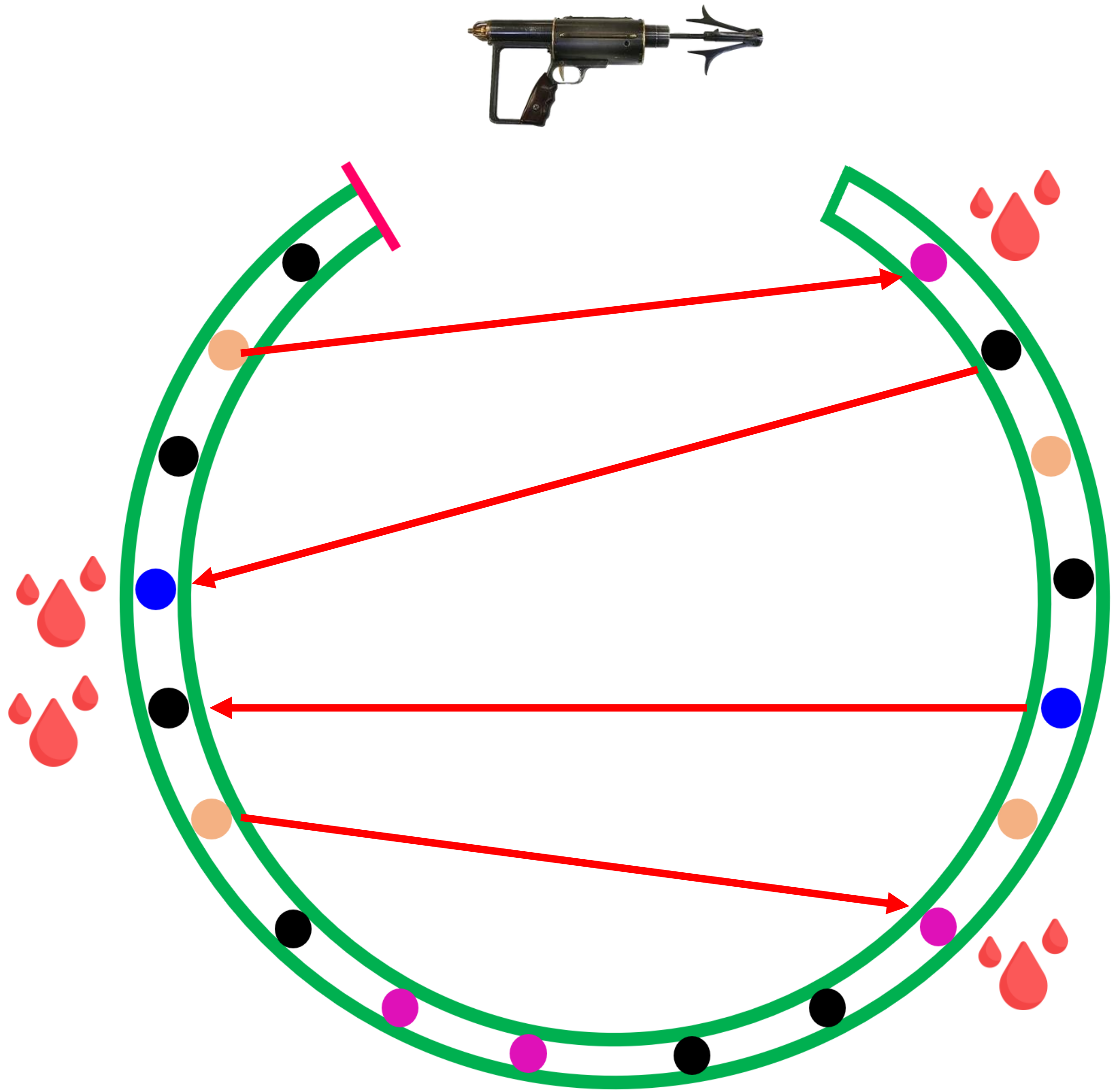




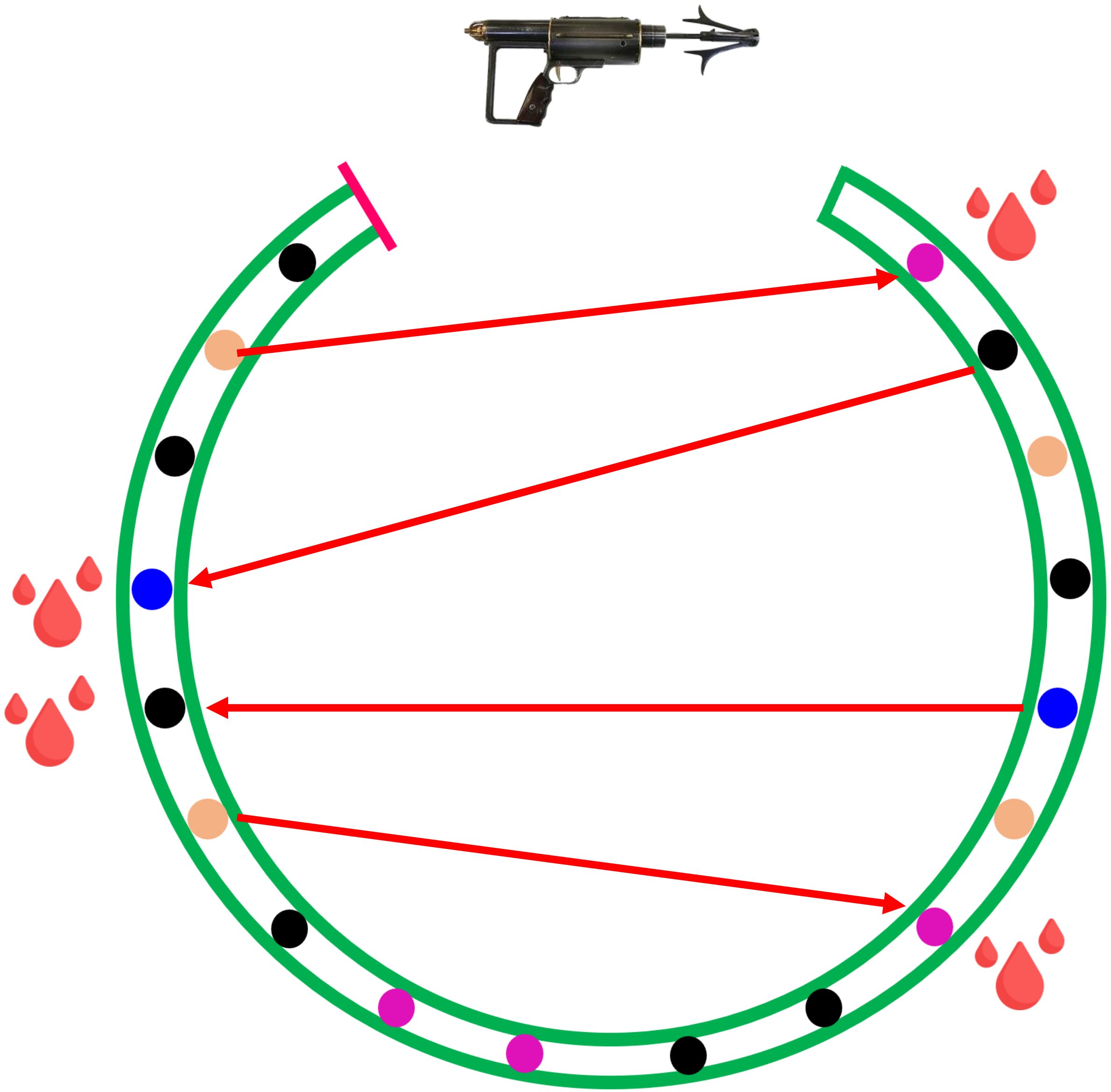






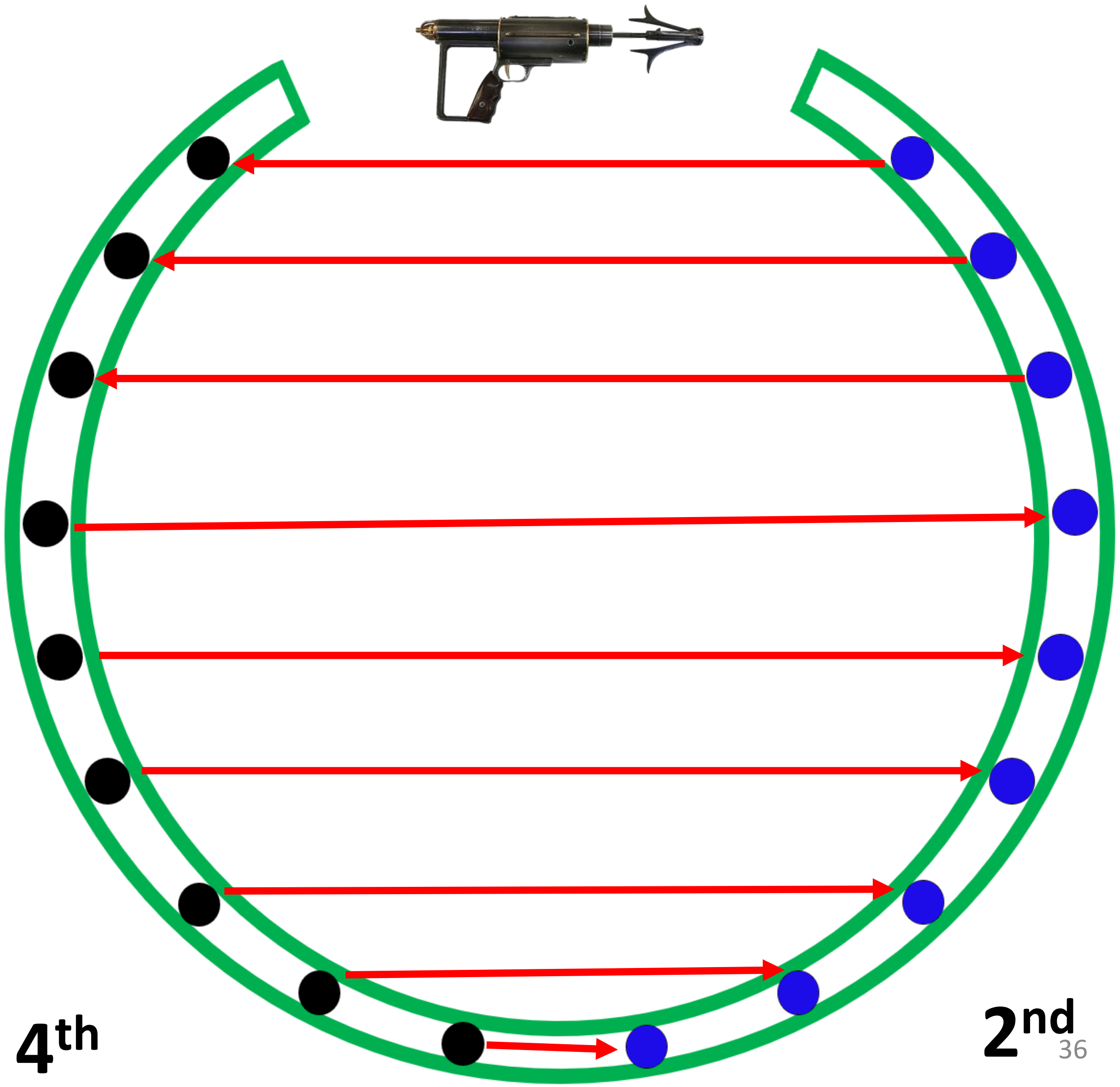


Structure S



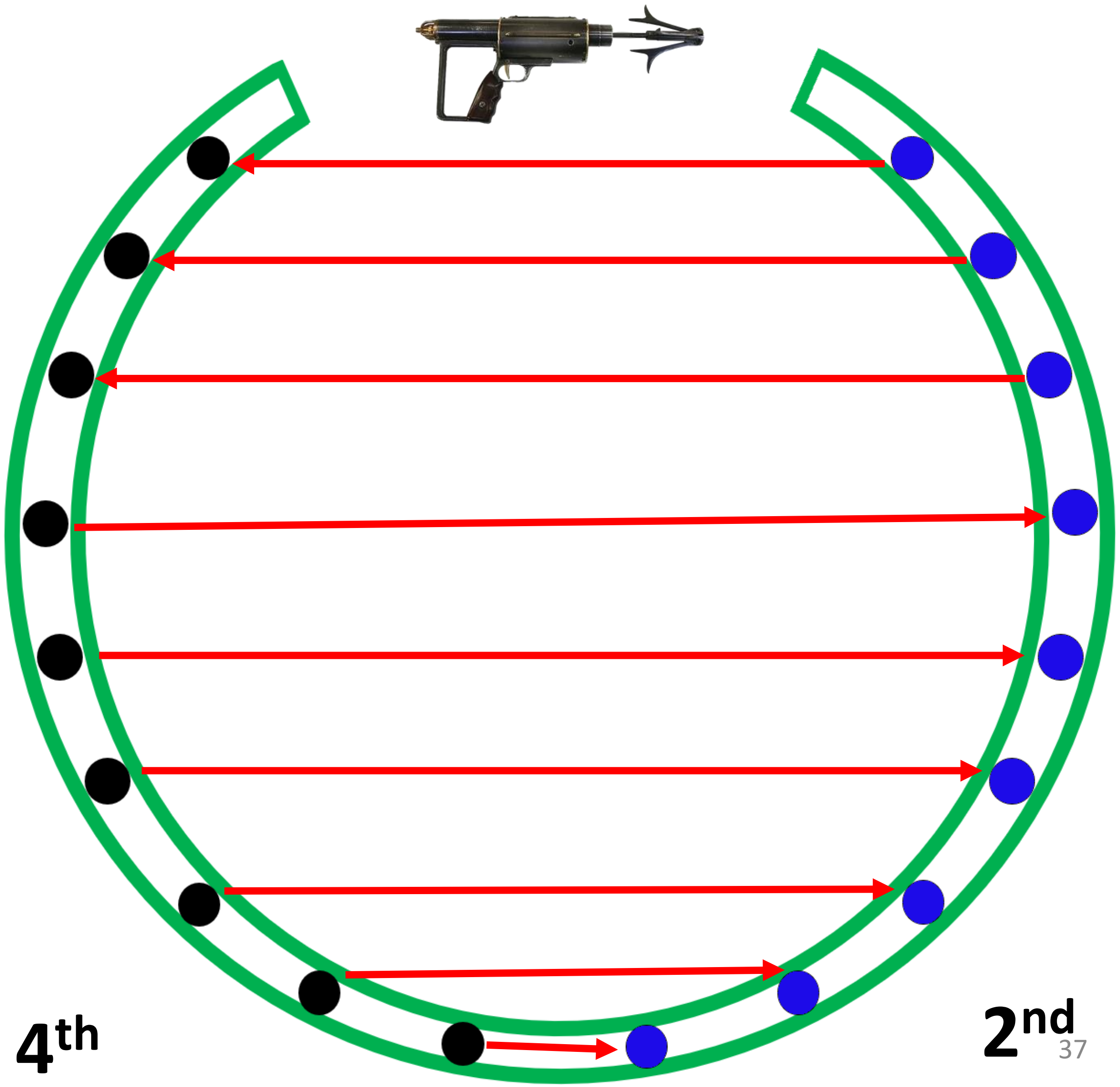
Structure S

$$N = 18$$



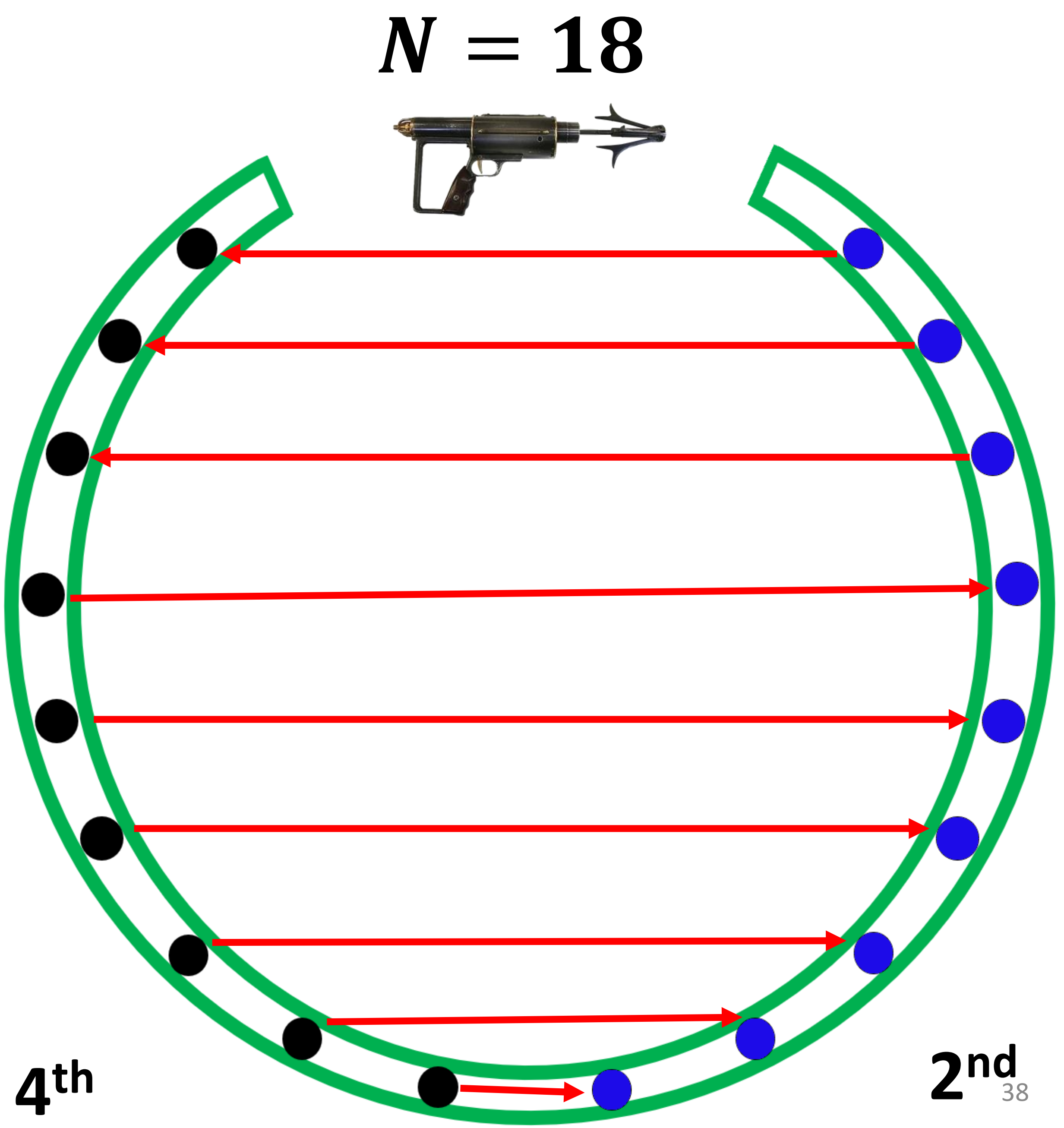
$$\# = \binom{9}{0} + \binom{9}{1} + \ldots + \binom{9}{9} = 2^9 = 2^{N/2}$$

$N = 18$



$$\# = \binom{9}{0} + \binom{9}{1} + \ \dots \ + \binom{9}{9} = 2^9 = 2^{N/2}$$

Ω: the set of all possible structures that respect the game rules

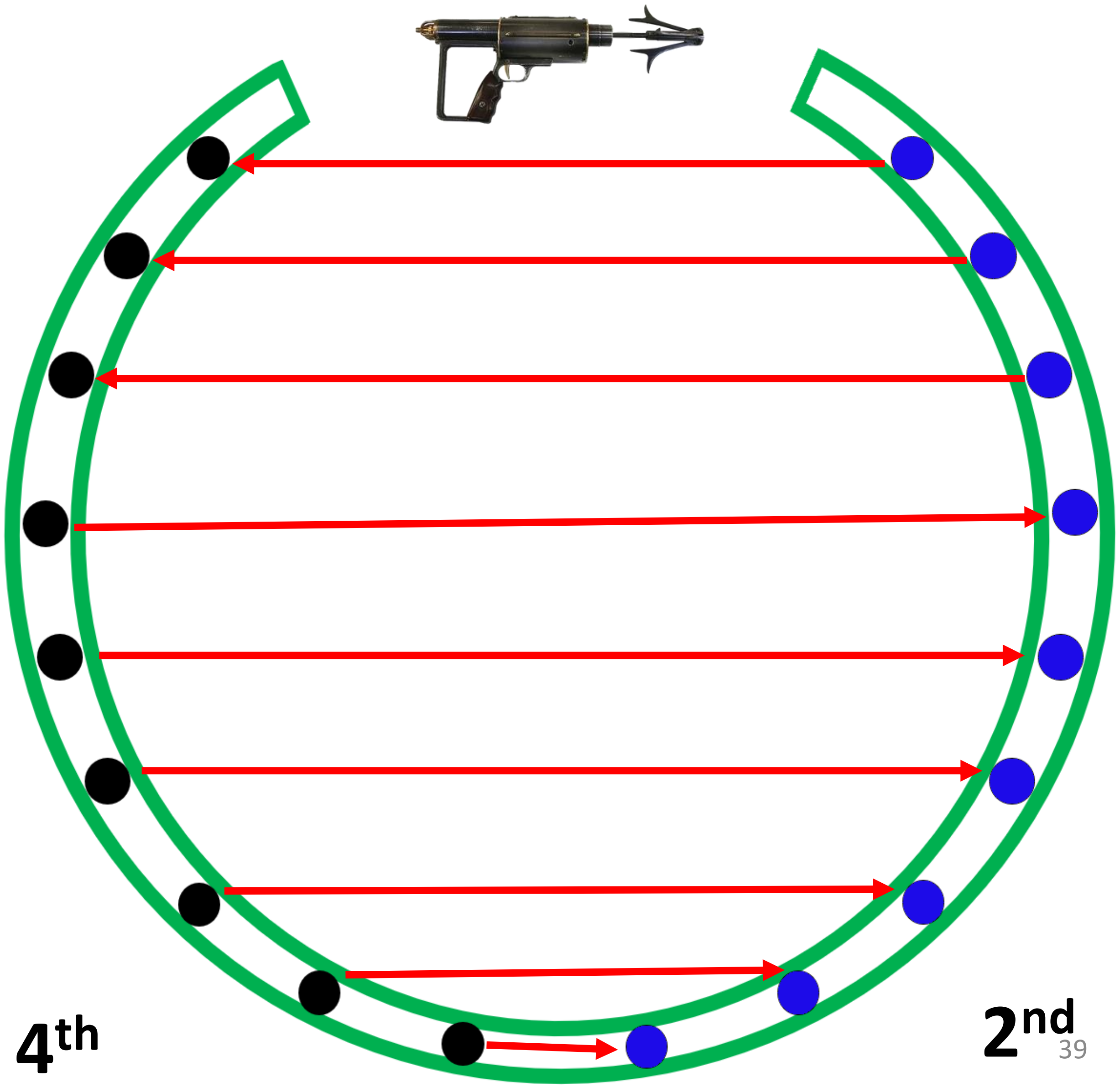


$$\# = \binom{9}{0} + \binom{9}{1} + \ldots + \binom{9}{9} = 2^9 = 2^{N/2}$$

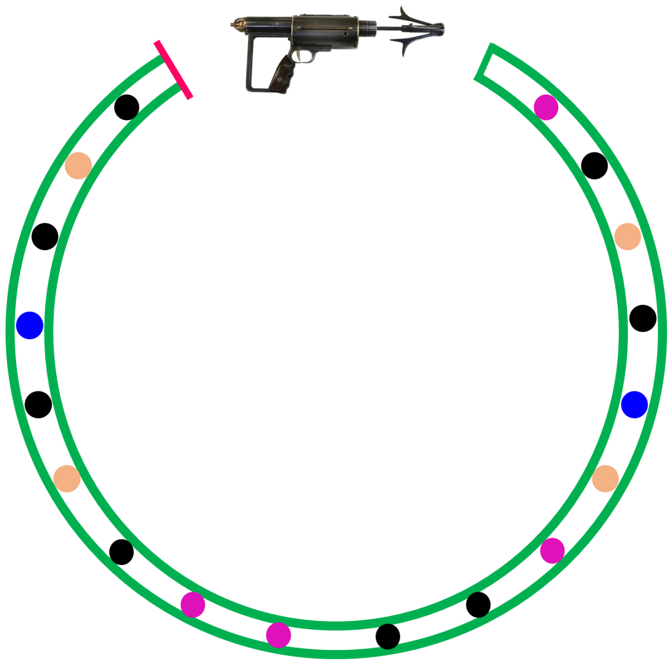
Ω: the set of all possible structures that respect the game rules

Huge

$N = 18$

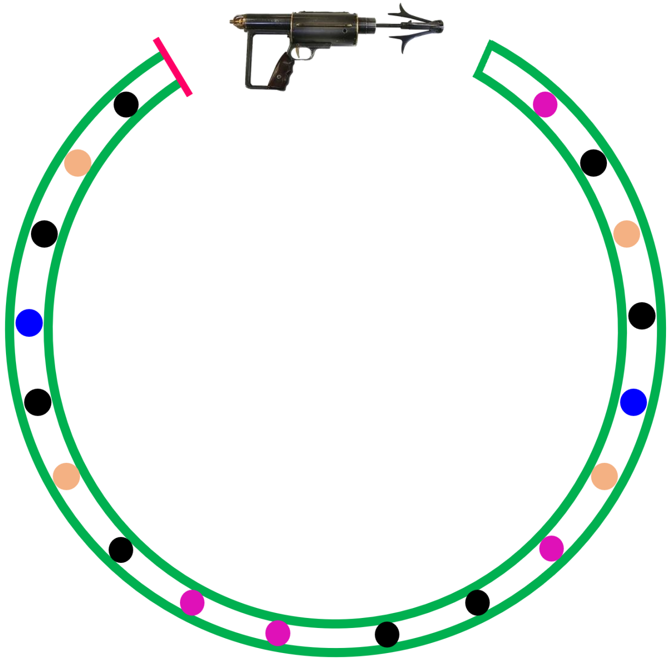


Possible scenarios



S_1

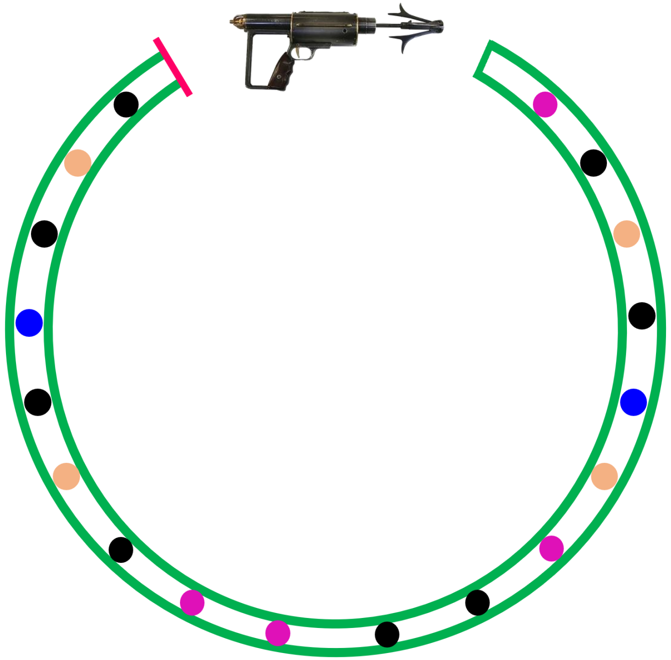
Possible scenarios



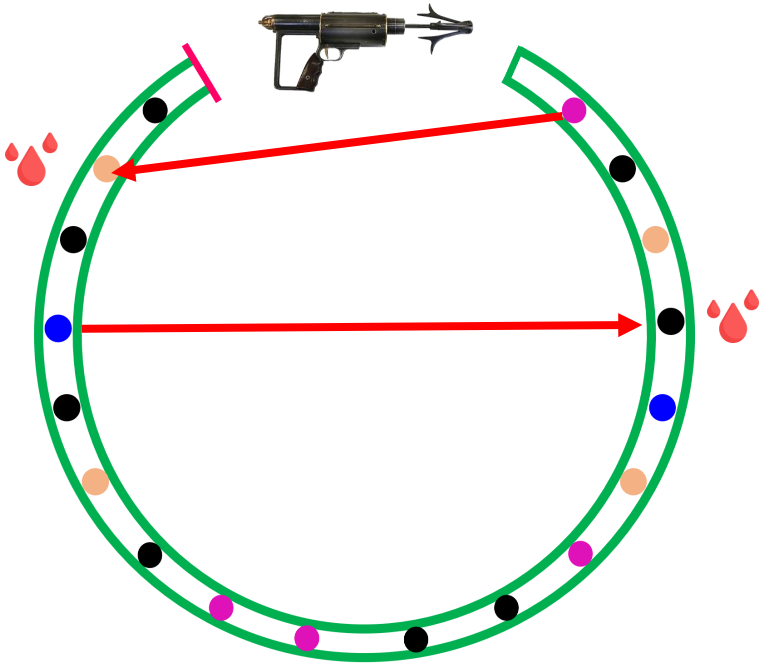
S_1

Not cool

Possible scenarios



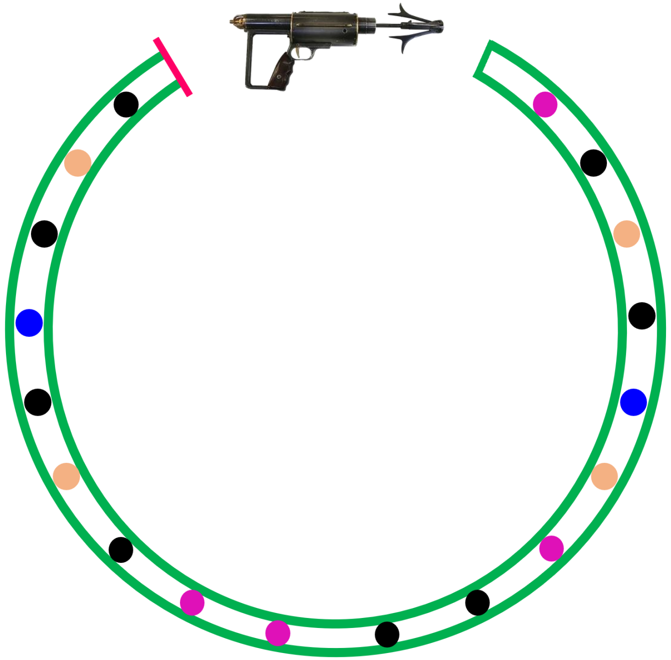
s_1



s_2

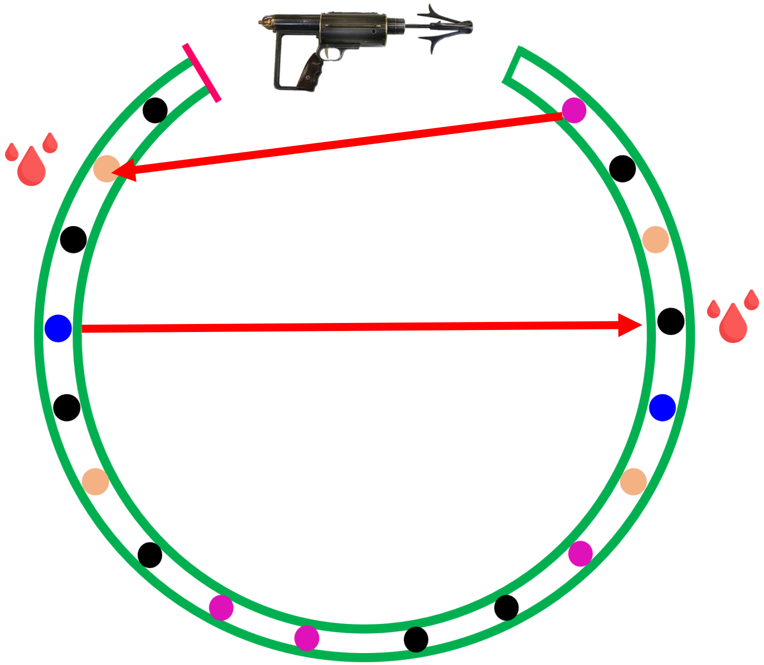
Not cool

Possible scenarios



s_1

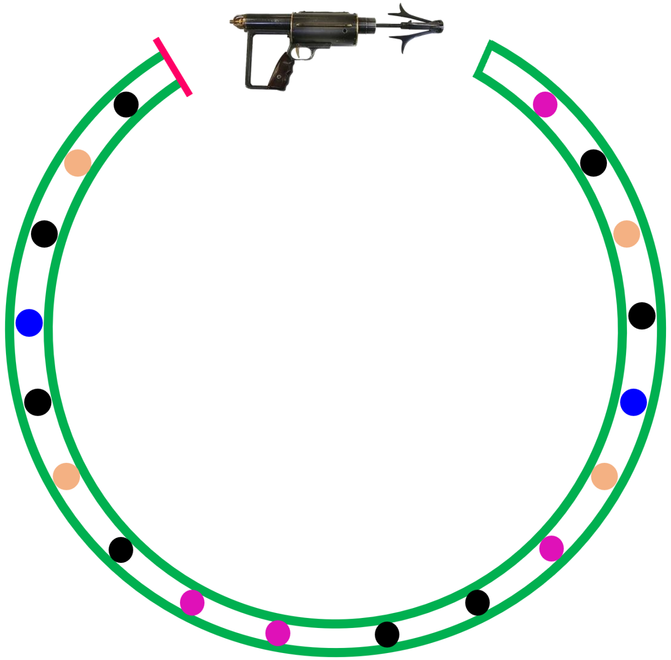
Not cool



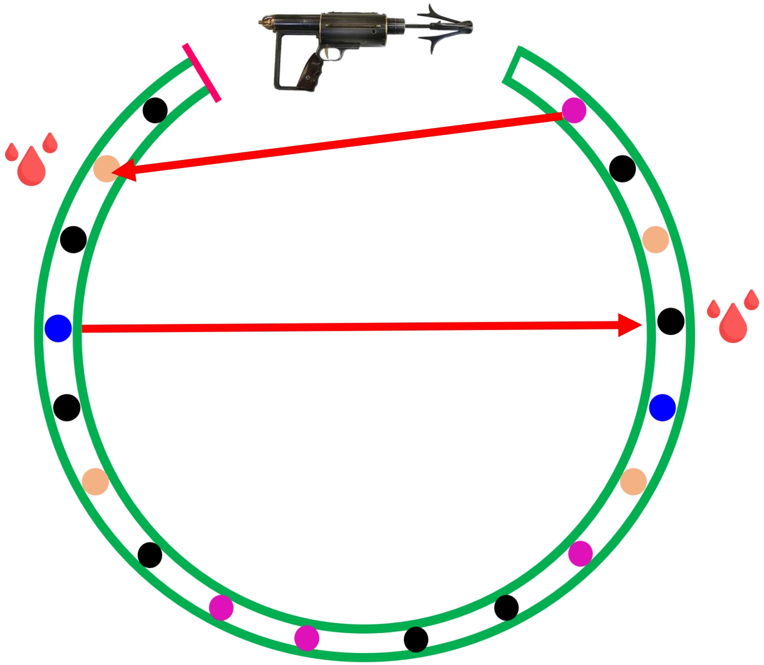
s_2

Getting better

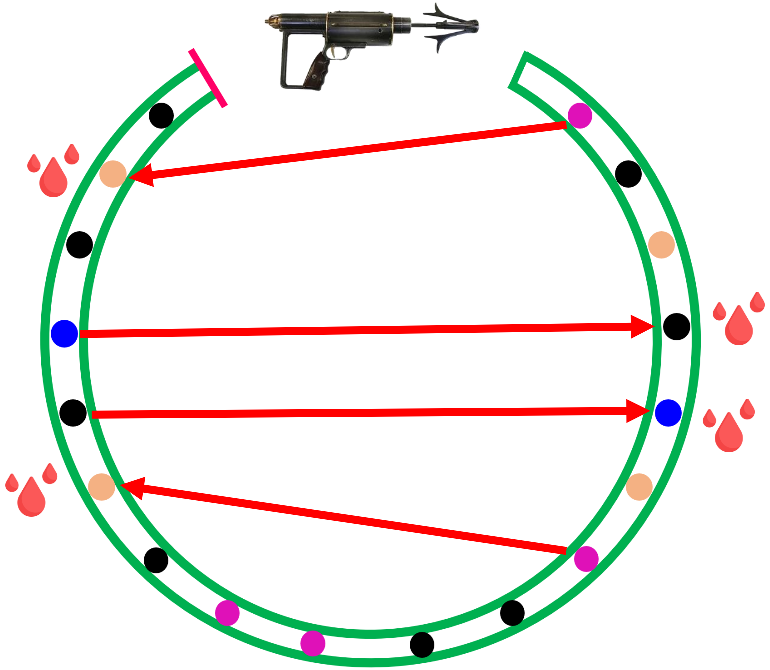
Possible scenarios



S_1



S_2

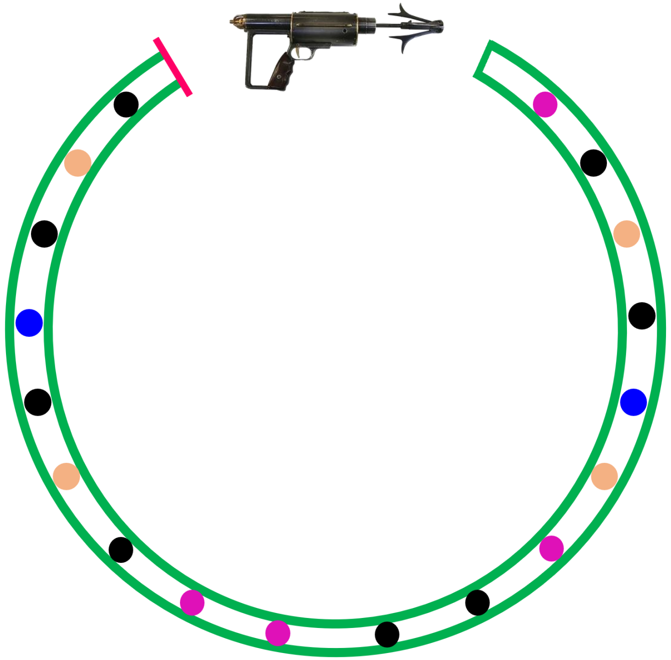


S_3

Not cool

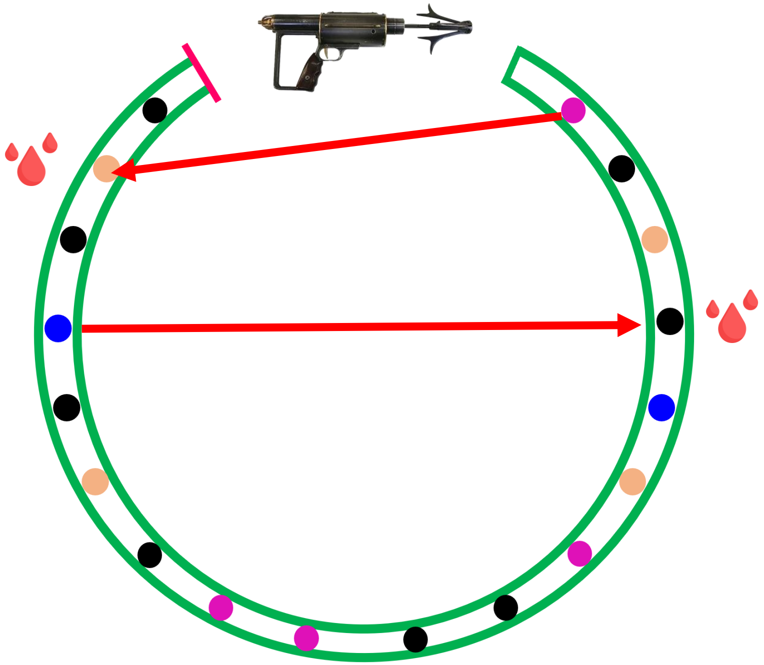
Getting better

Possible scenarios



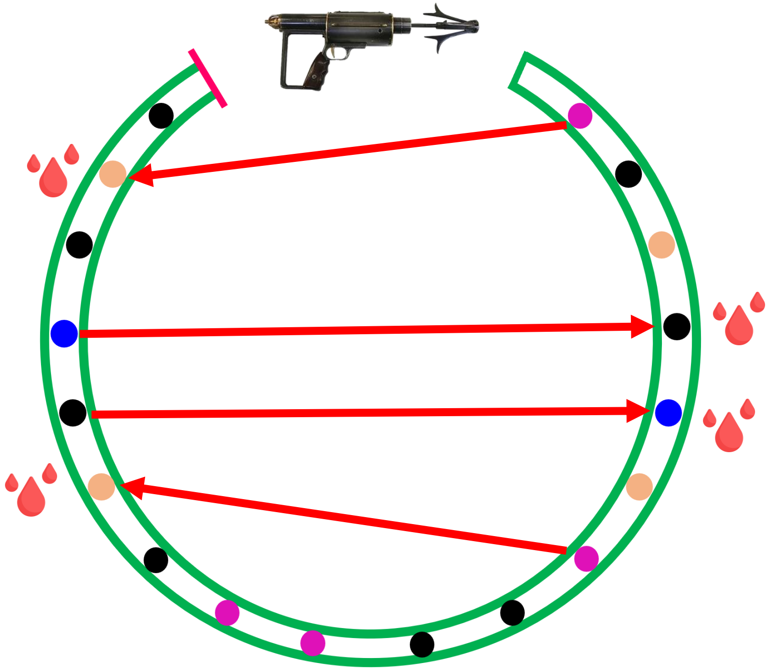
S_1

Not cool



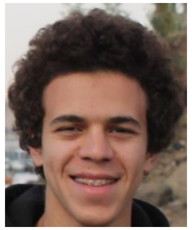
S_2

Getting better



S_3

Much better



Ahmed's goal

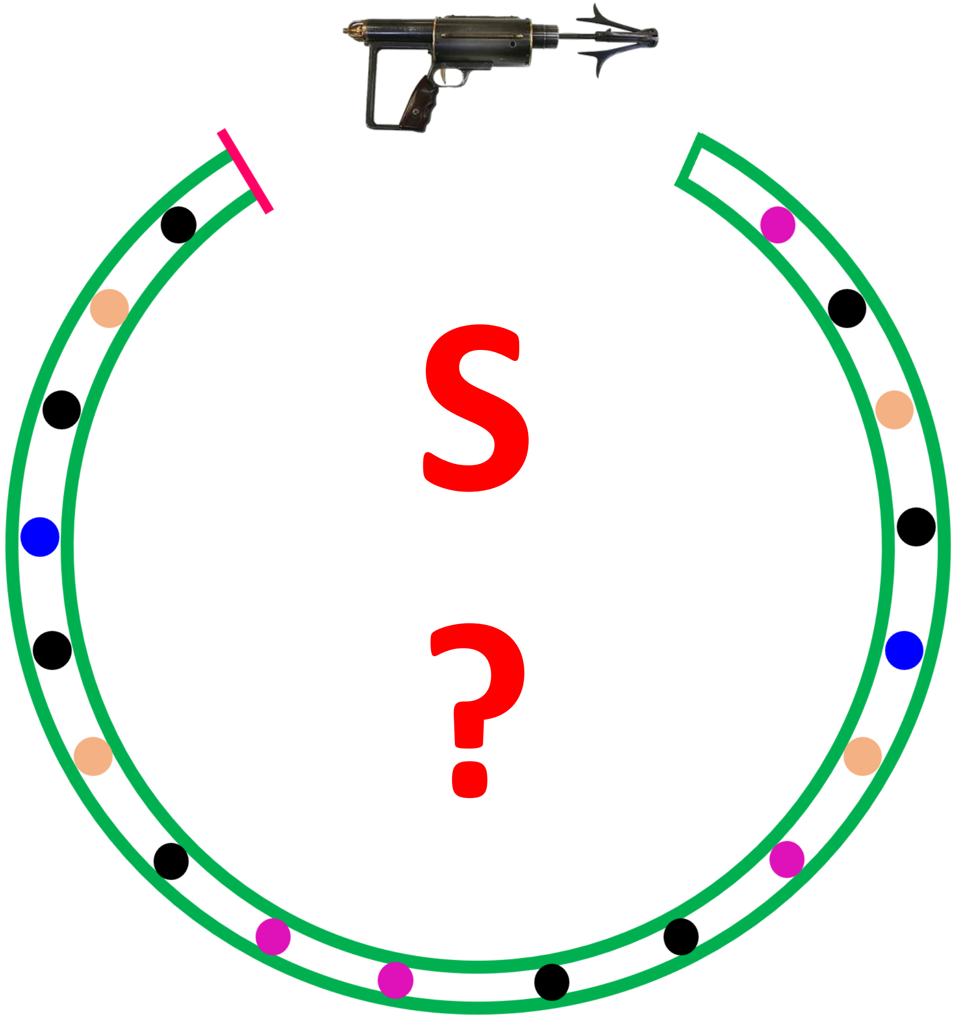
PI

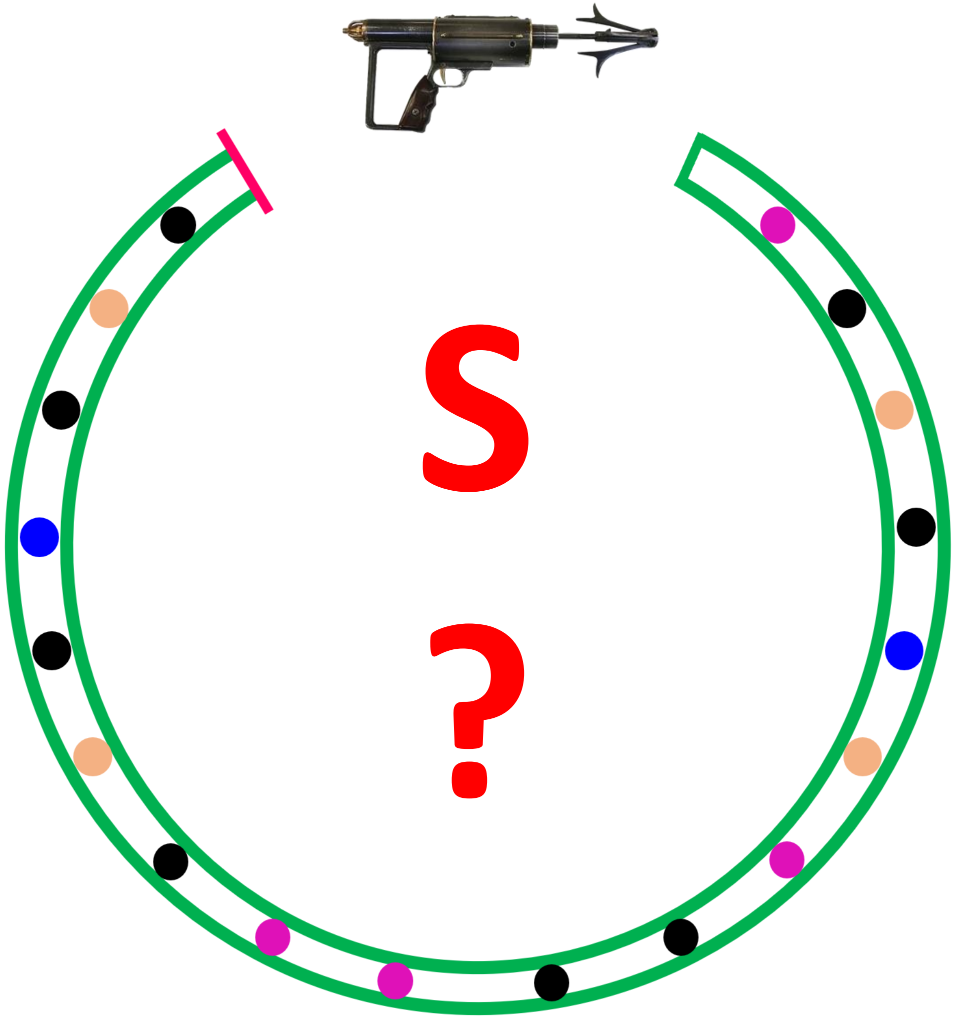
Loves more blood

?

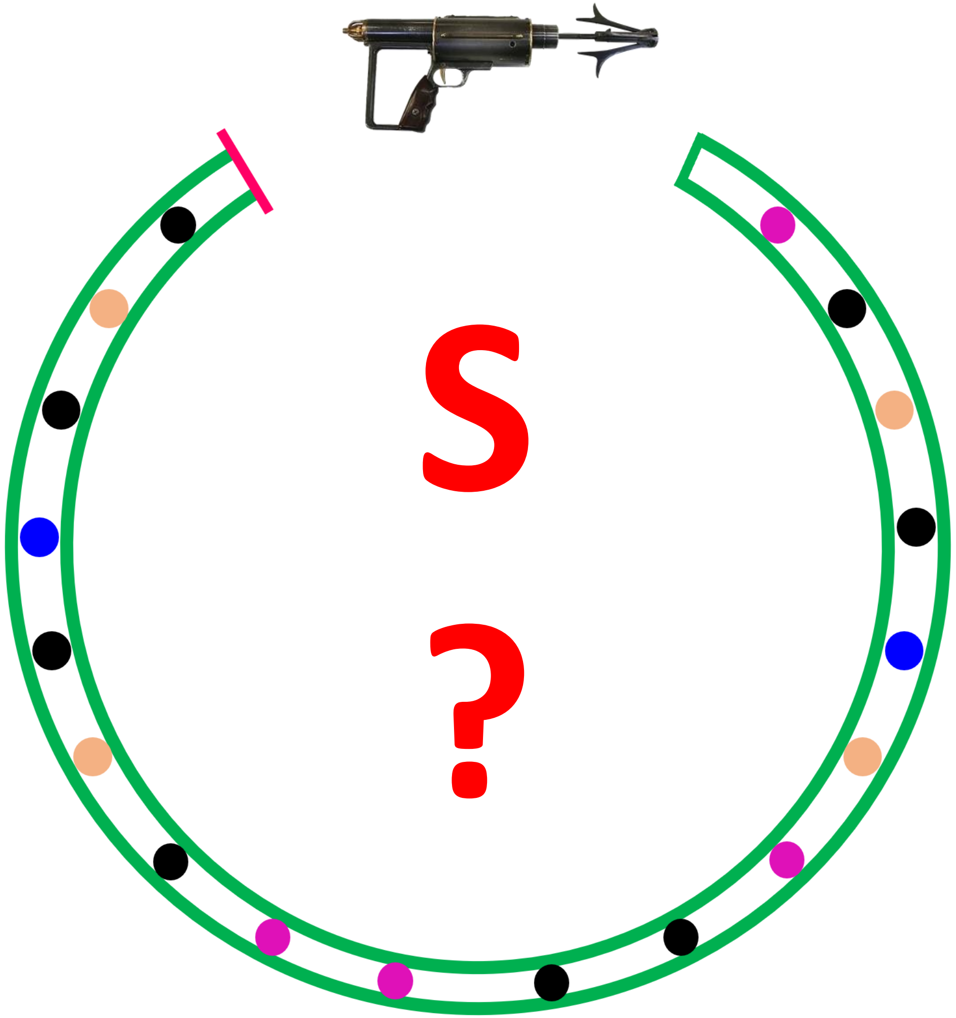
?

?


S
?

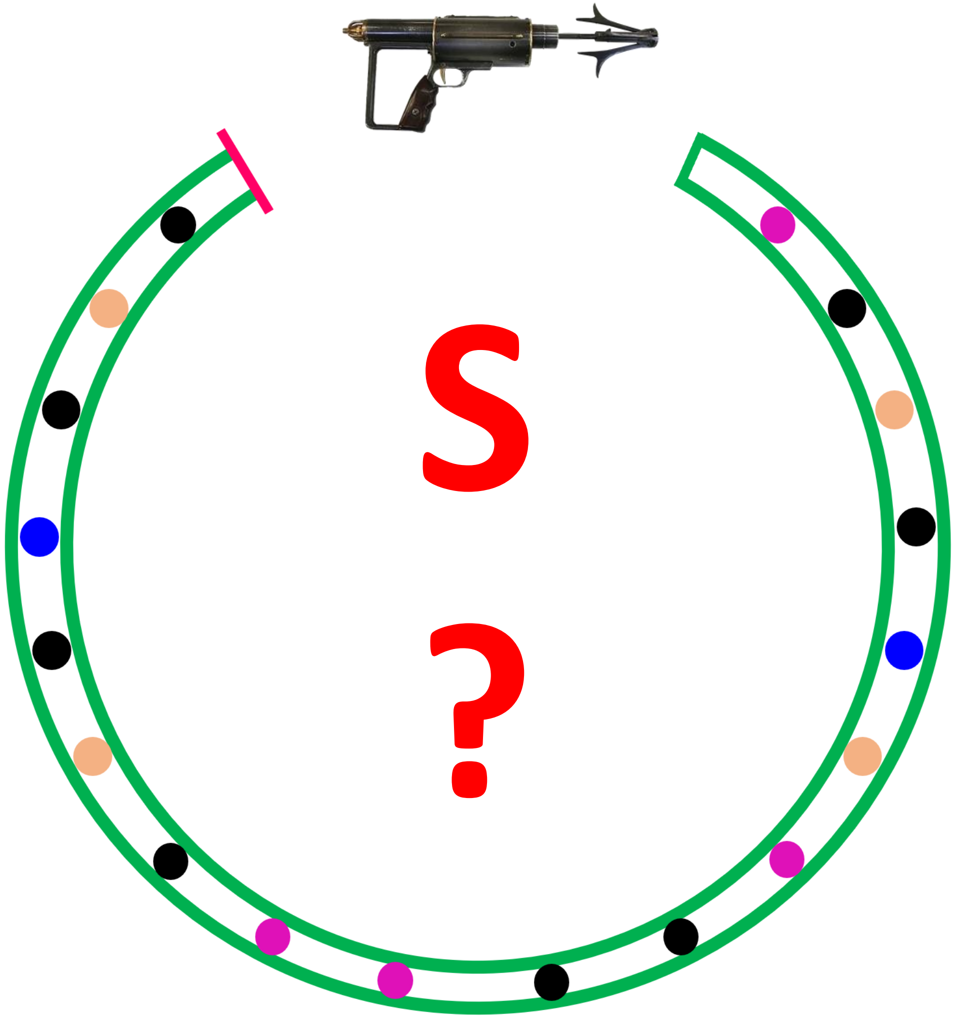


That is so cool!



Some Criteria/Model ?

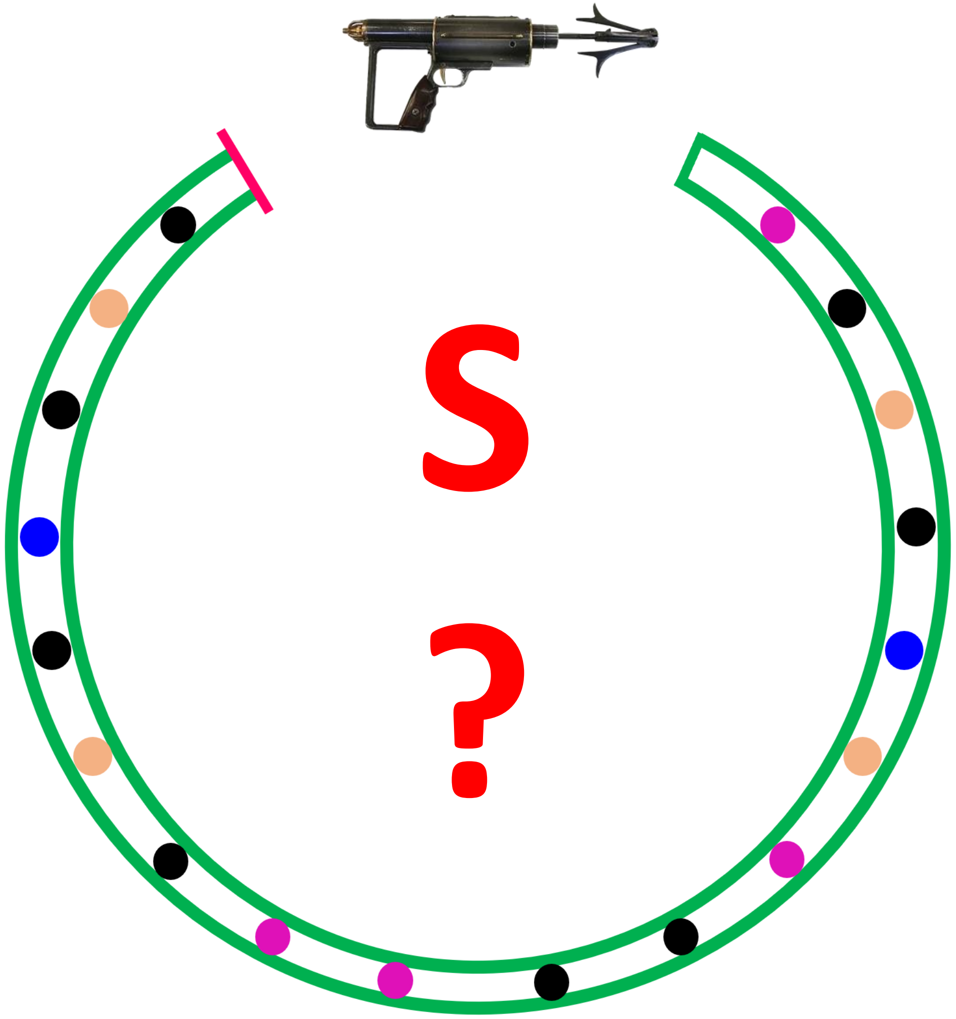
That is so cool!



Some Criteria/Model ?

$$B(S) = \#\text{killed PhDs}$$

That is so cool!



That is so cool!

Some Criteria/Model ?

$$B(S) = \#\text{killed PhDs}$$

$$\max_{S \in \Omega} B(S)$$

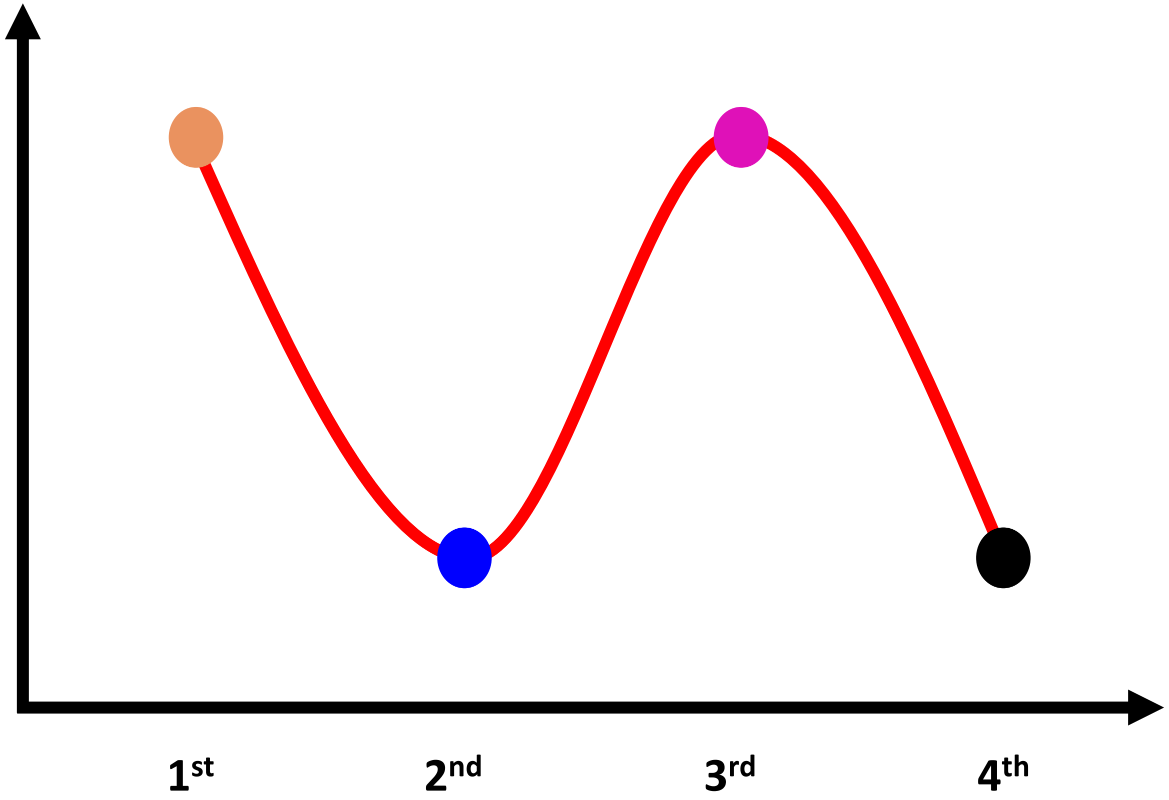
Ω is the set of all possible structures that respect the game rules

How to compute this fast?

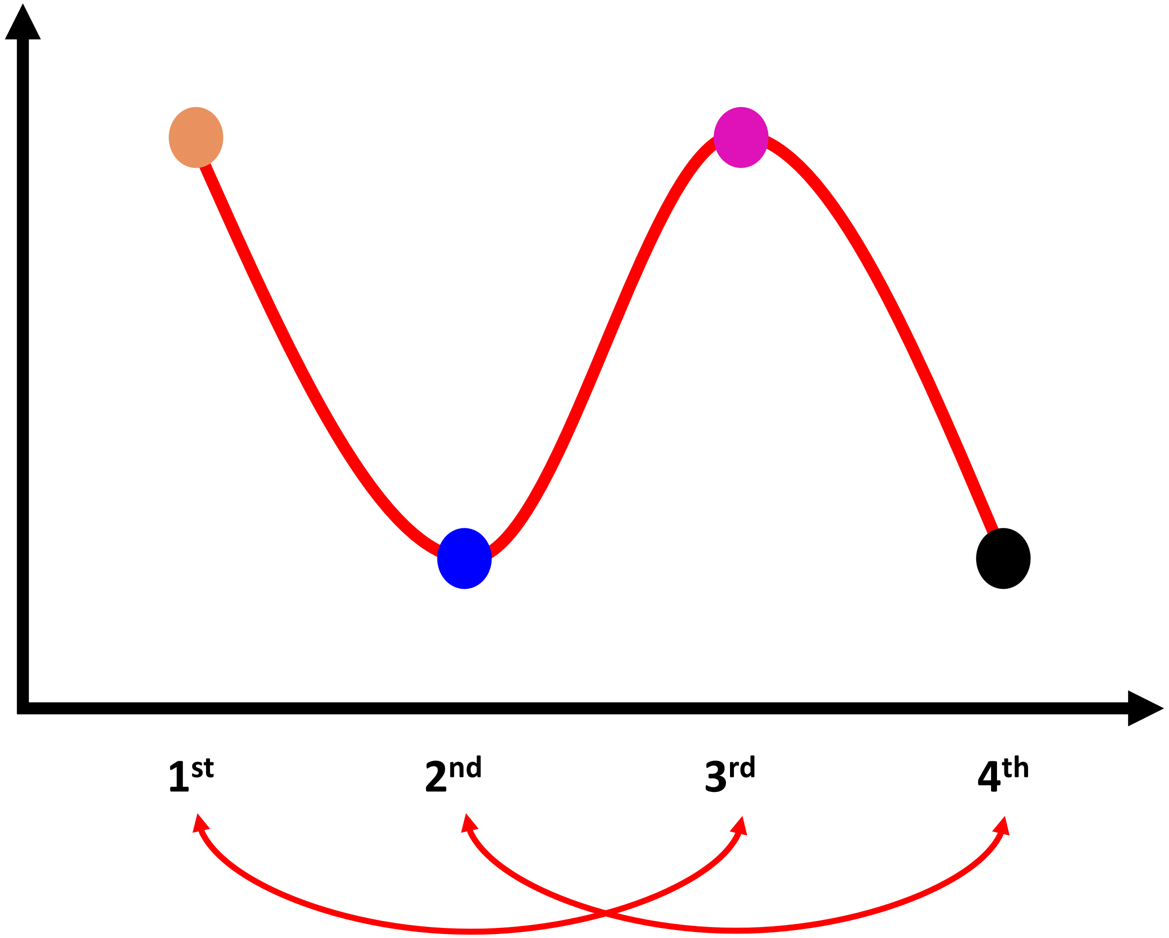
Level 2

After playing that game over and over

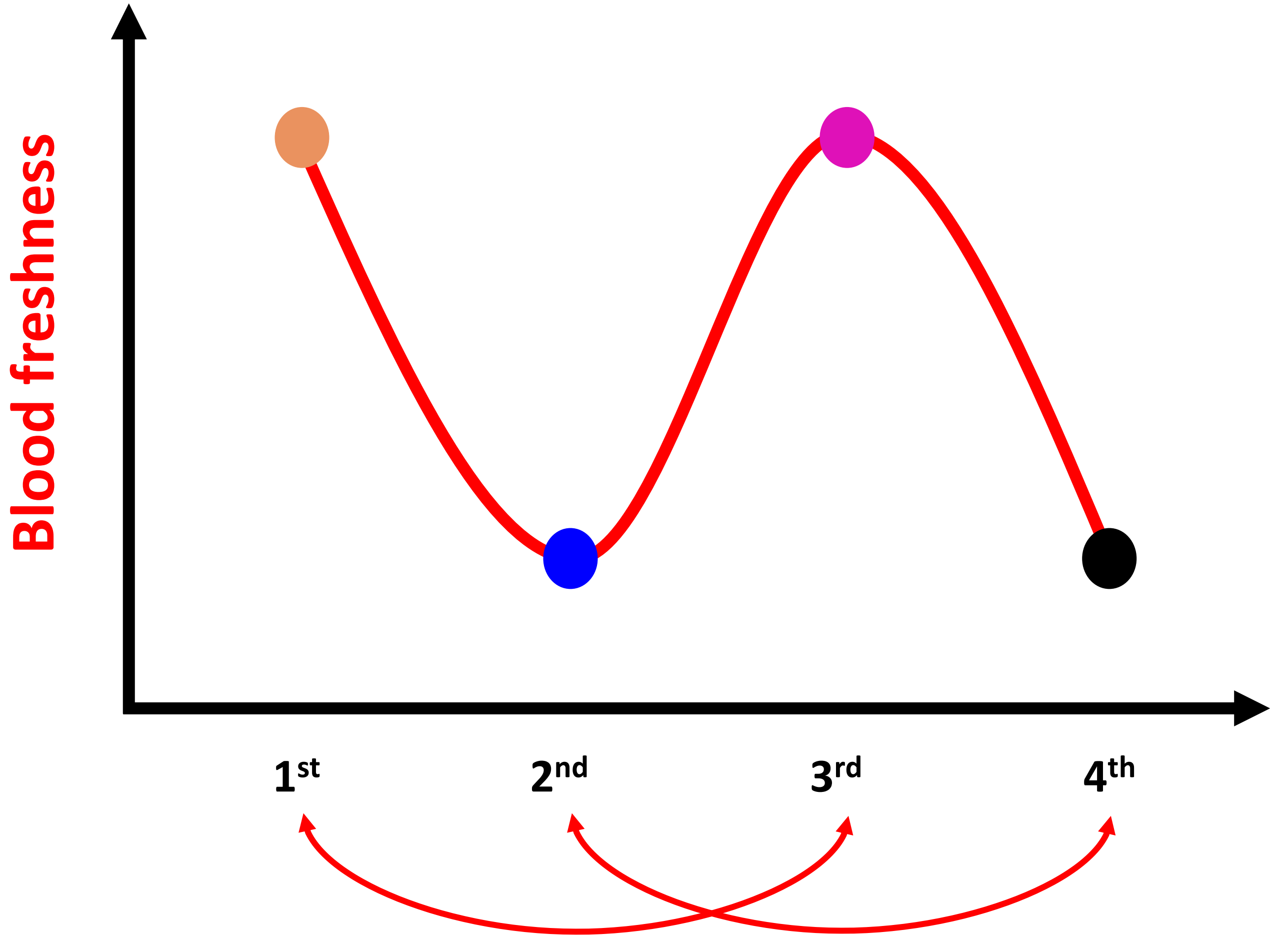
After playing that game over and over

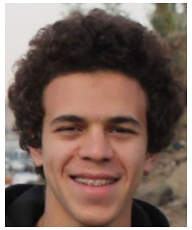


After playing that game over and over



After playing that game over and over





Ahmed's goal

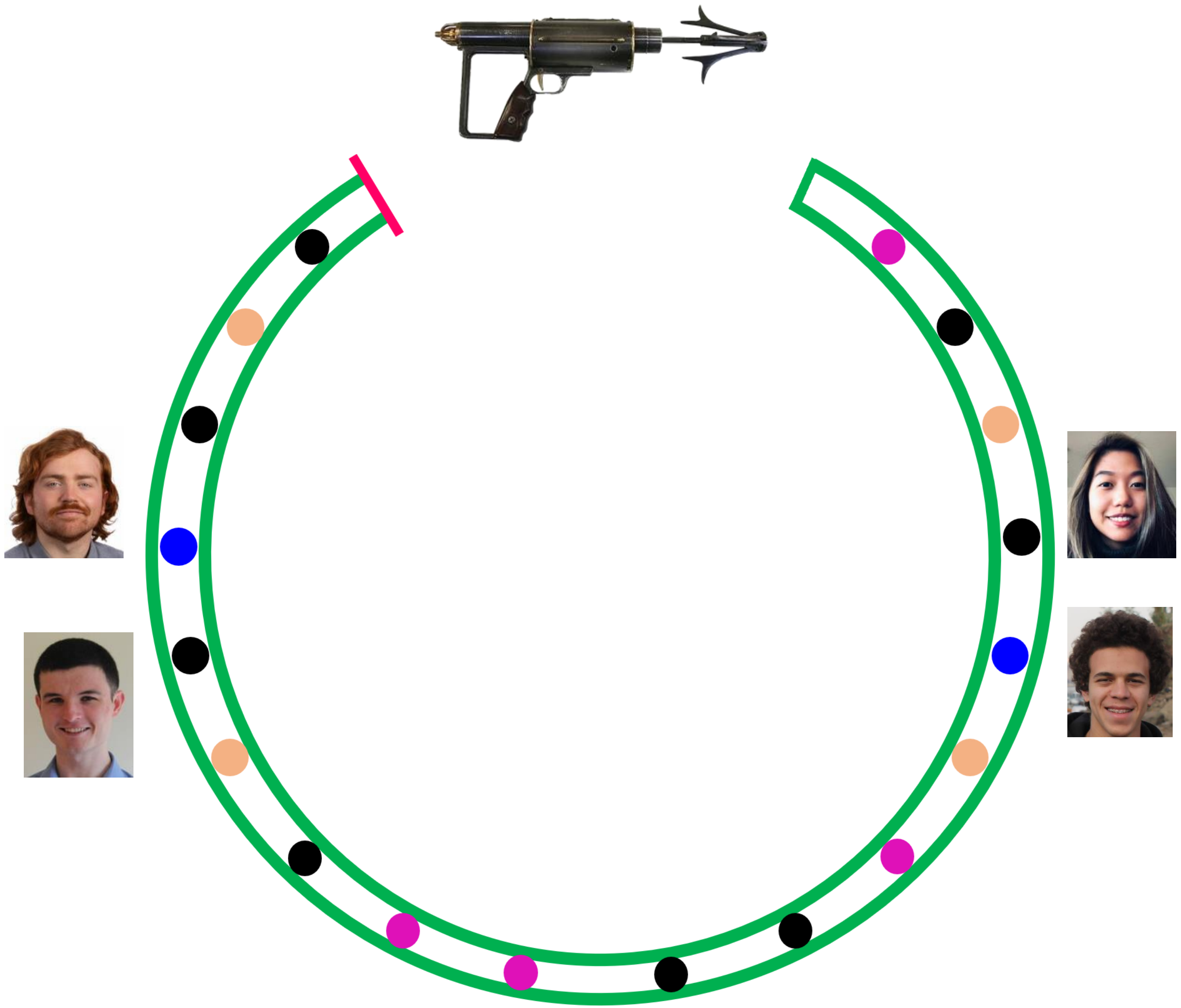
PI

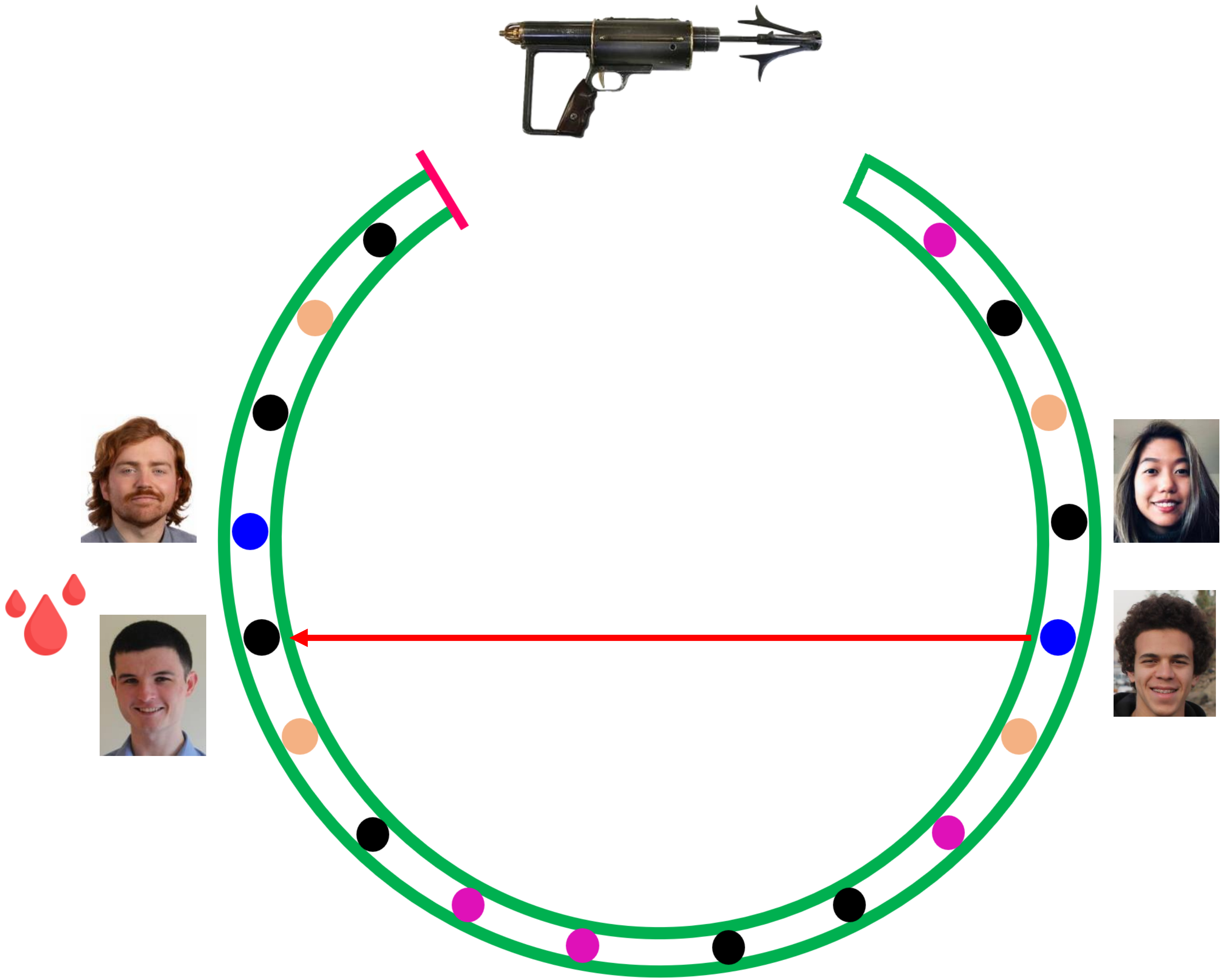
Loves high quality blood

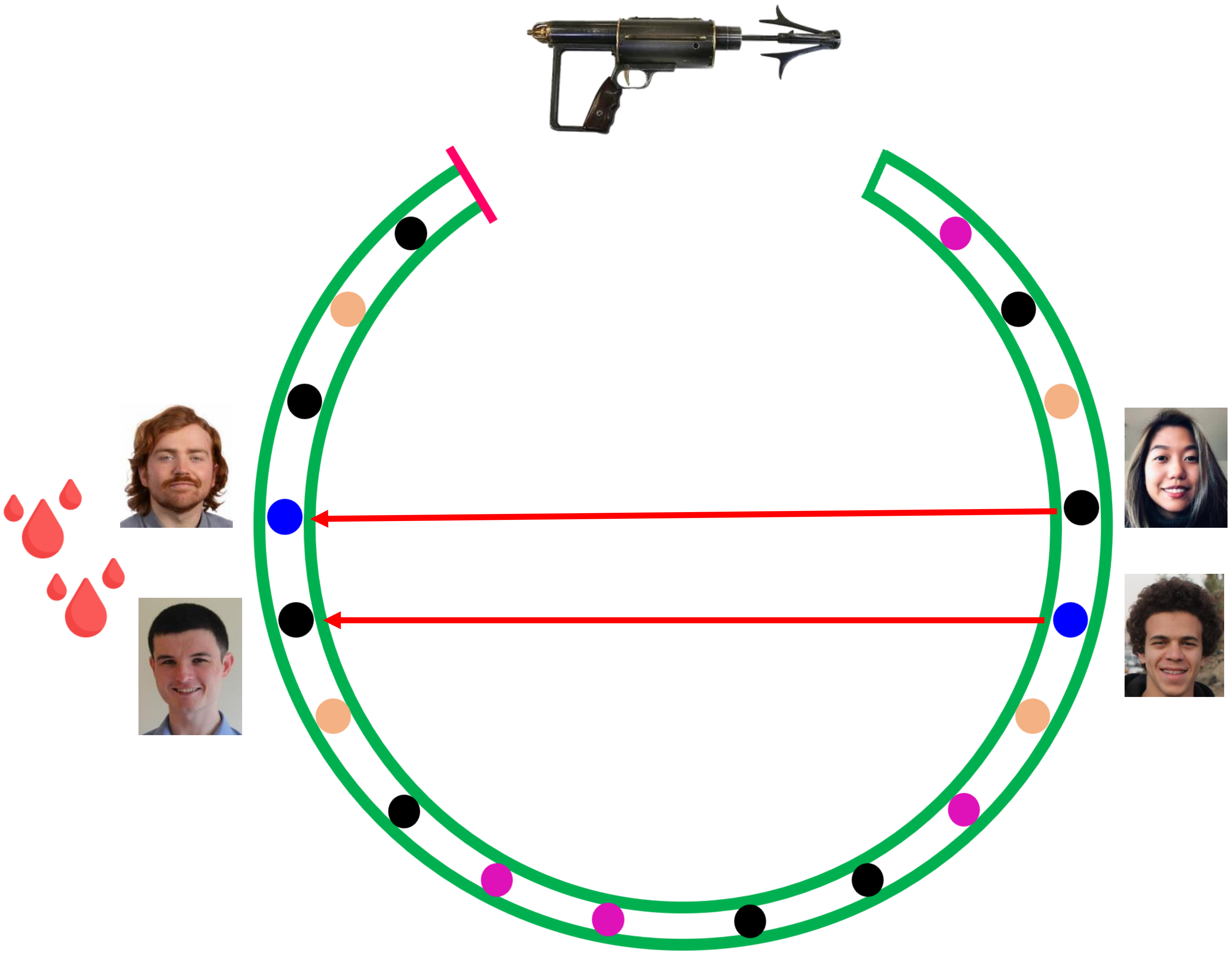
?

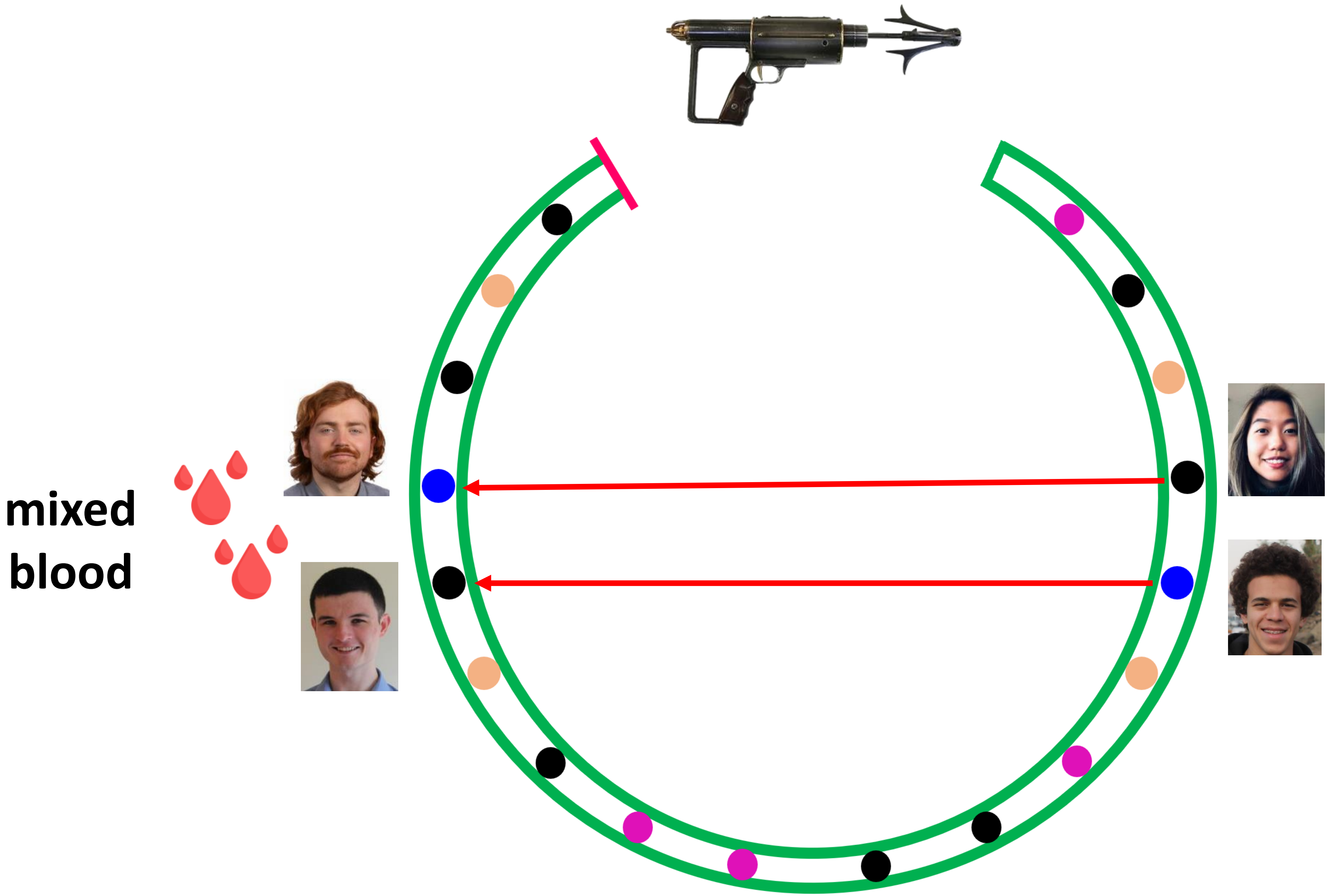
?

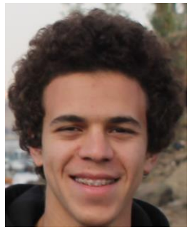
?








mixed
blood



Ahmed's goal

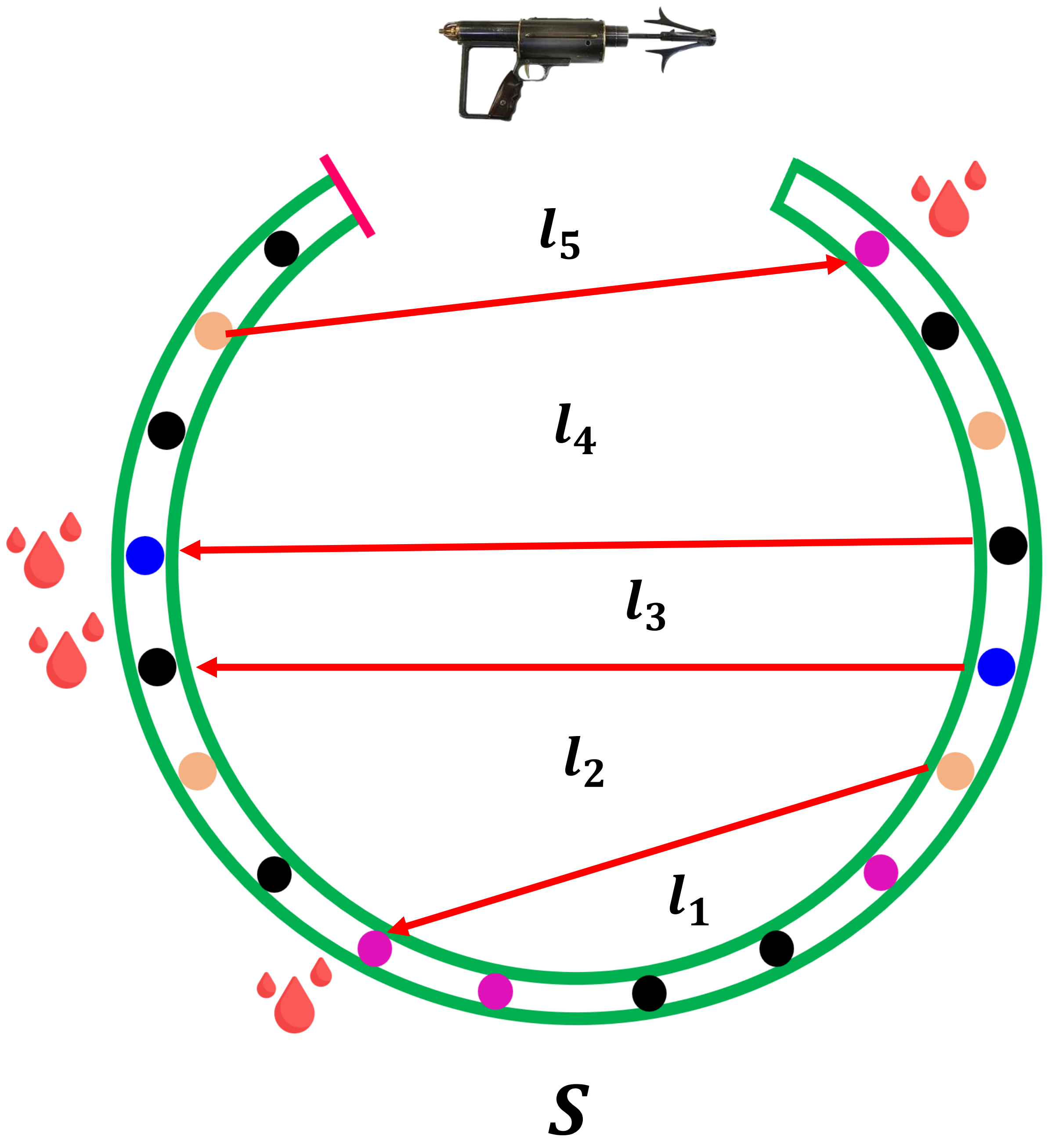
PI

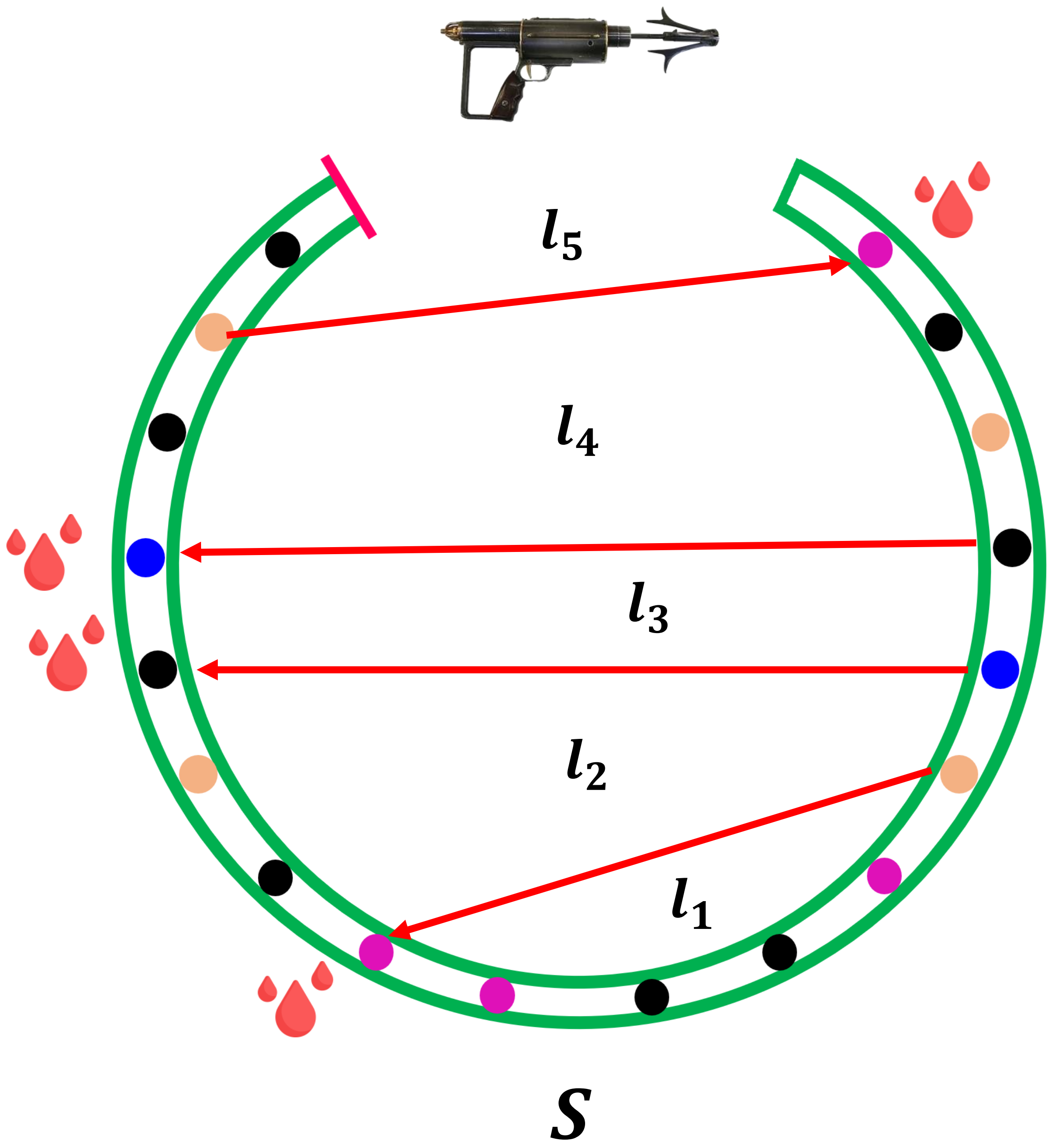
Loves high quality blood

Loves mixed blood

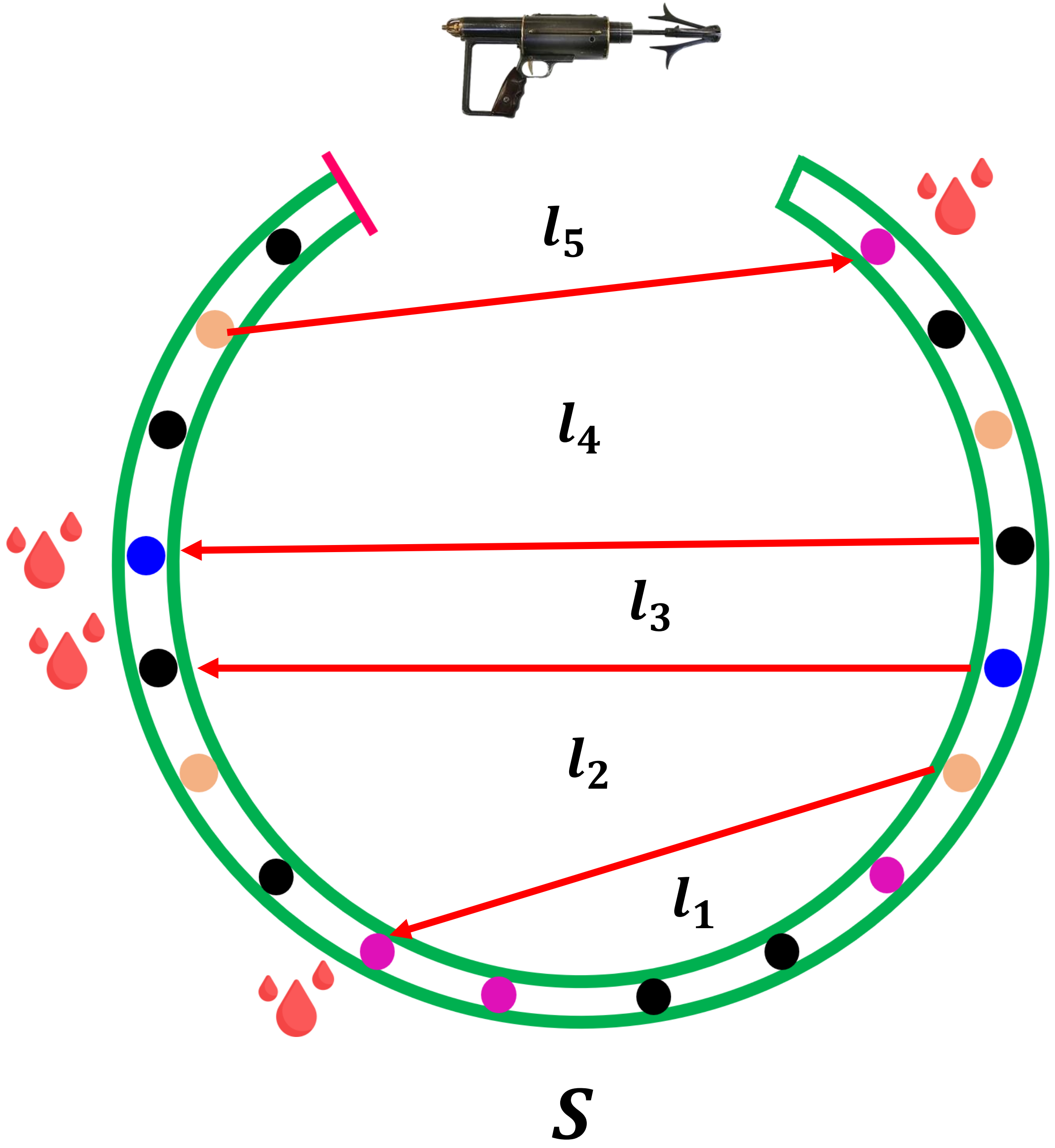
?

?


l_5
l_4
l_3
l_2
l_1
S

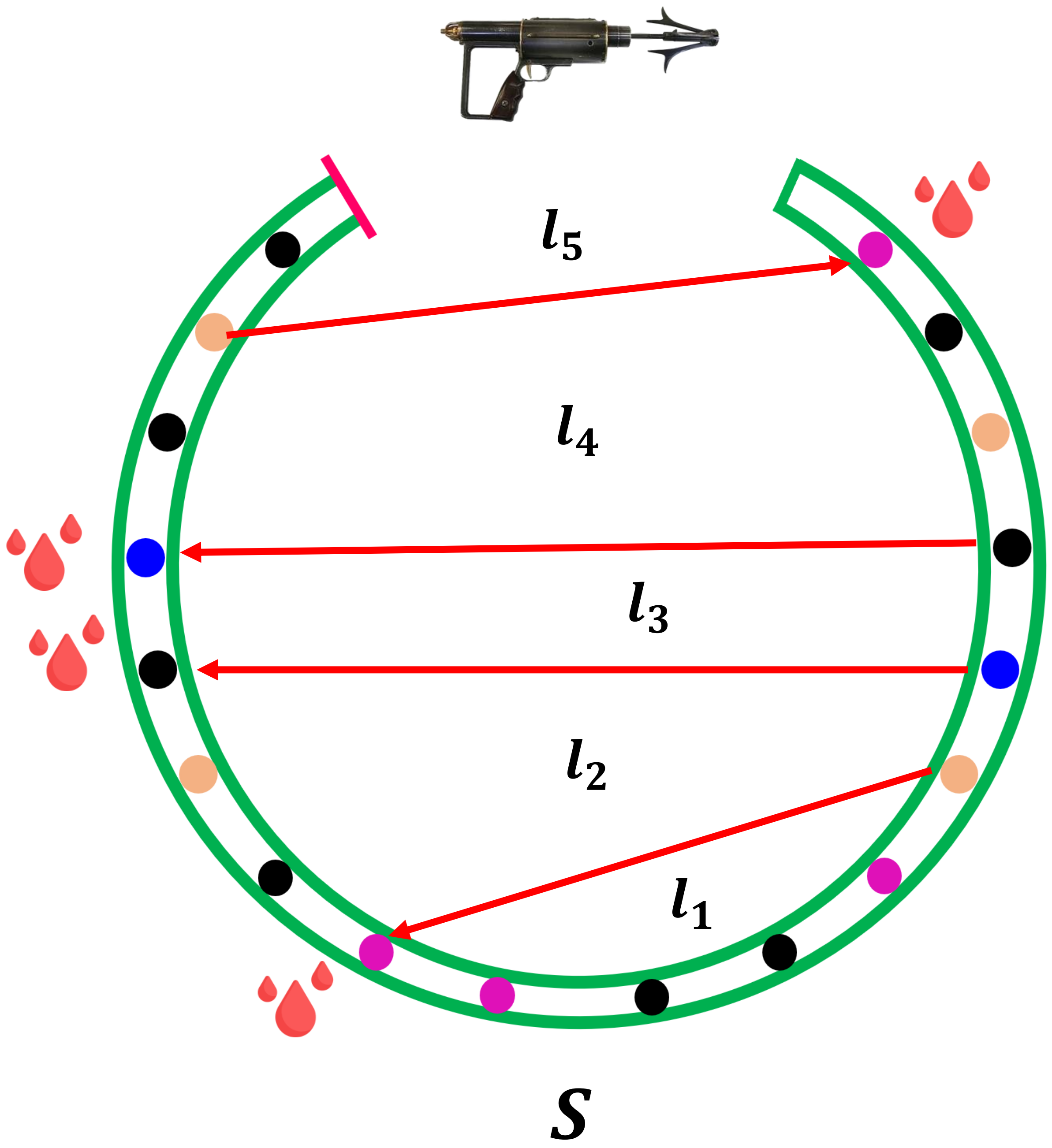


Some Criteria/Model ?



Some Criteria/Model ?

$$B(S) = \sum_{l} B(l)$$



Some Criteria/Model ?

$$B(S) = \sum_{l} B(l)$$

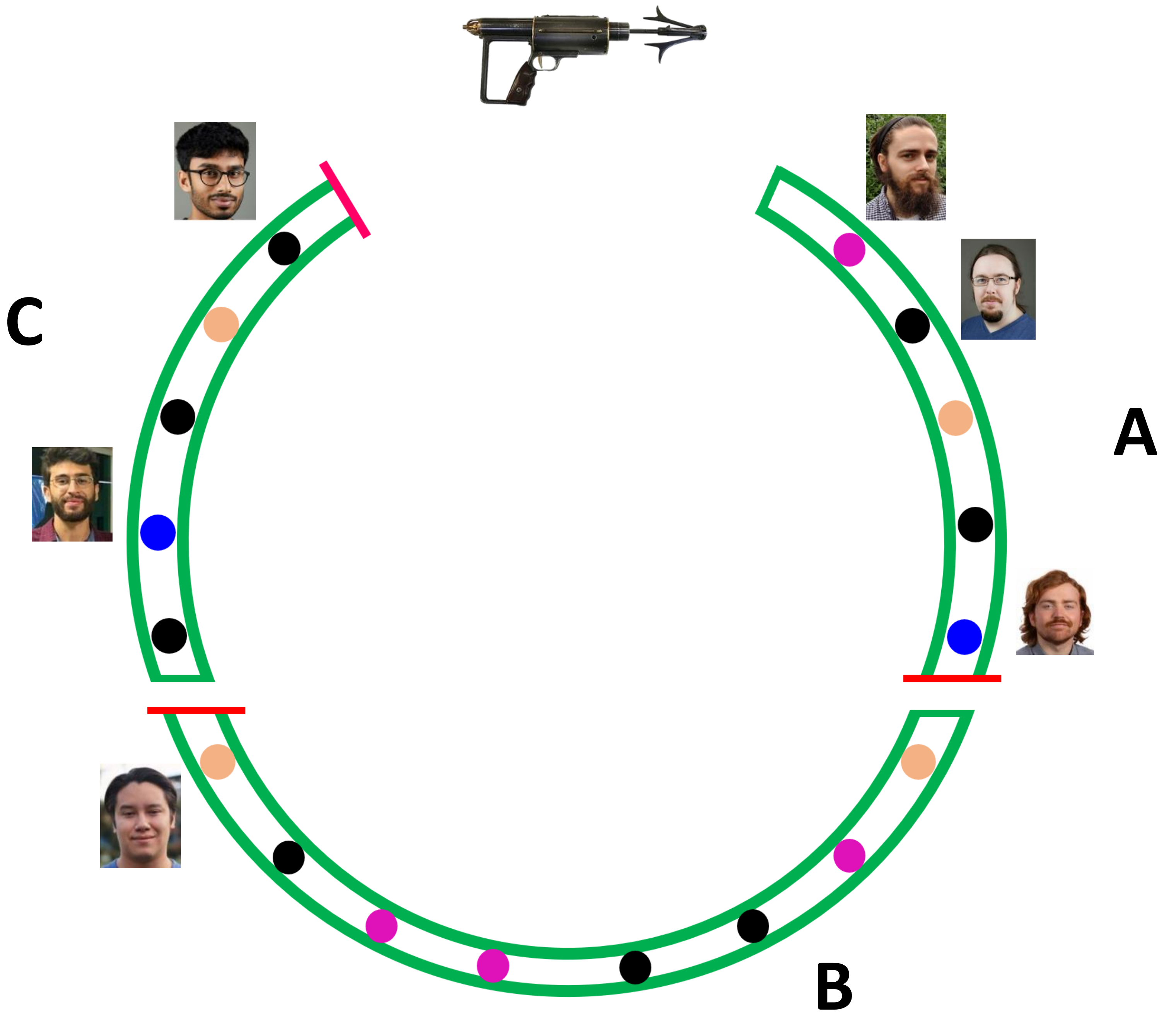
$$\max_{S \in \Omega} B(S)$$

How to compute this fast?

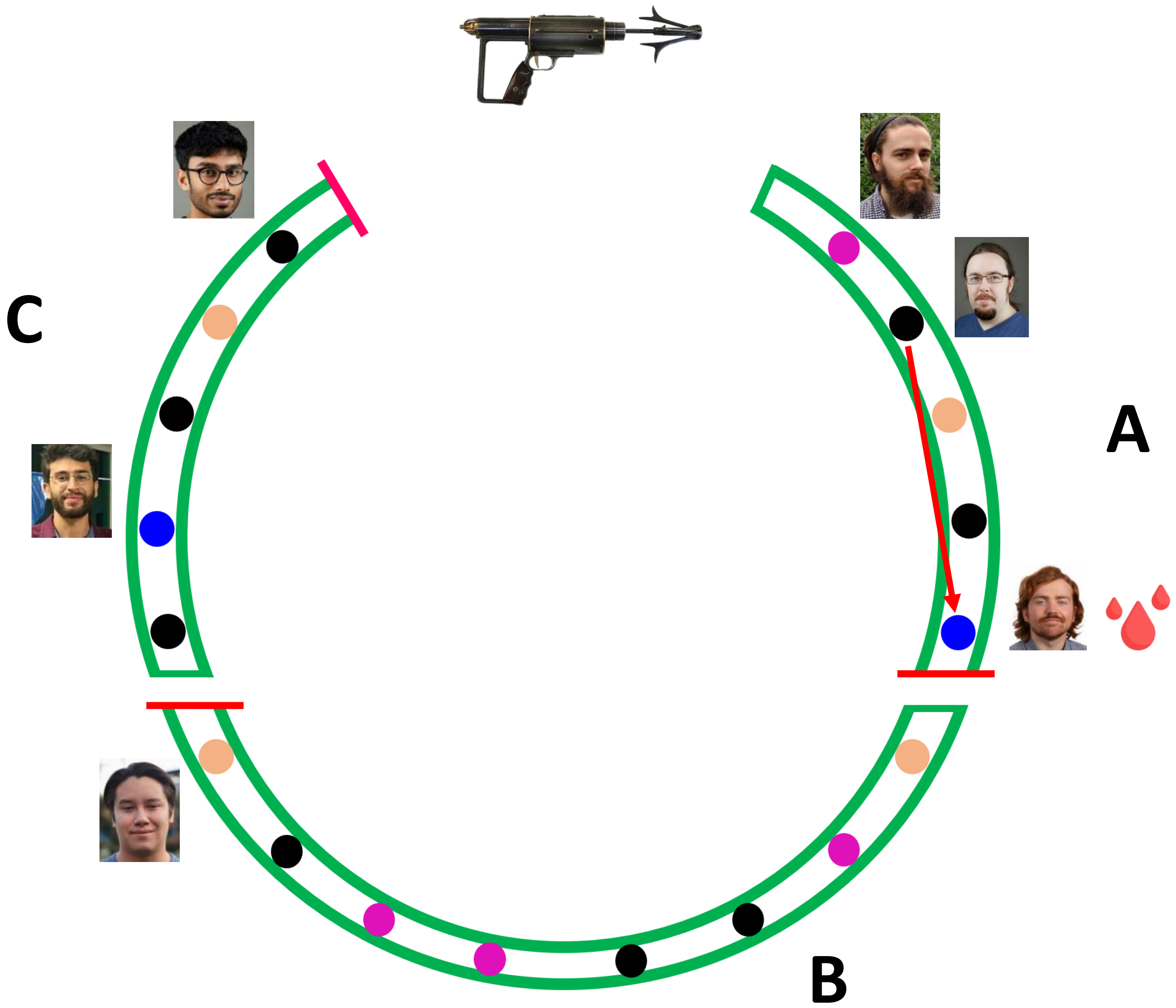
Level 3


FIRE POINT

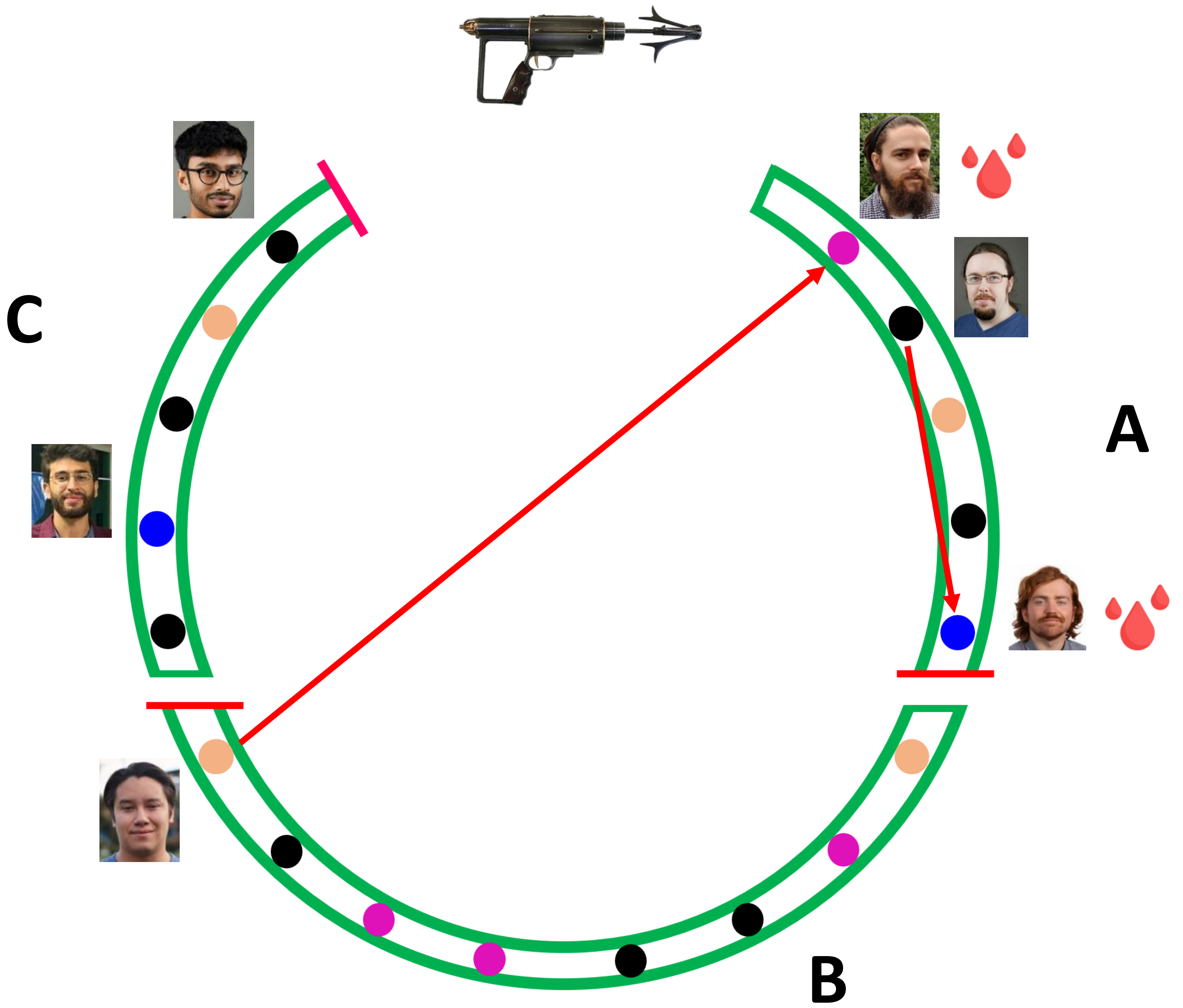
c = 3 sofas



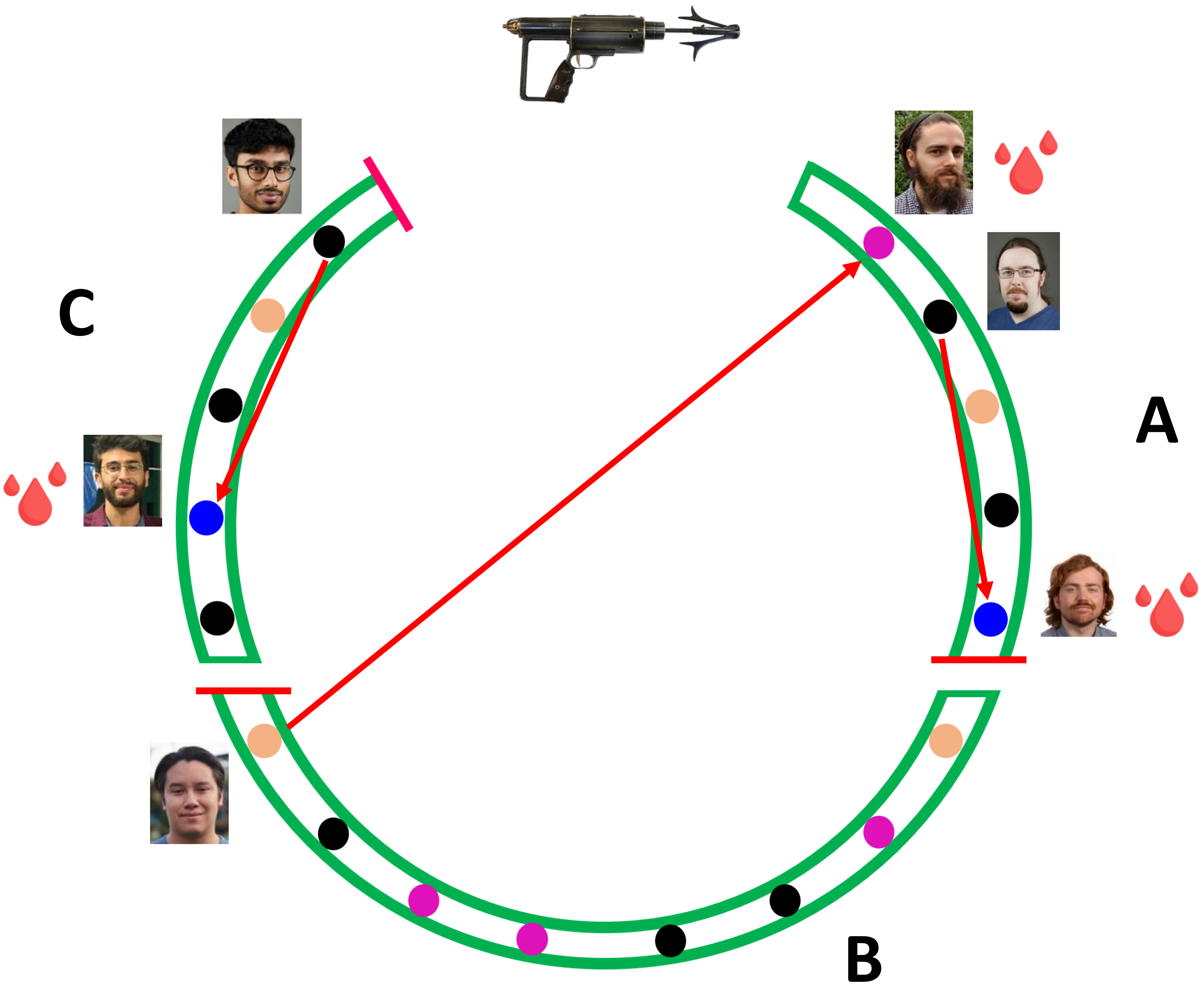
c = 3 sofas



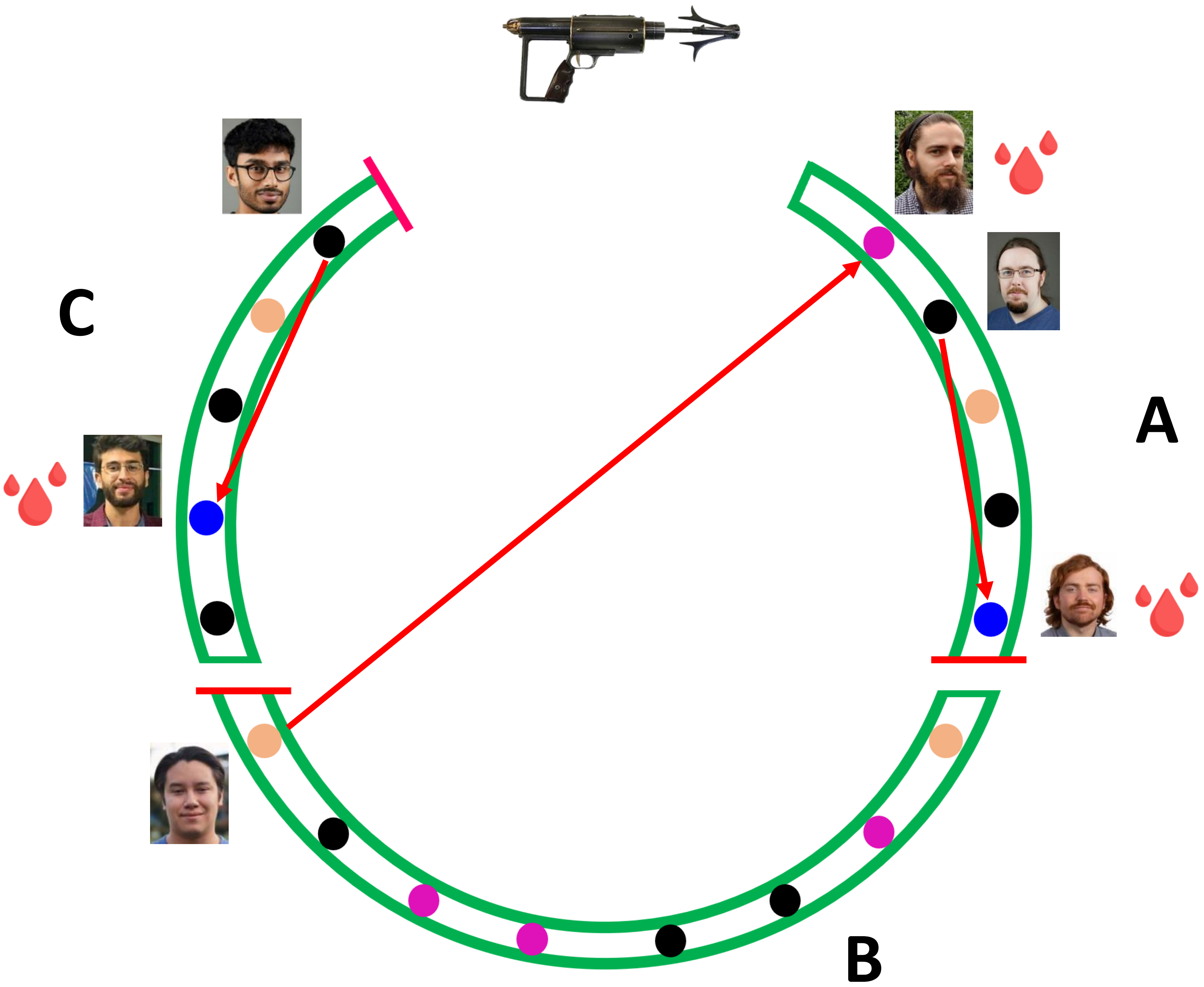
c = 3 sofas



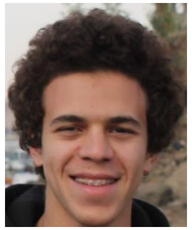
c = 3 sofas



c = 3 sofas



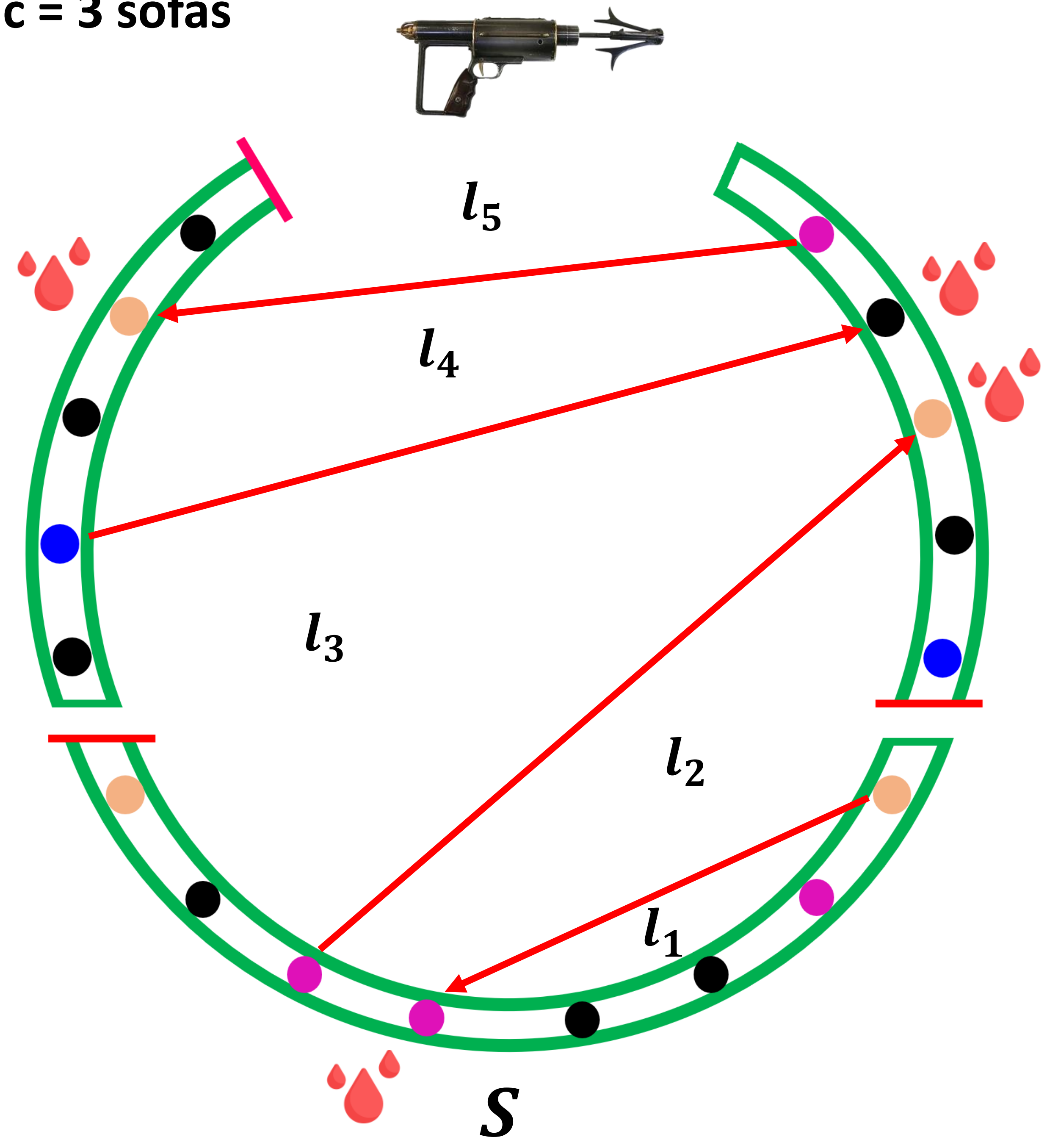
That is so bad!



Ahmed's goal

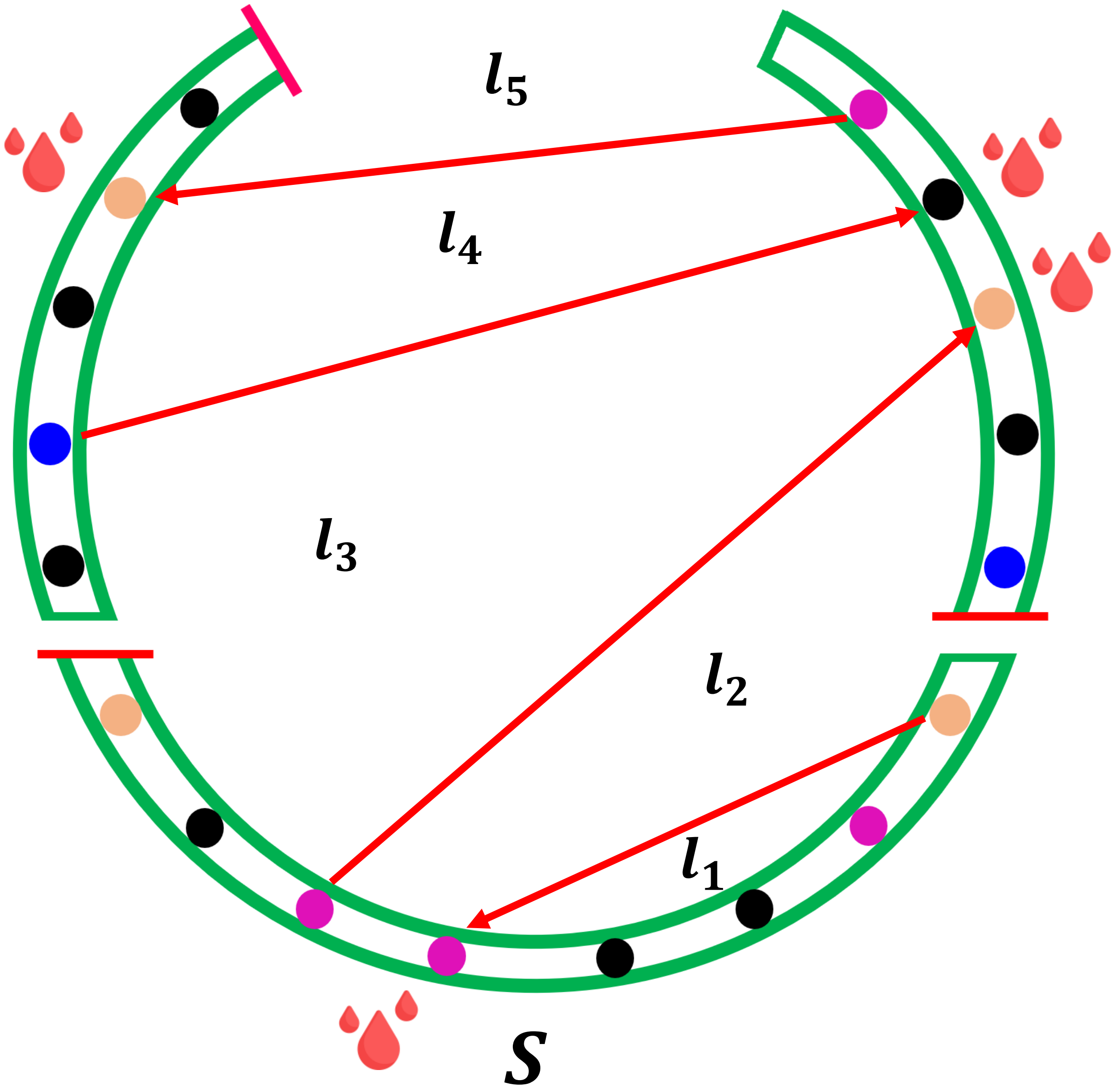
PI
Loves high quality blood
Loves mixed blood
Hates disconnectedness
?

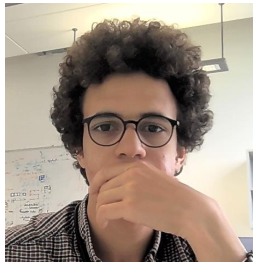
c = 3 sofas



Ω: the set of all connected structures that respect the game rules

c = 3 sofas

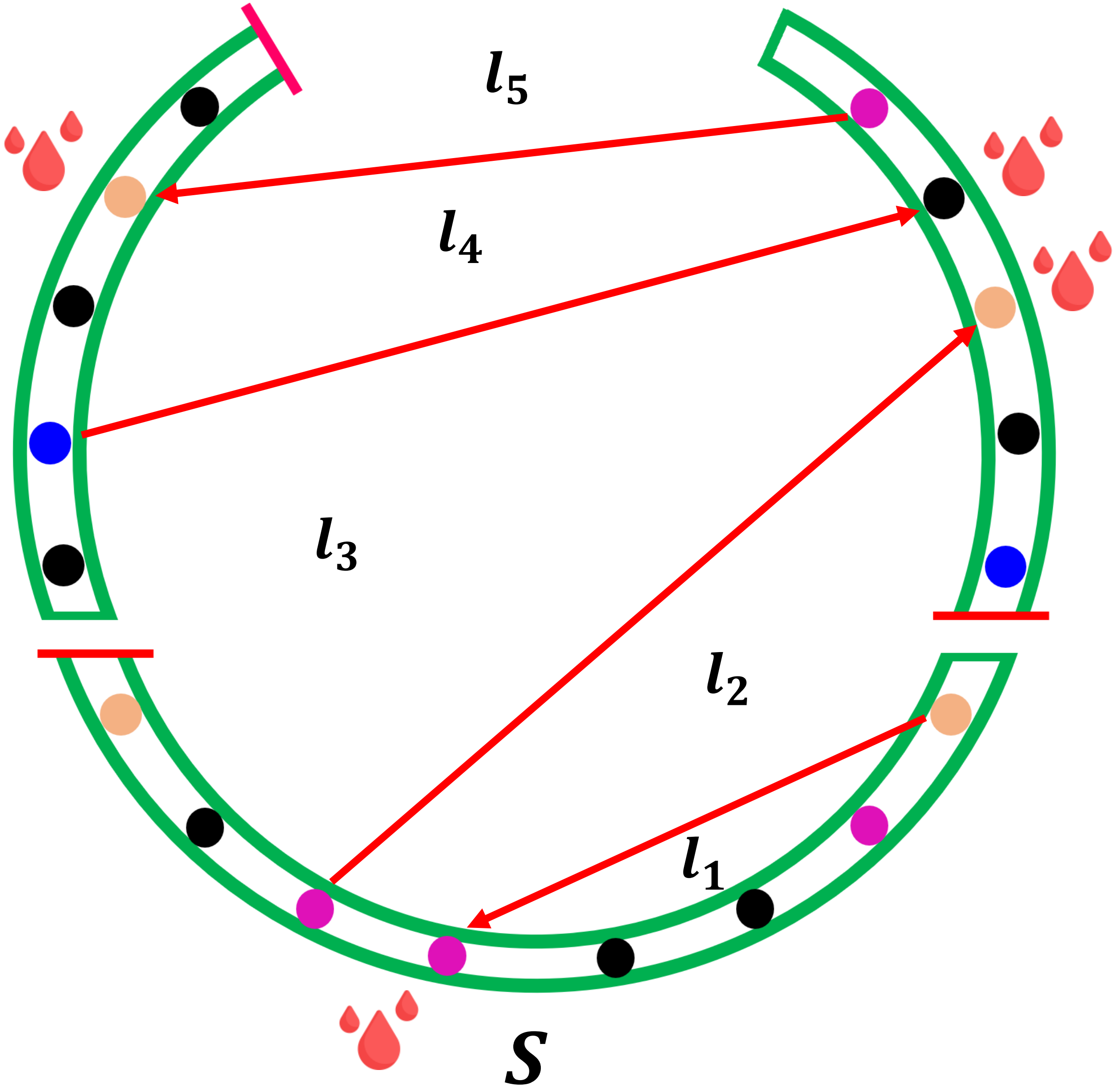


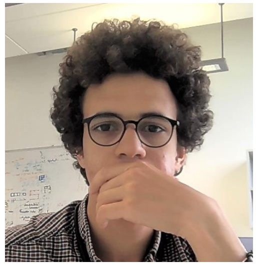


Some Criteria/Model ?

Ω: the set of all connected structures that respect the game rules

c = 3 sofas



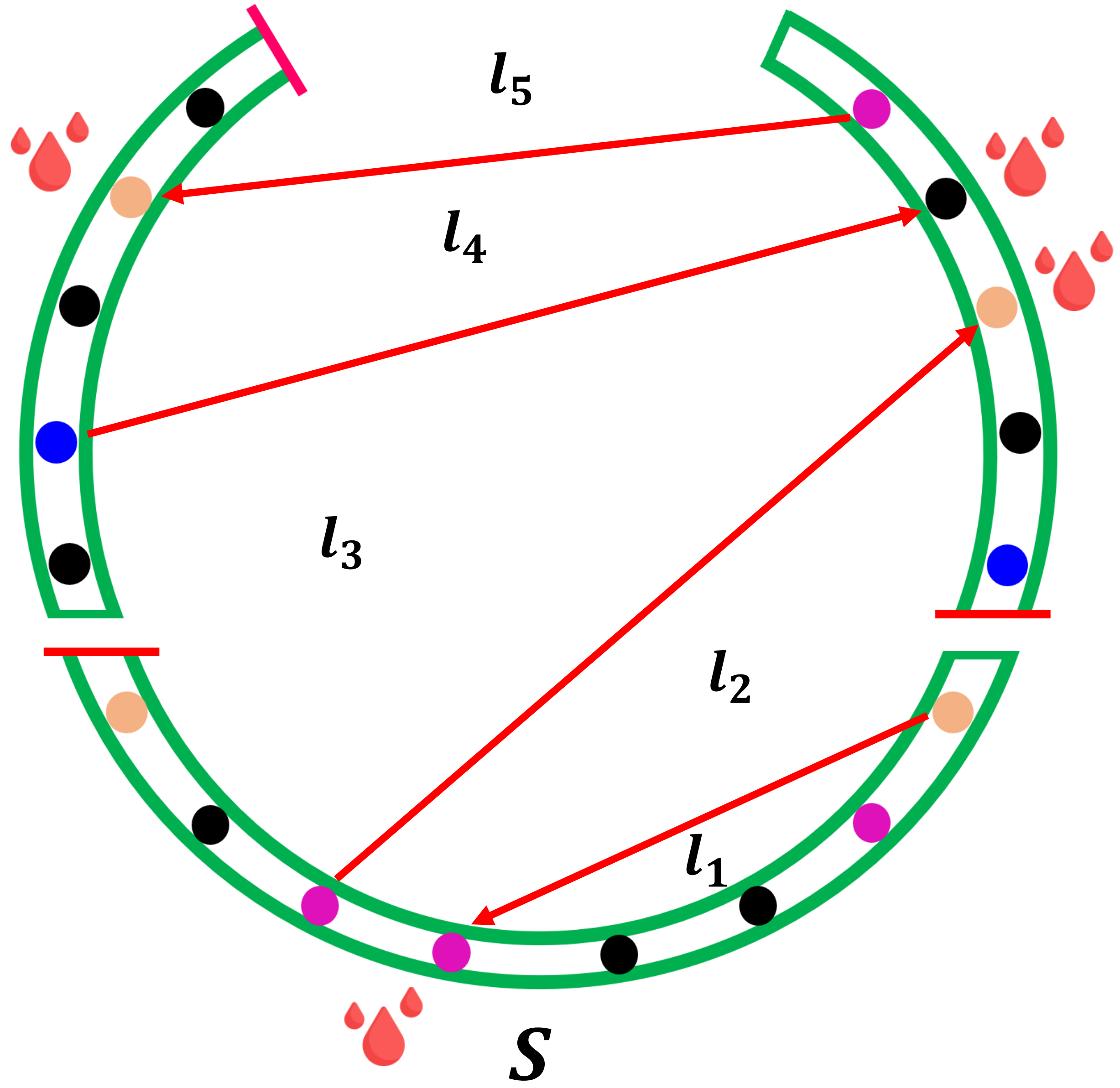


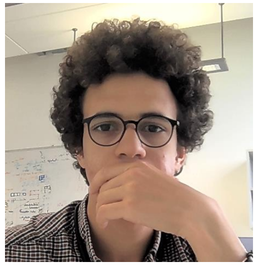
Some Criteria/Model ?

$$B(S) = \sum_{l} B(l) - (c-1)\, B^{\text{assoc}}$$

Ω: the set of all connected structures that respect the game rules

c = 3 sofas





Some Criteria/Model ?

$$B(S) = \sum_{l} B(l) - (c-1)\, B^{\mathrm{assoc}}$$

$$\max_{S \in \Omega} B(S)$$

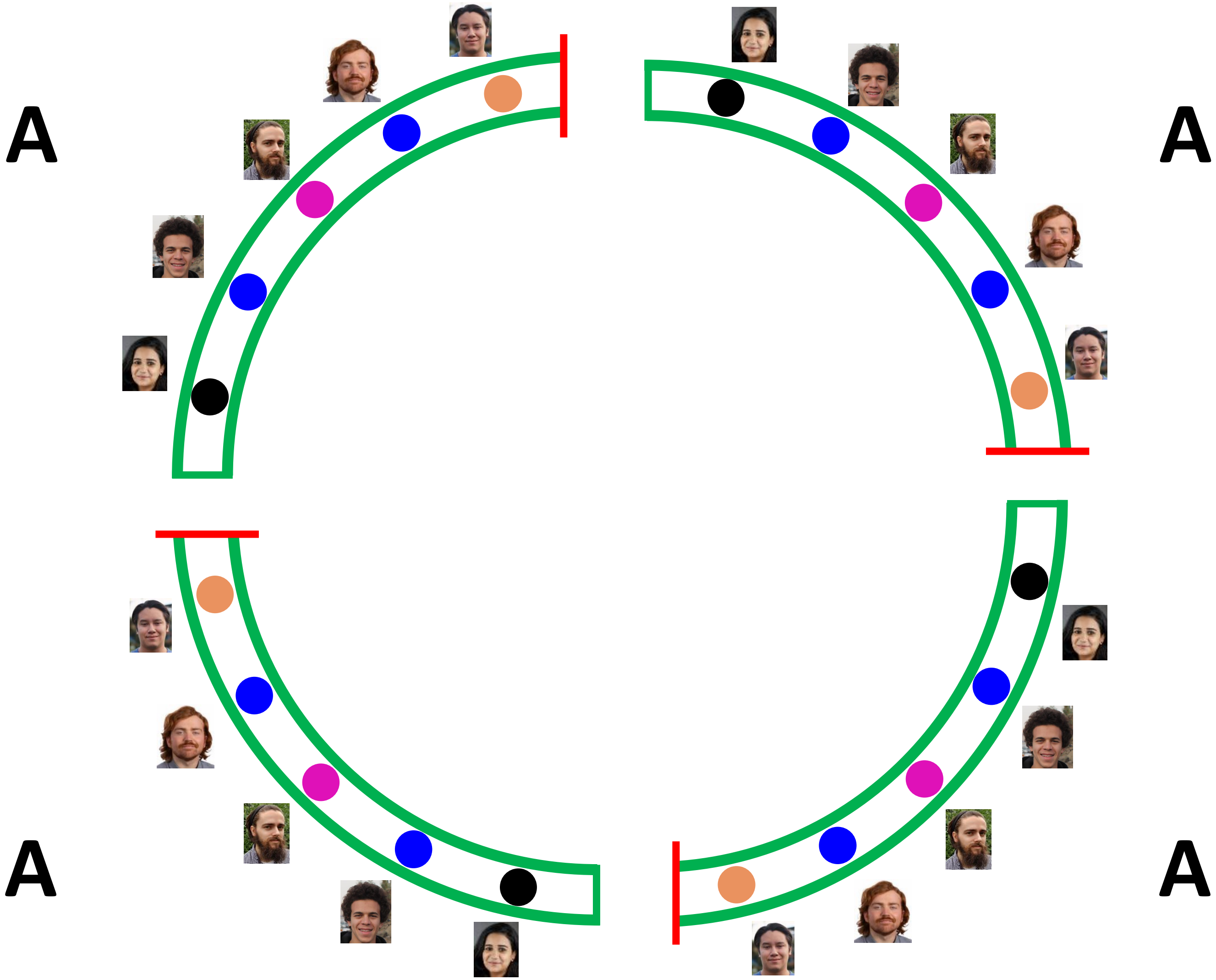
Ω: the set of all connected structures that respect the game rules

How to compute this fast?

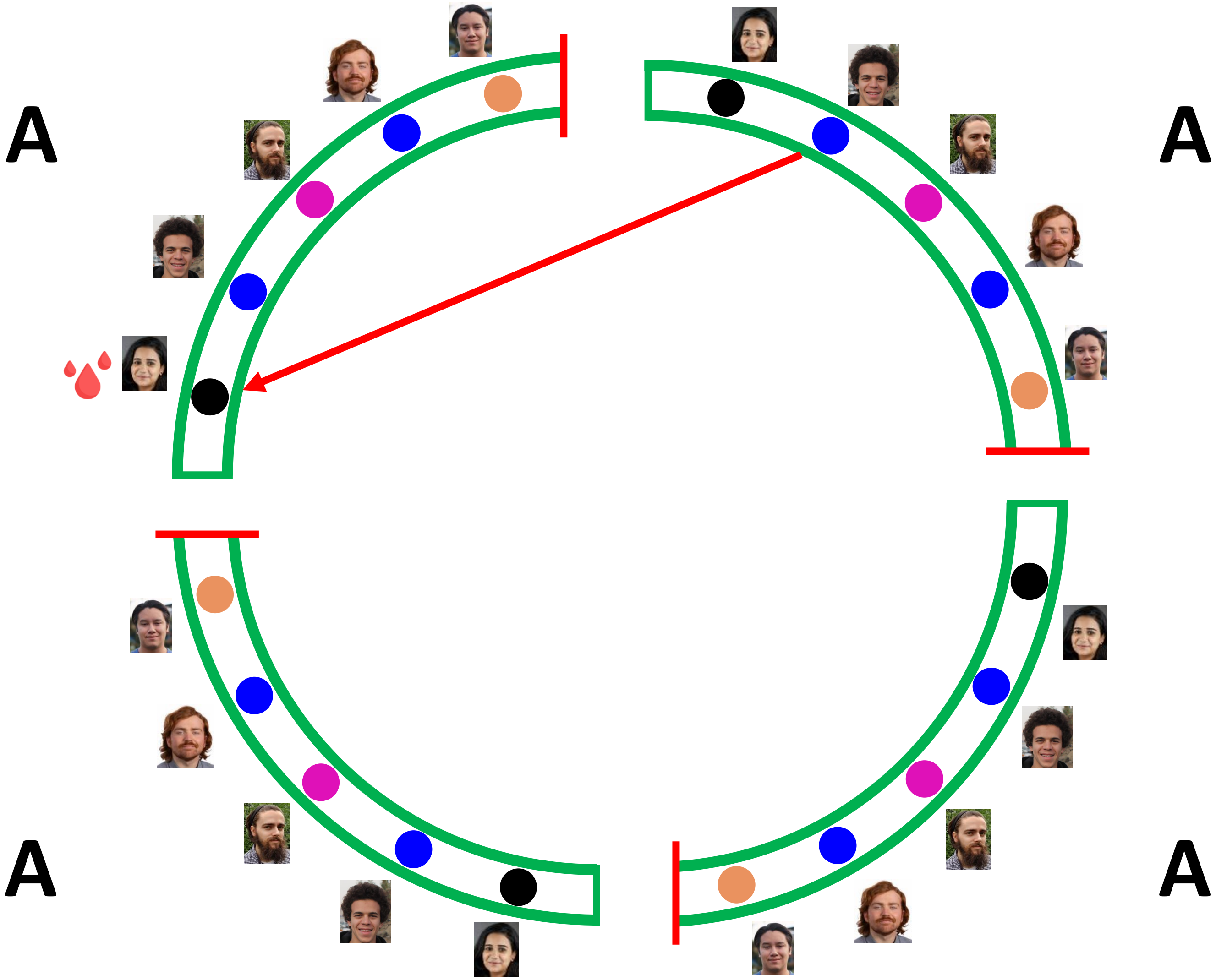
Level 4


FIRE POINT

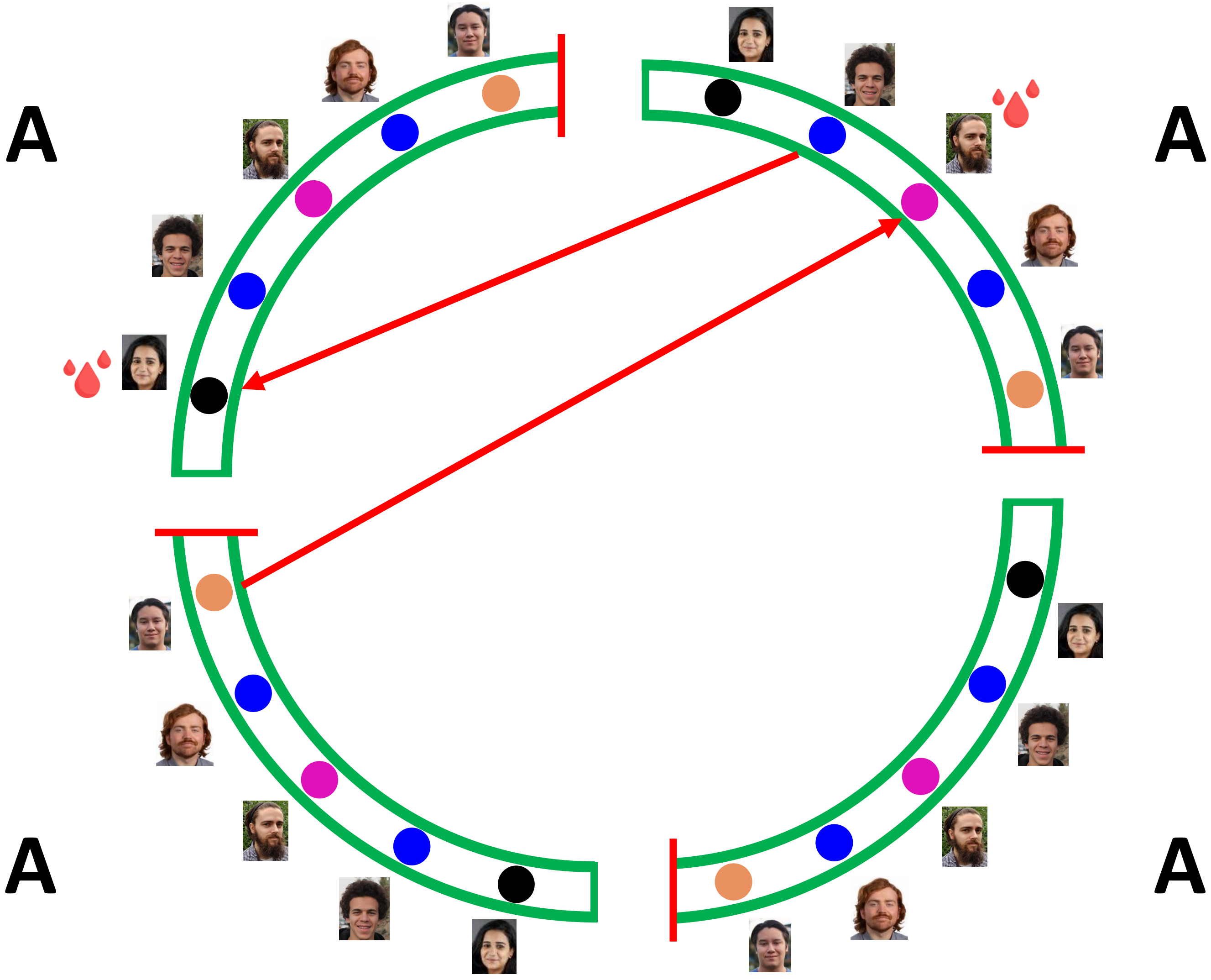
c = 4 sofas



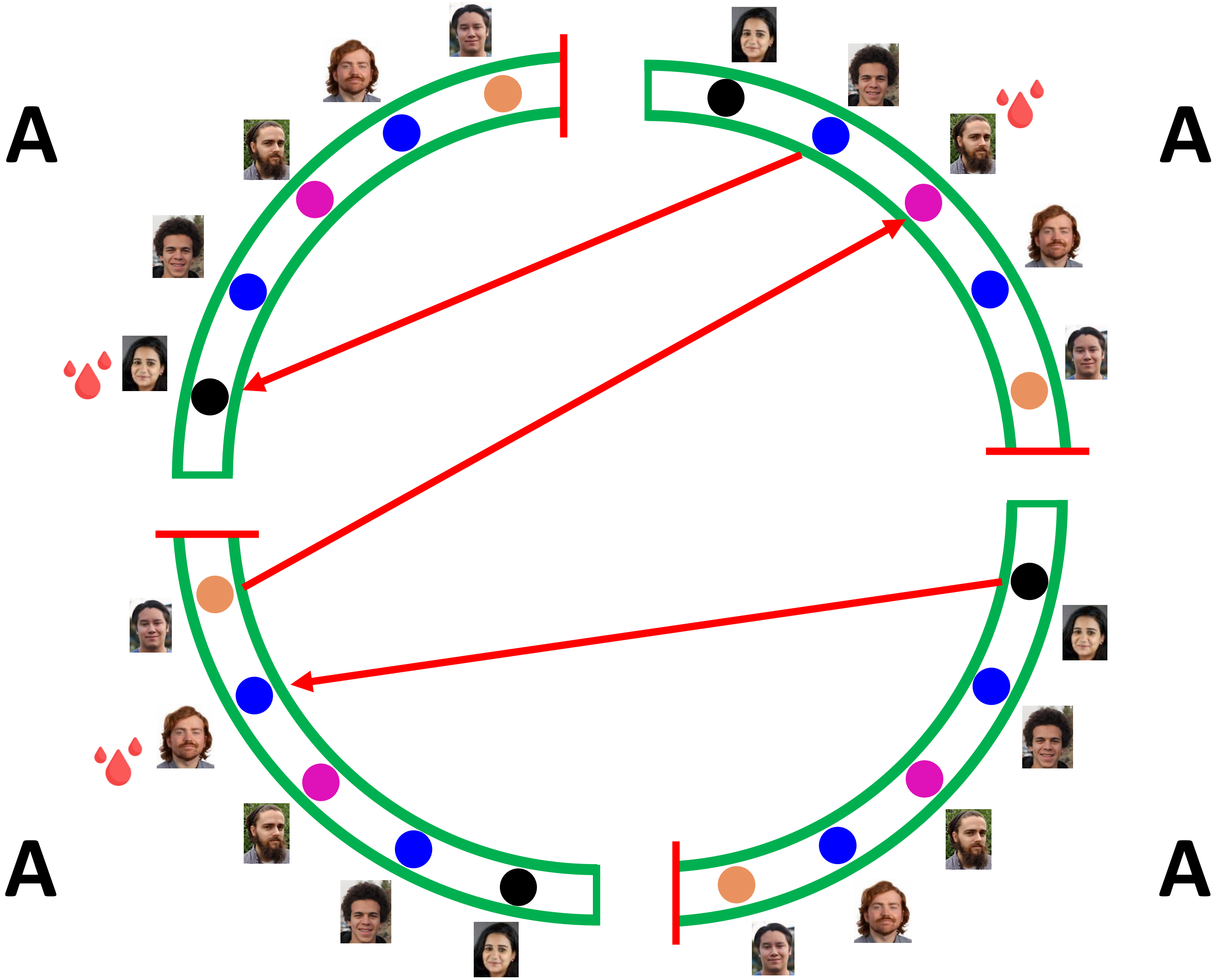
c = 4 sofas



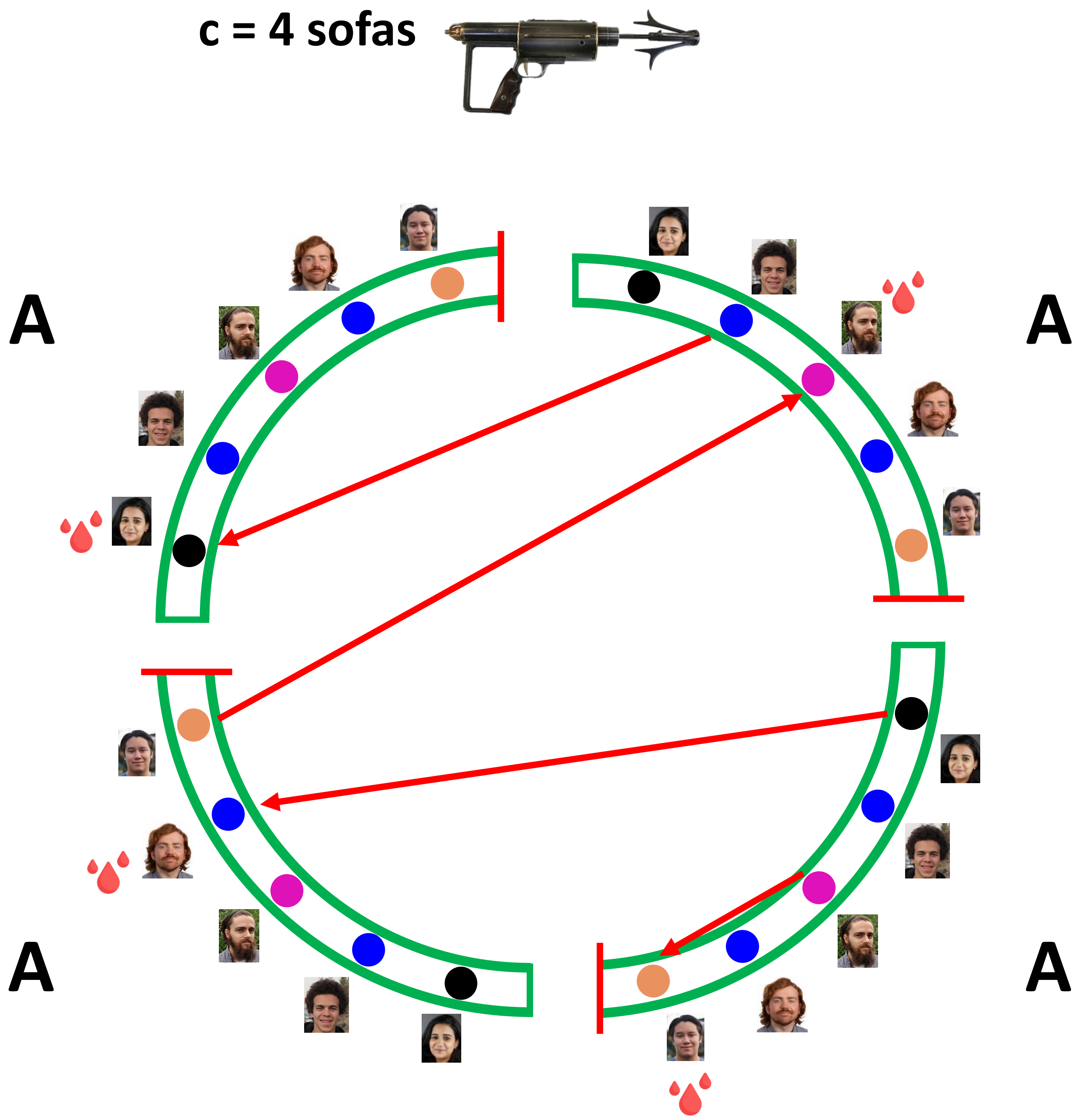
c = 4 sofas



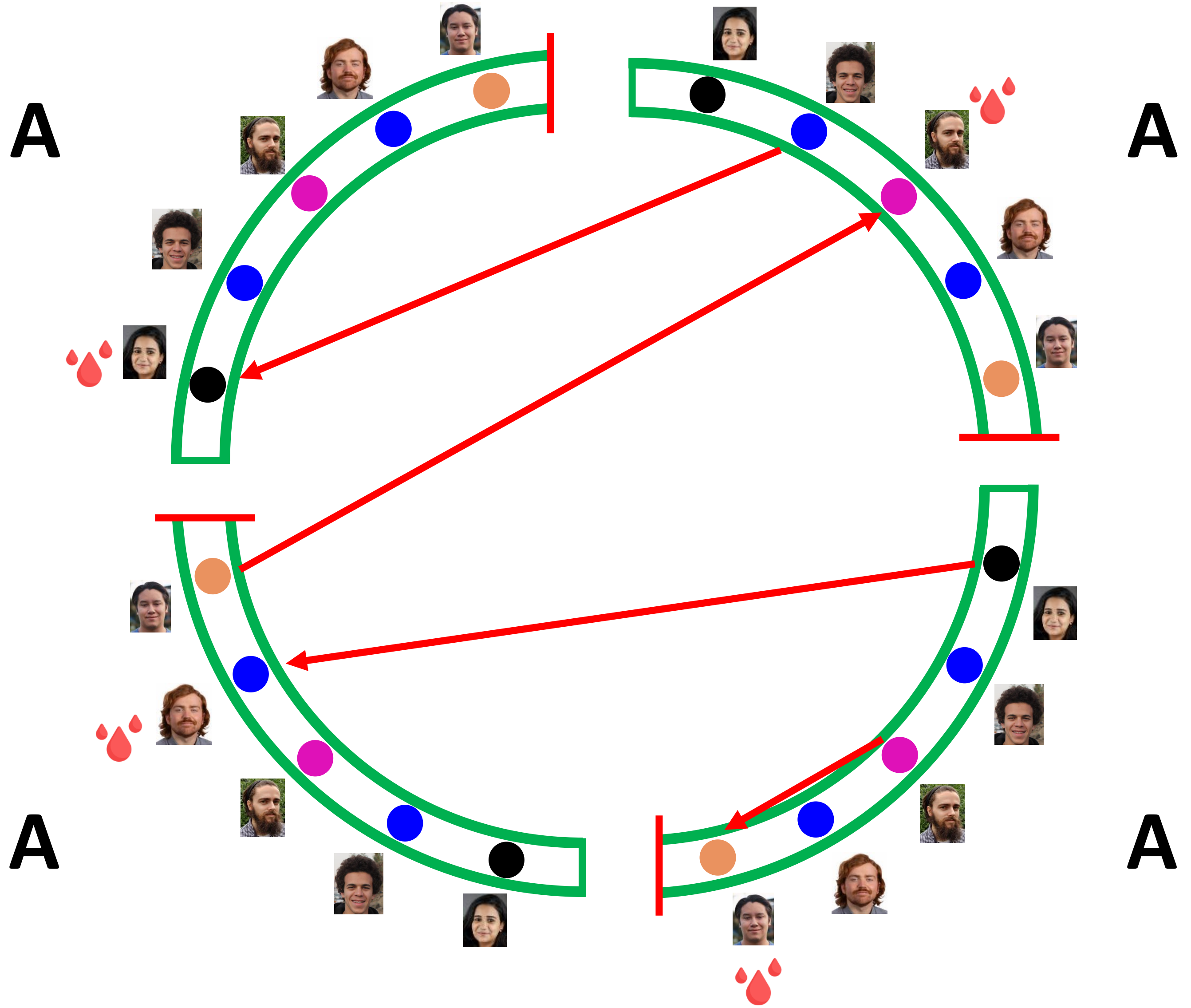
c = 4 sofas



c = 4 sofas

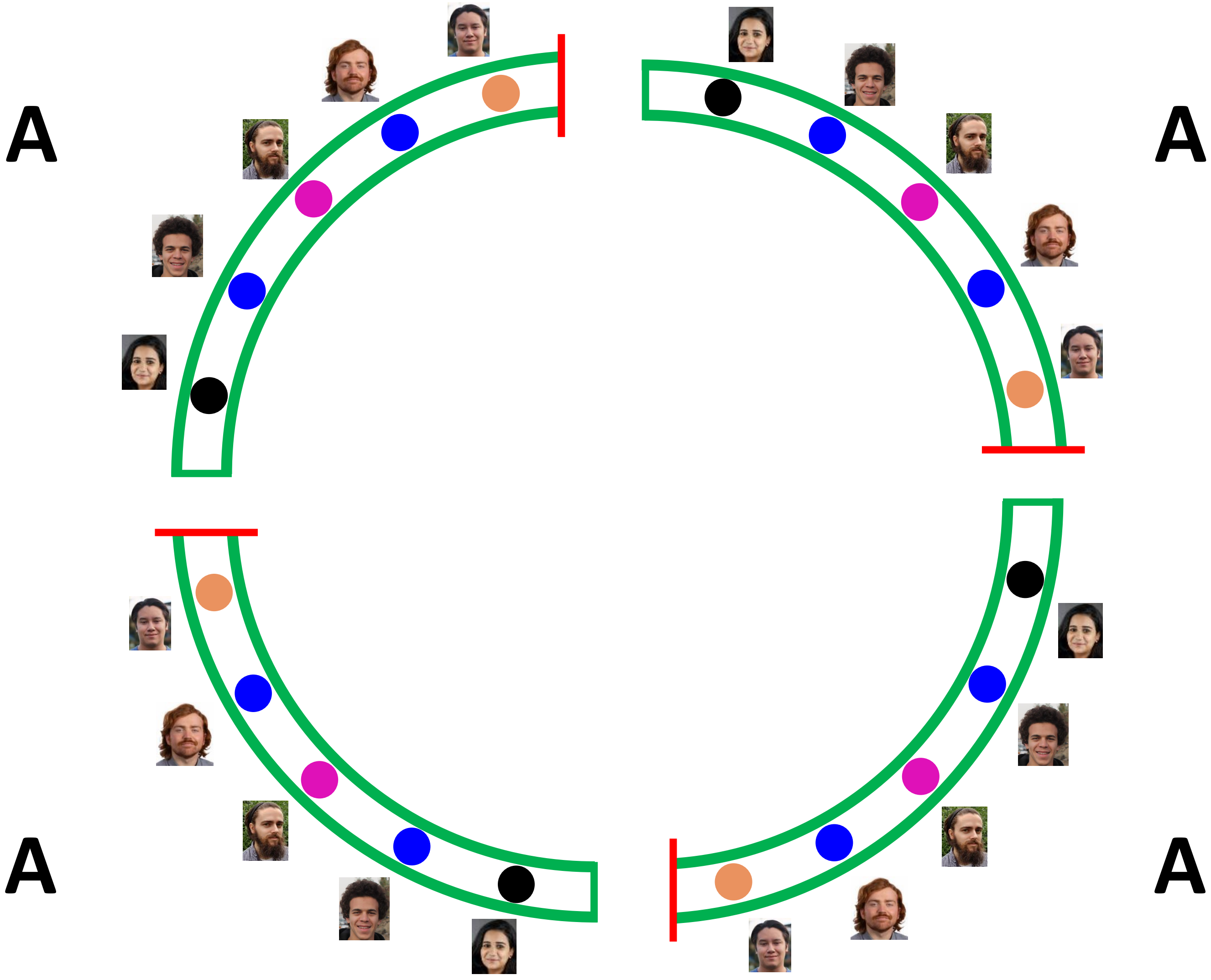


c = 4 sofas

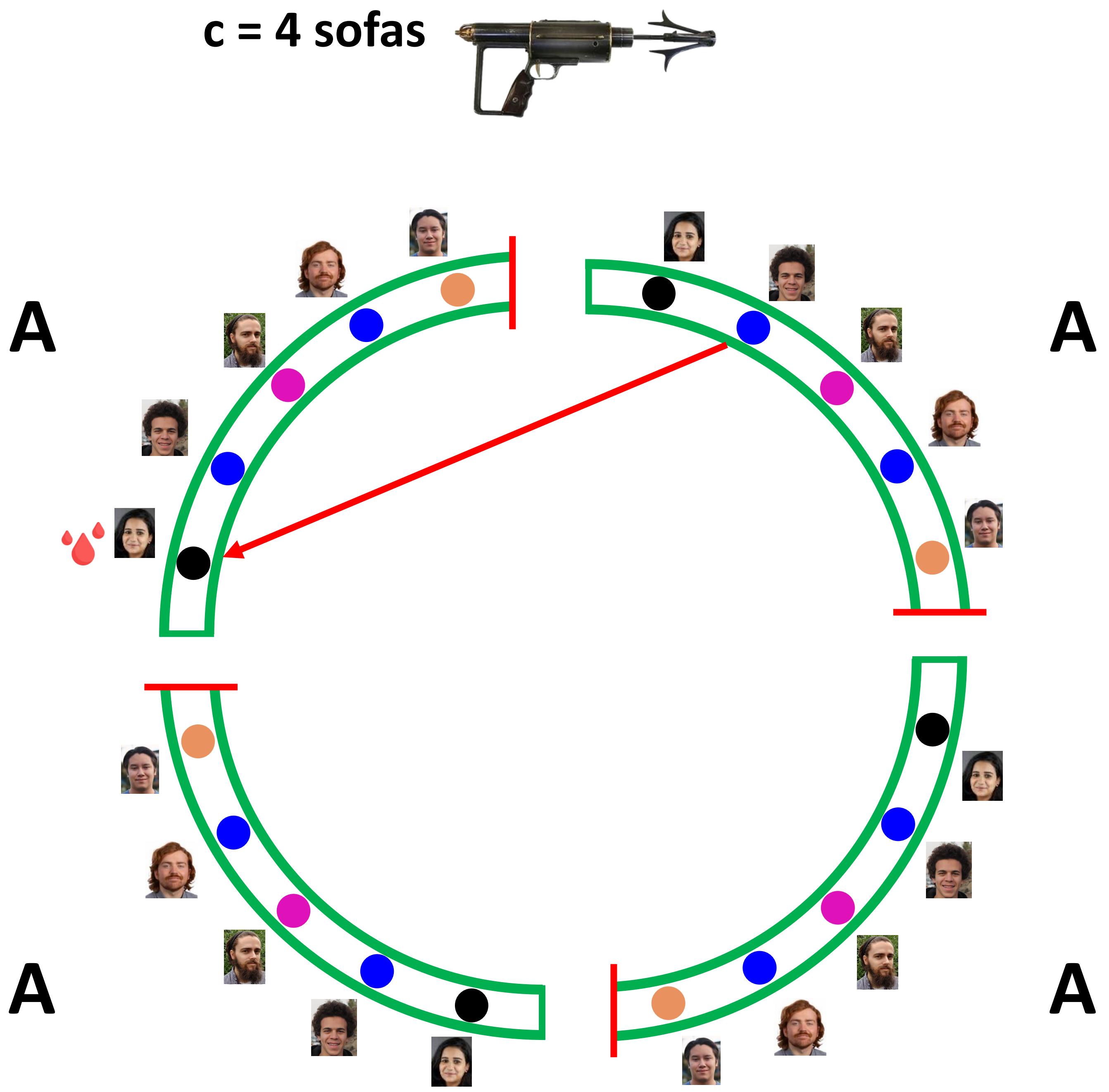


That is ok!

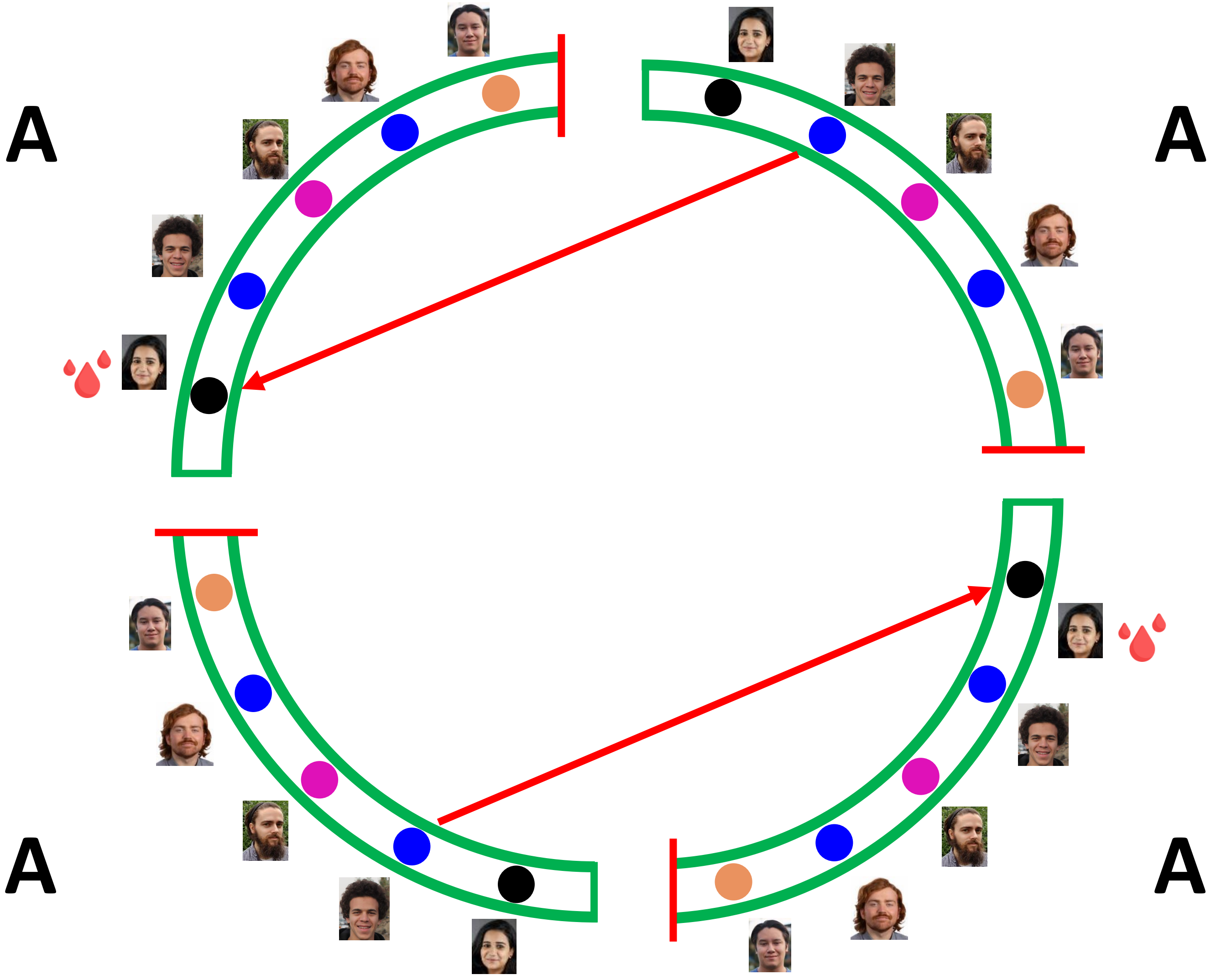
c = 4 sofas



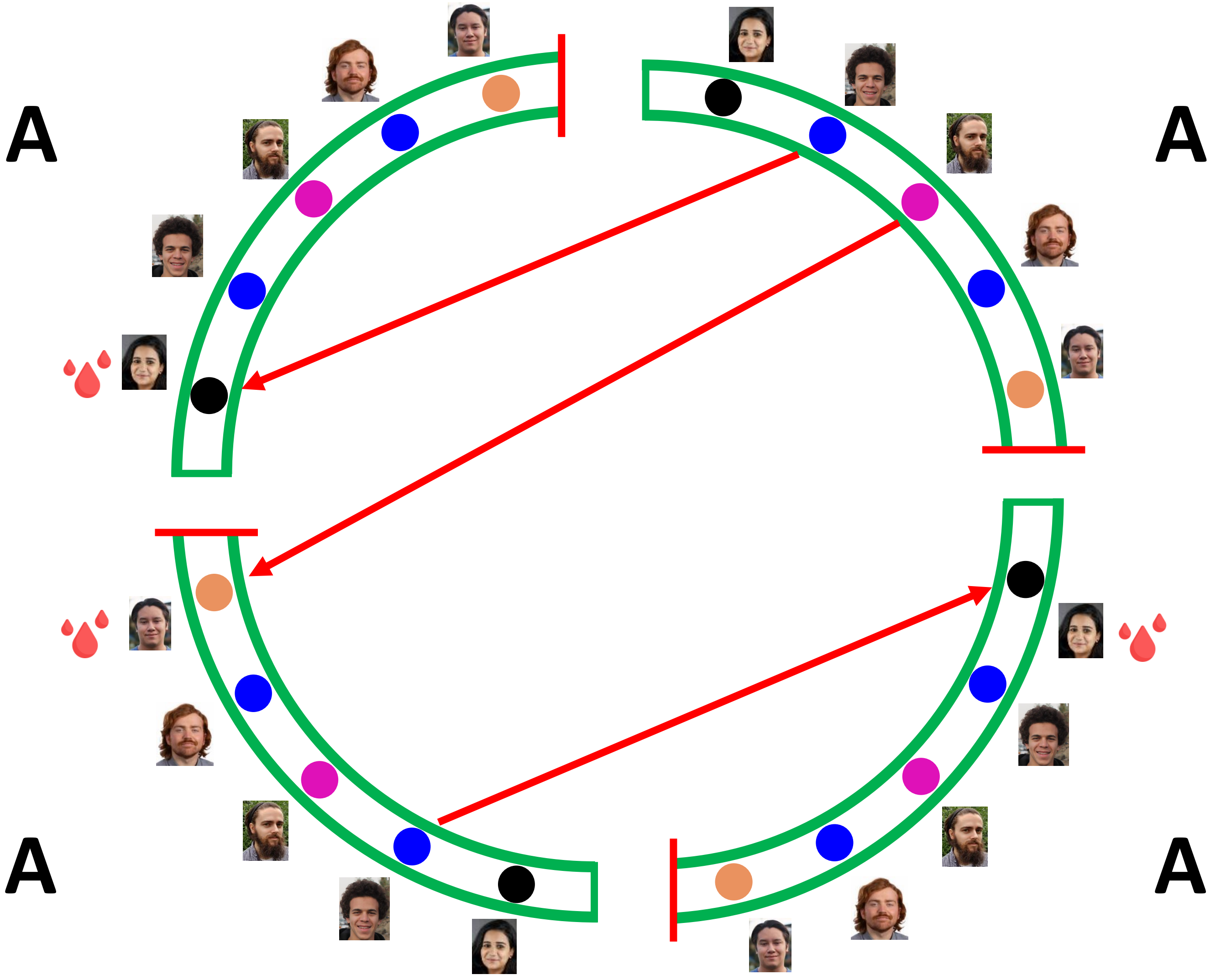
c = 4 sofas



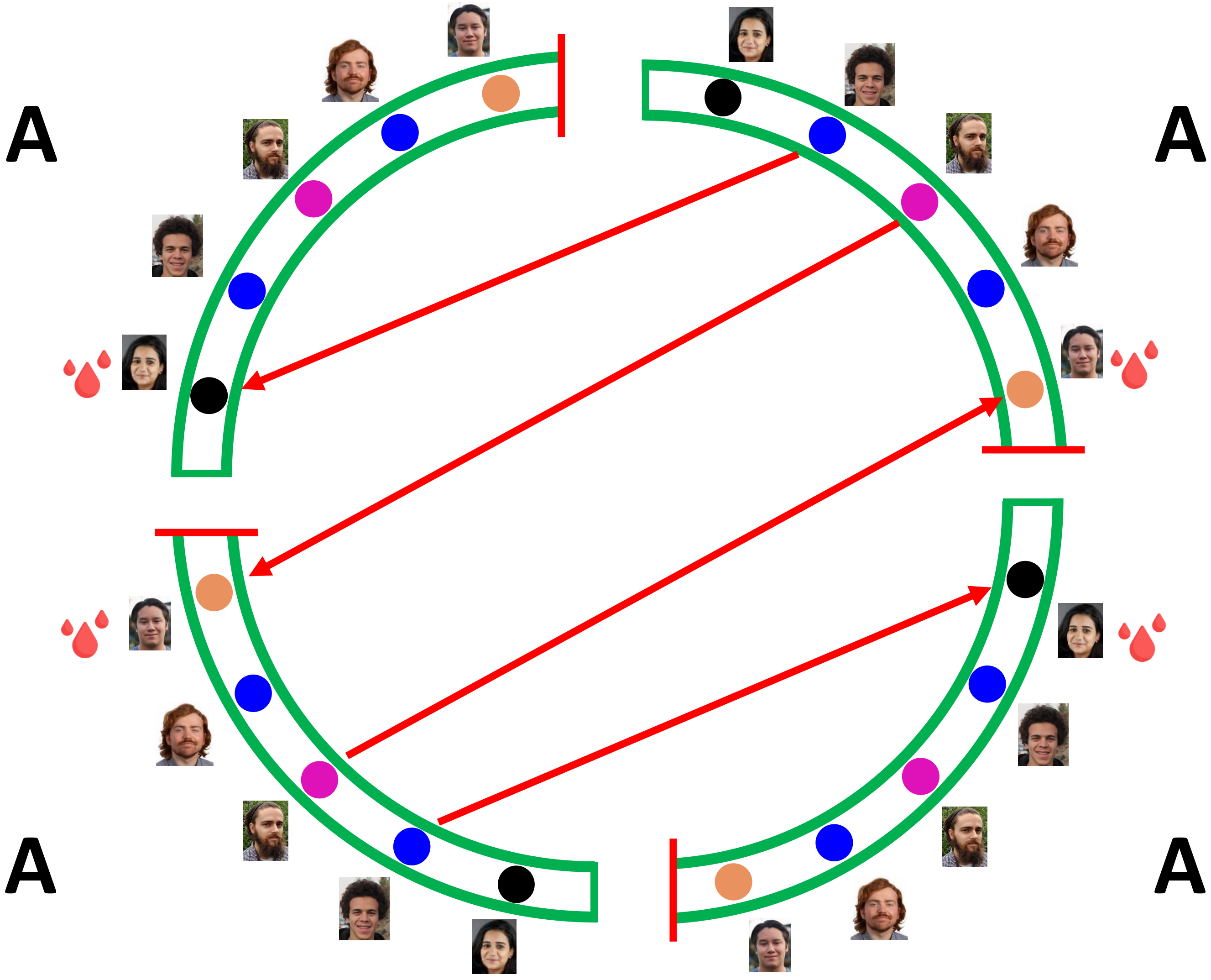
c = 4 sofas



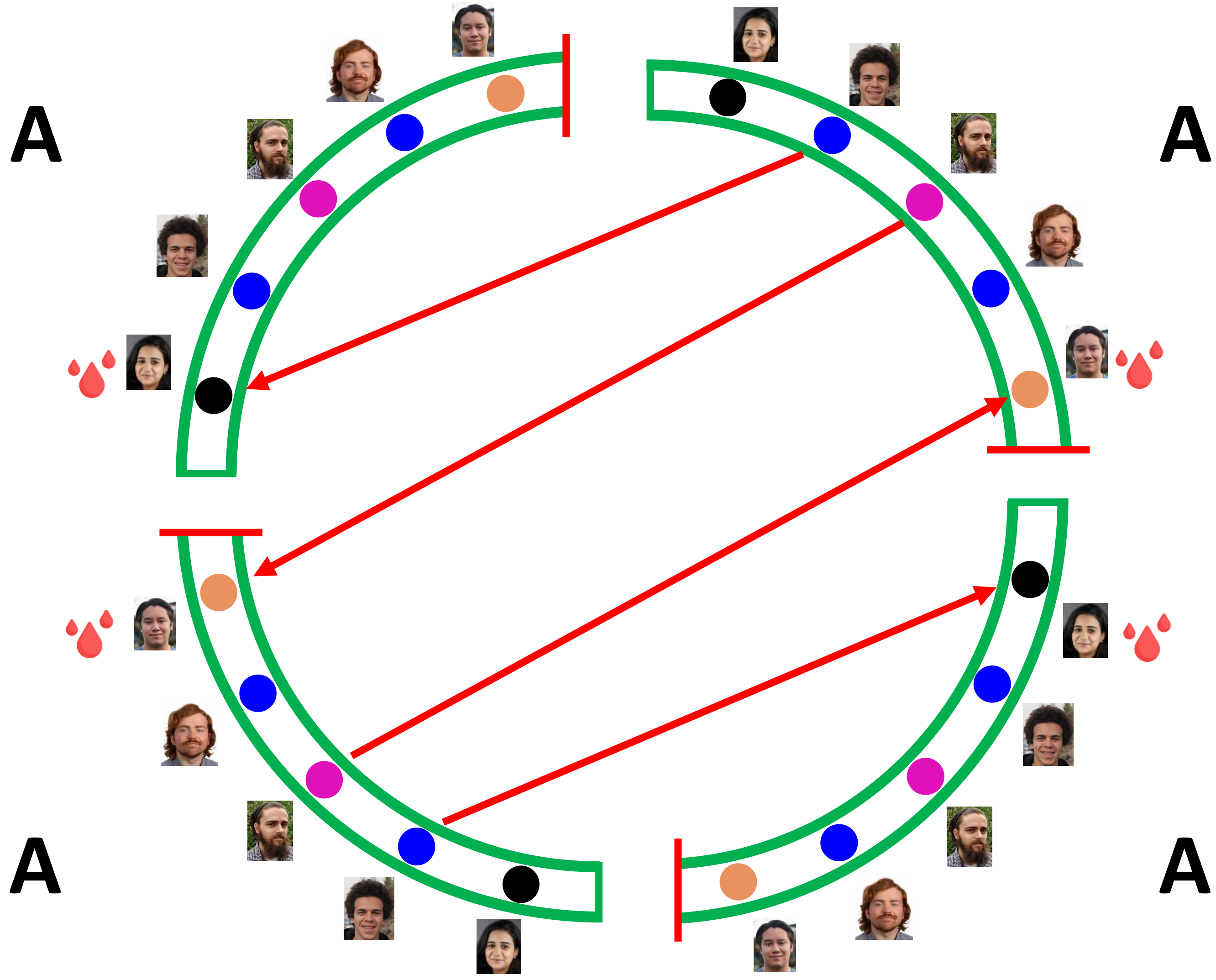
c = 4 sofas



c = 4 sofas

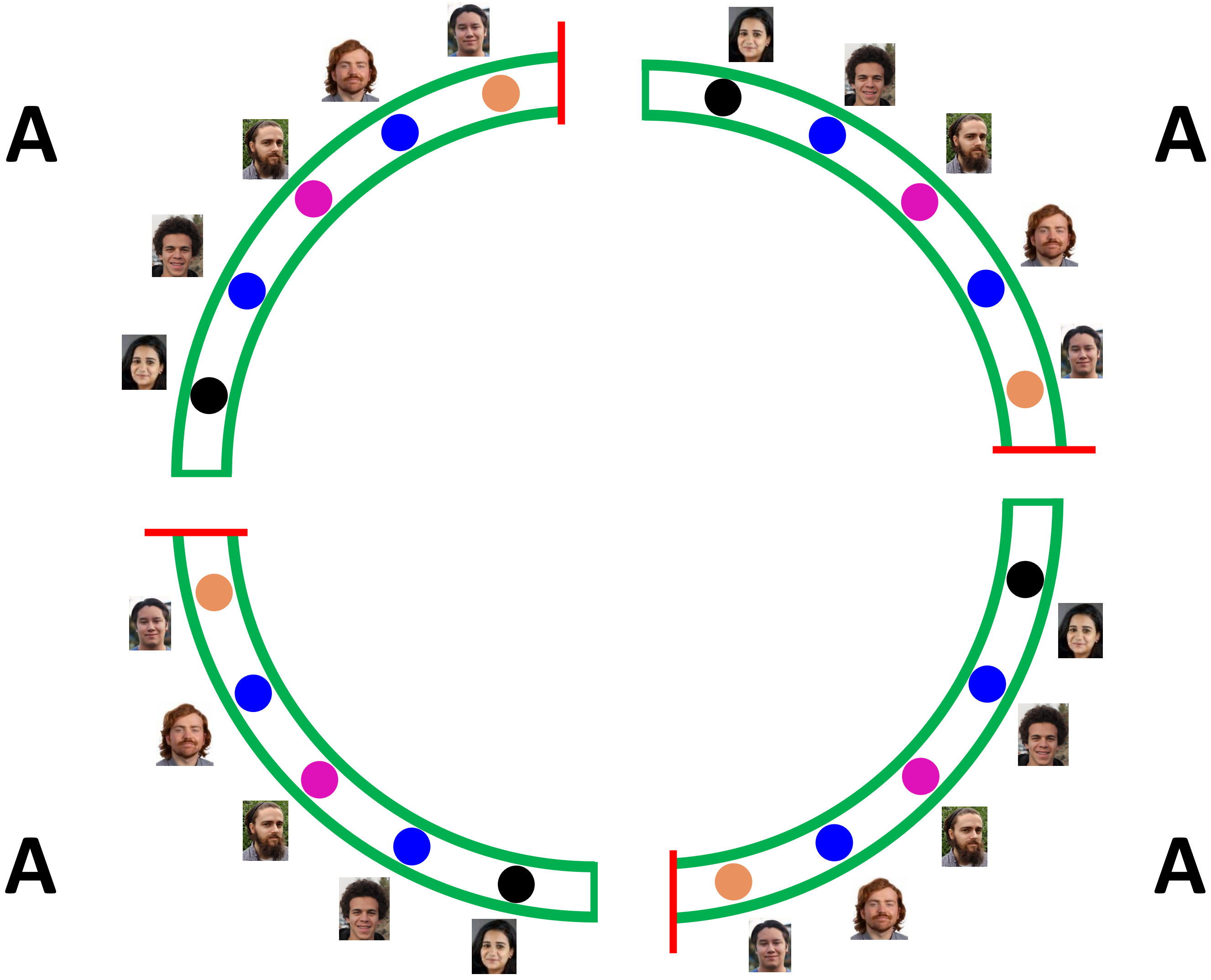


c = 4 sofas

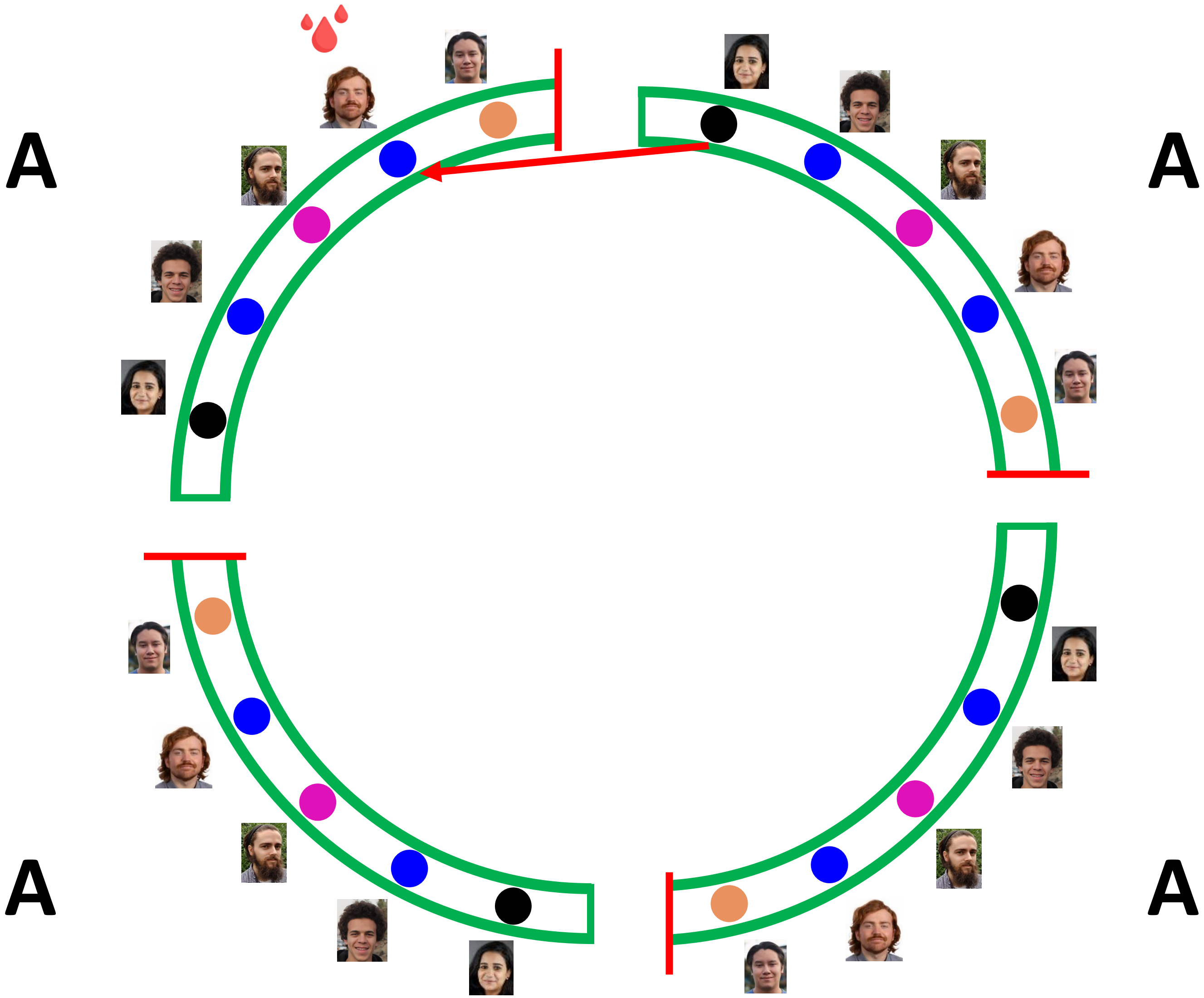


That is ugh!

c = 4 sofas



c = 4 sofas

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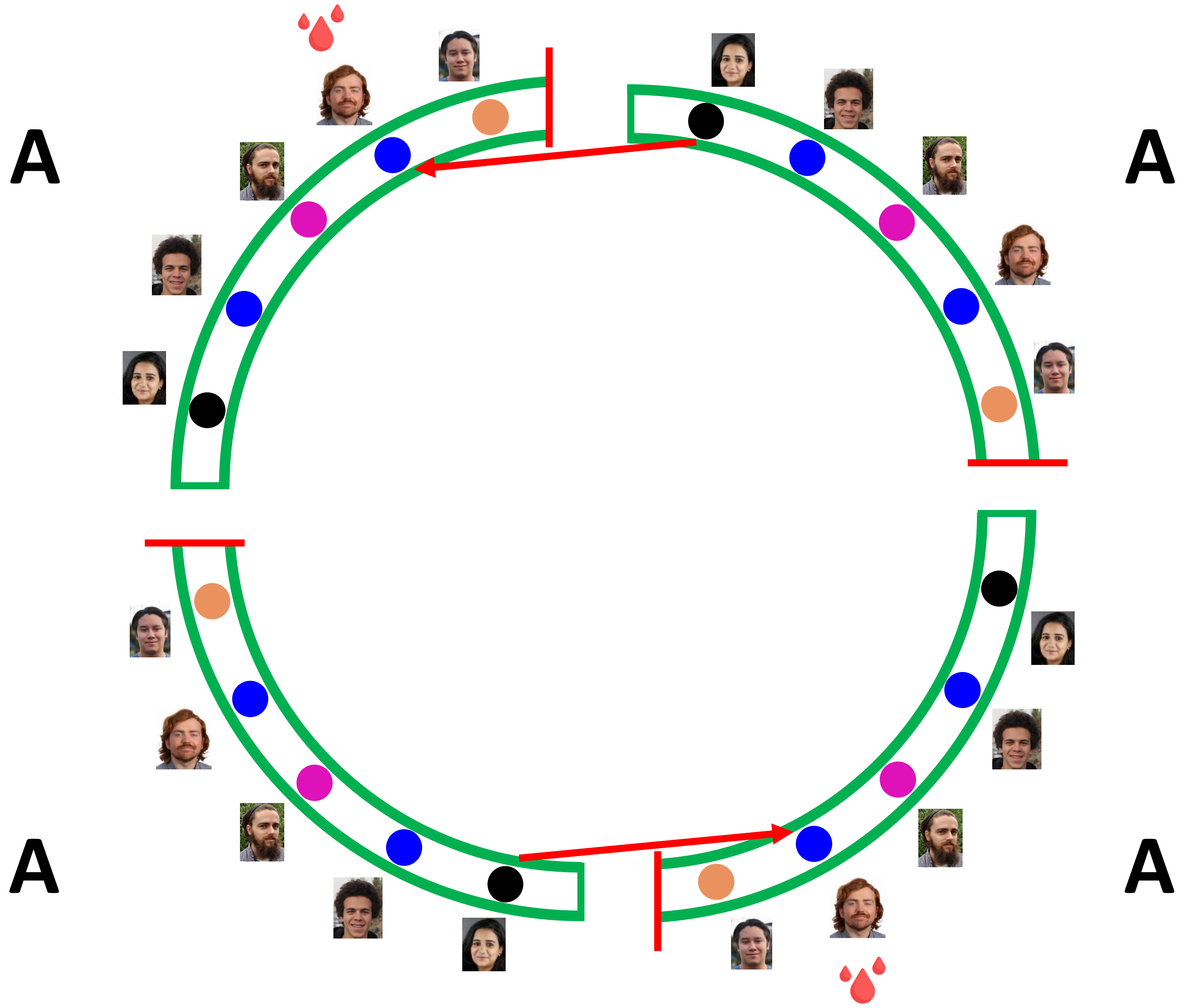
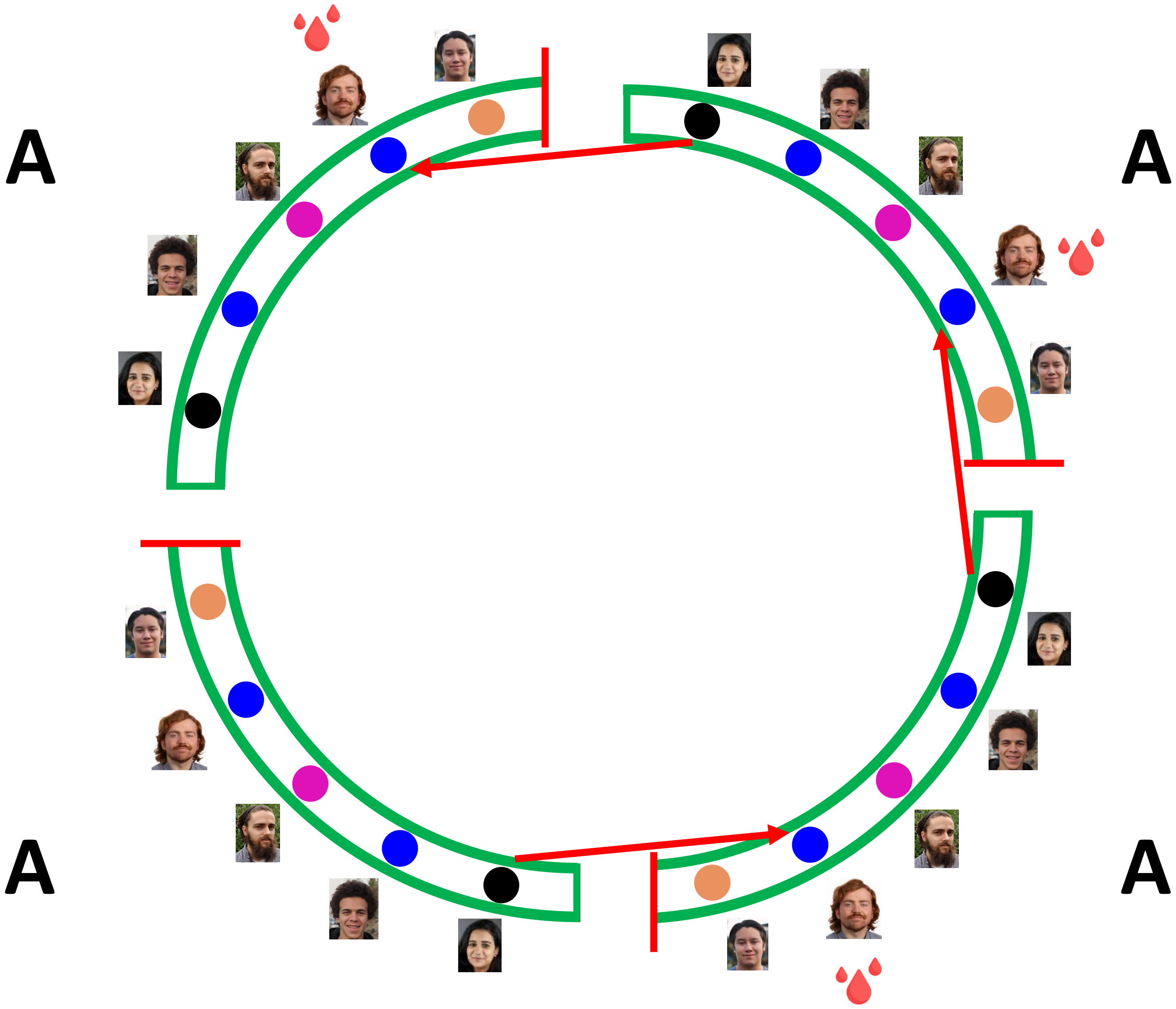
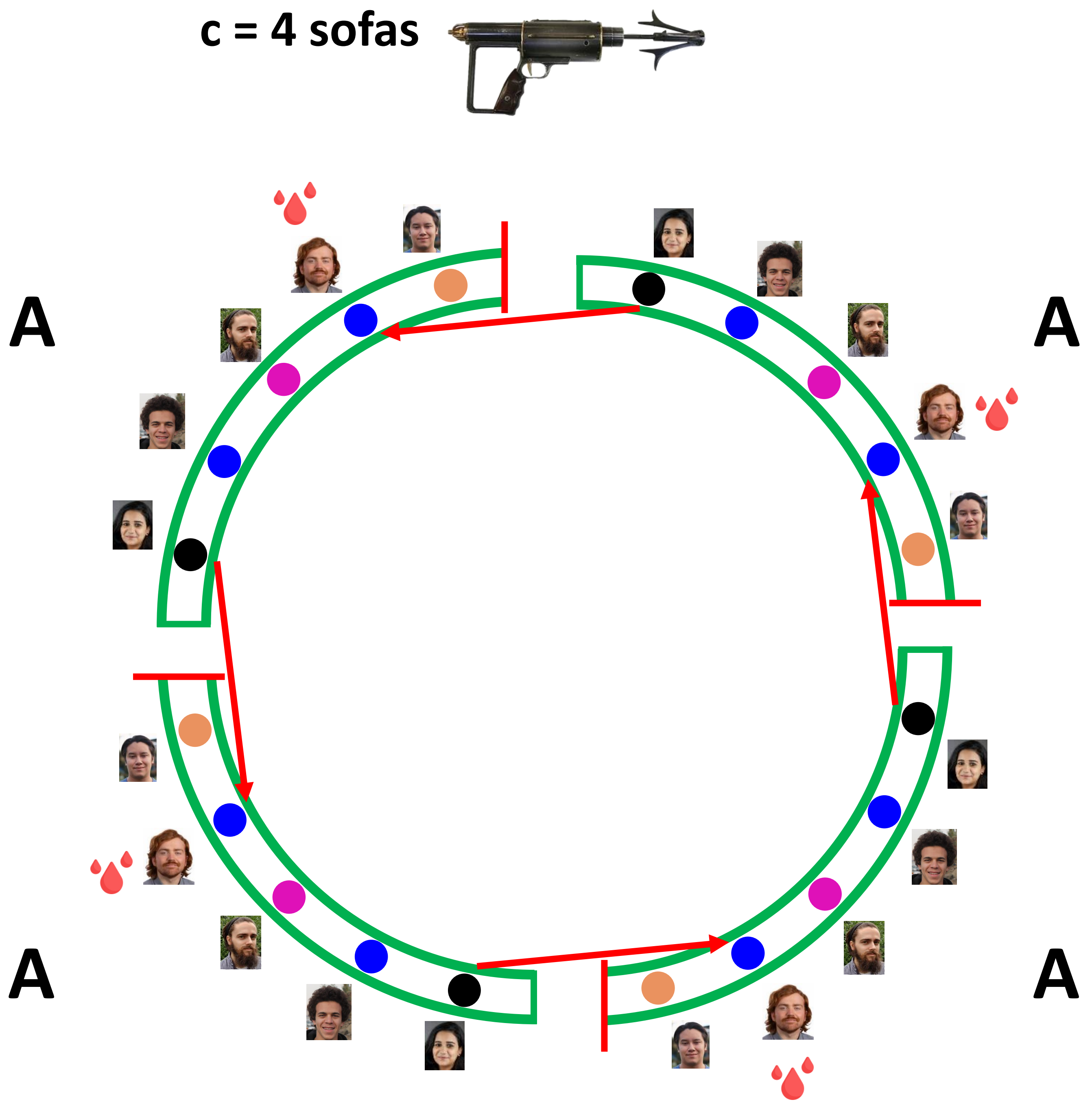


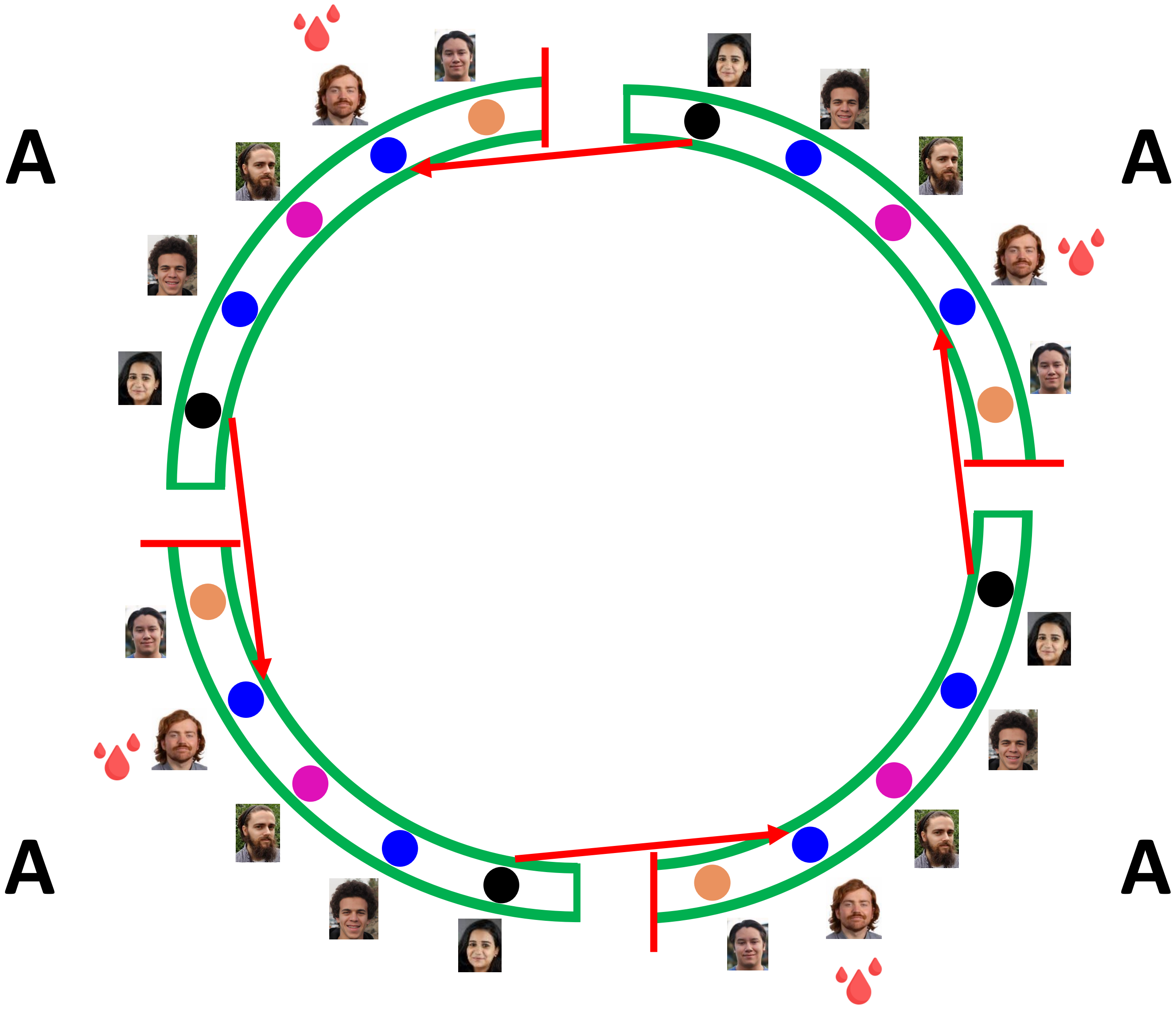
c = 4 sofas



c = 4 sofas

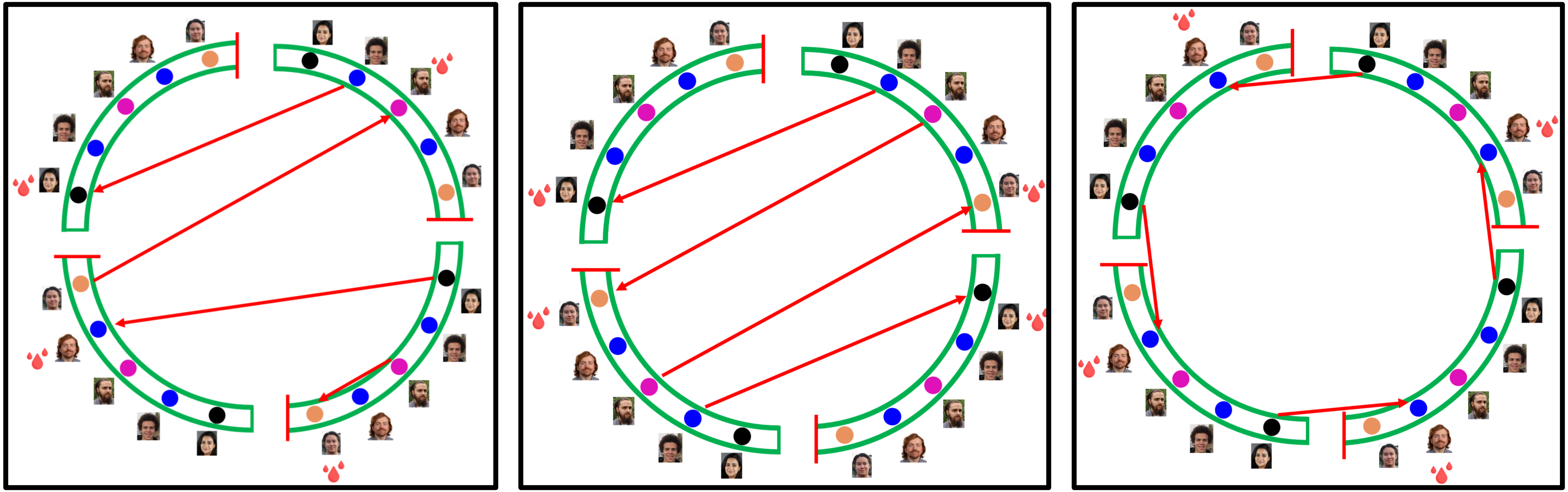


c = 4 sofas

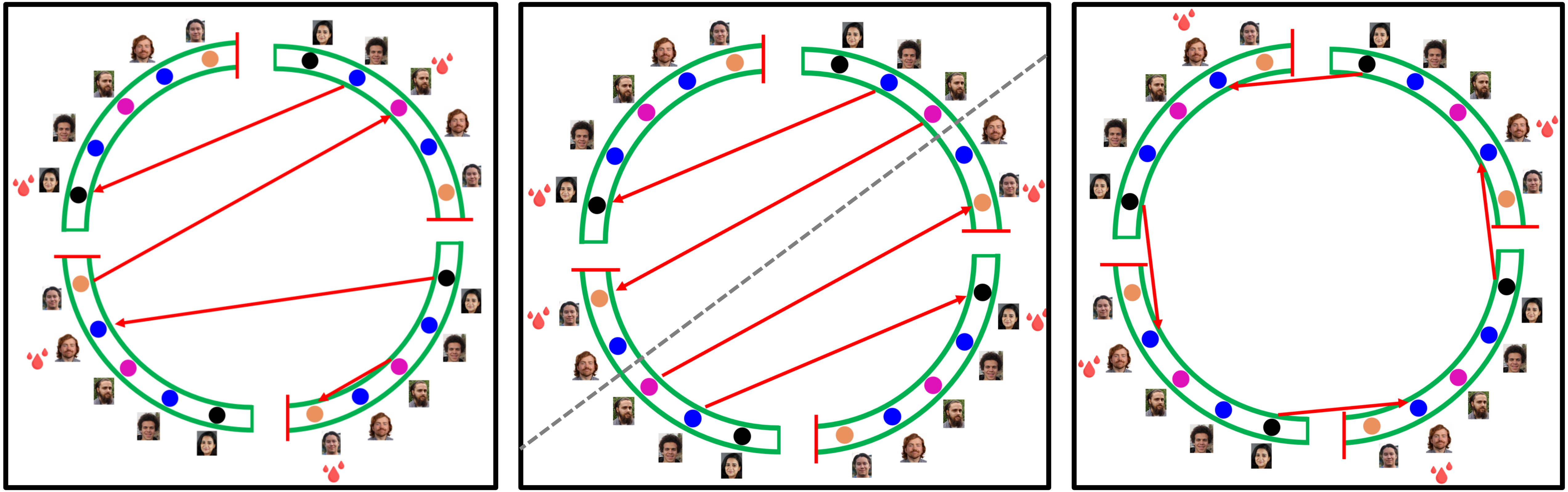


That is ugh ugh!

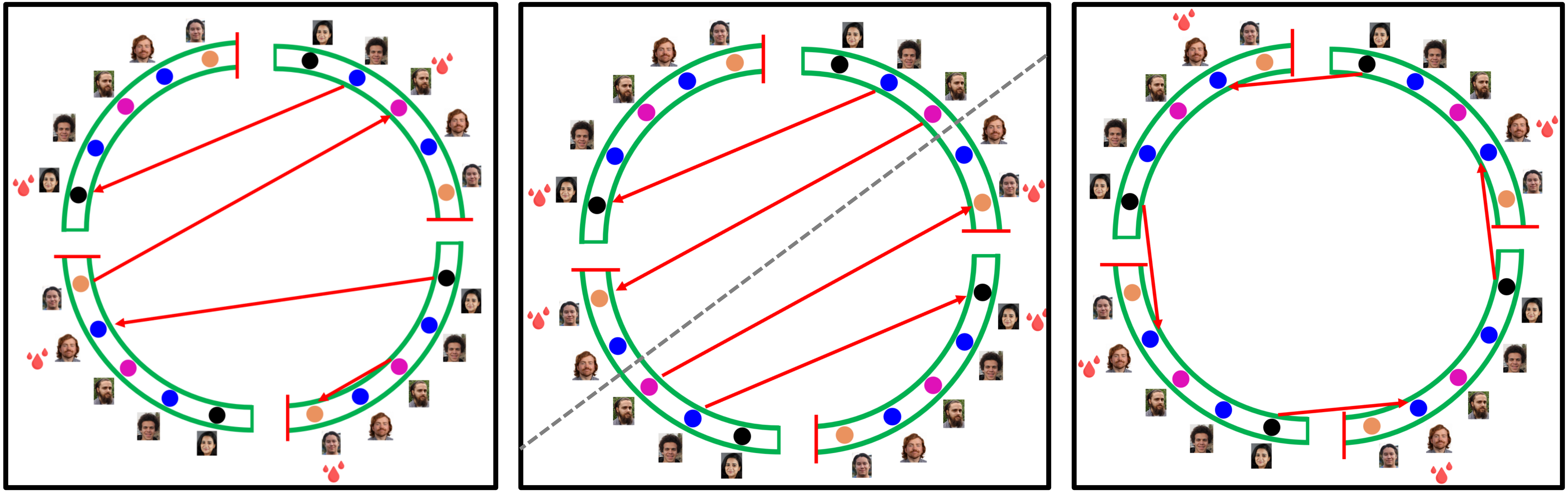
Let’s analyse this



Let’s analyse this

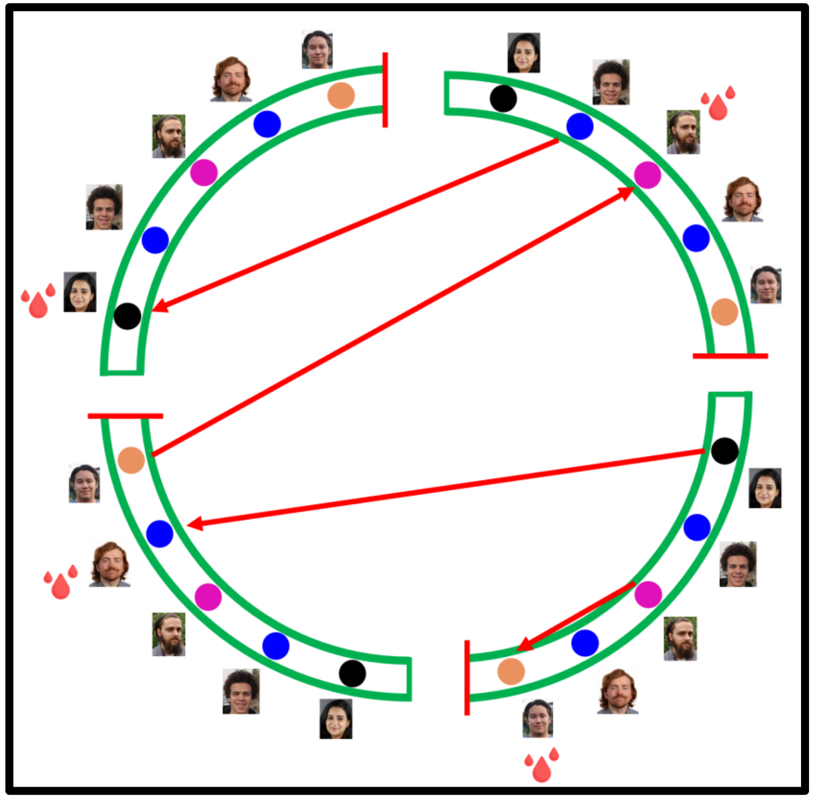


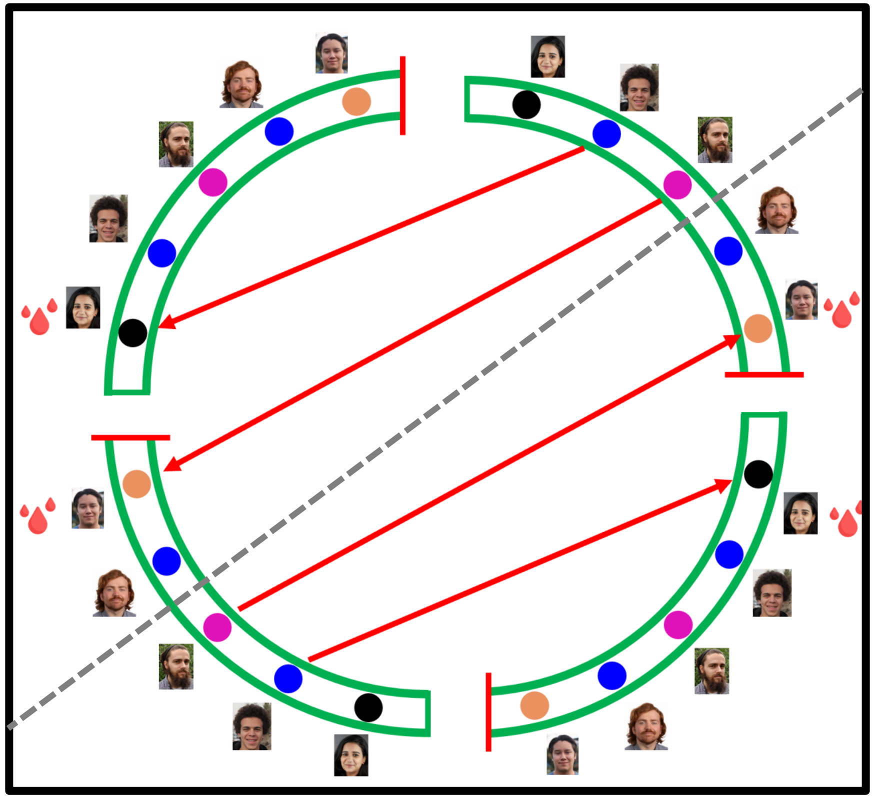
Let’s analyse this



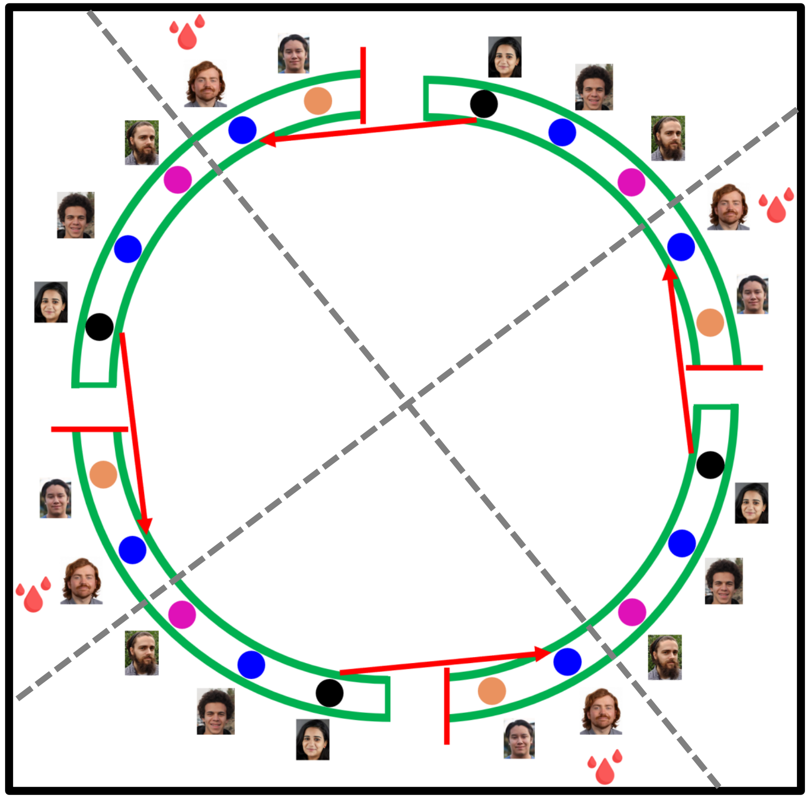
Rotate by 180 degrees

Let’s analyse this

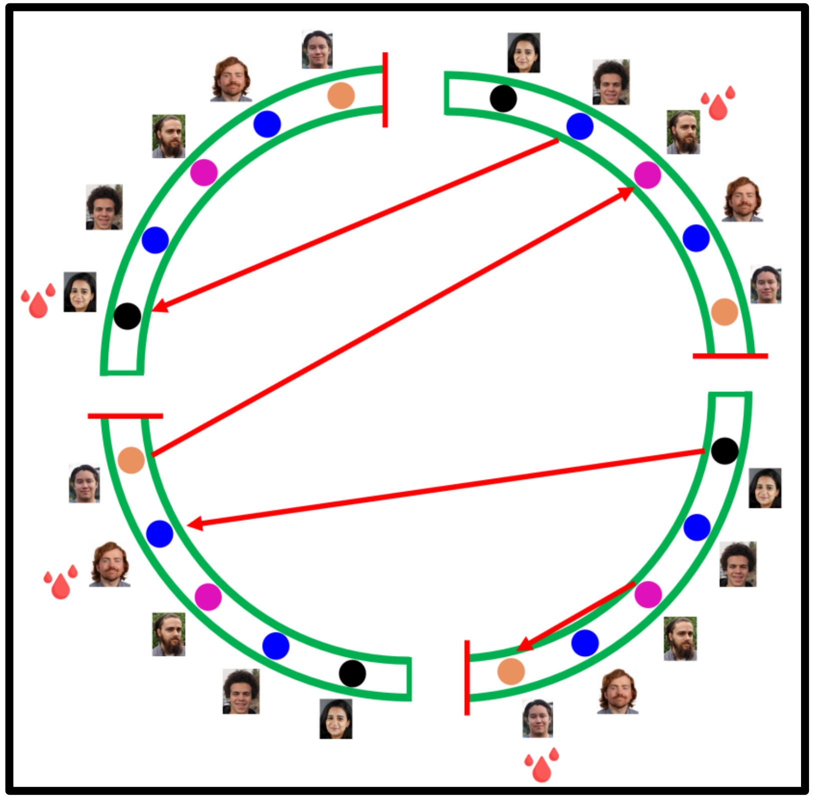


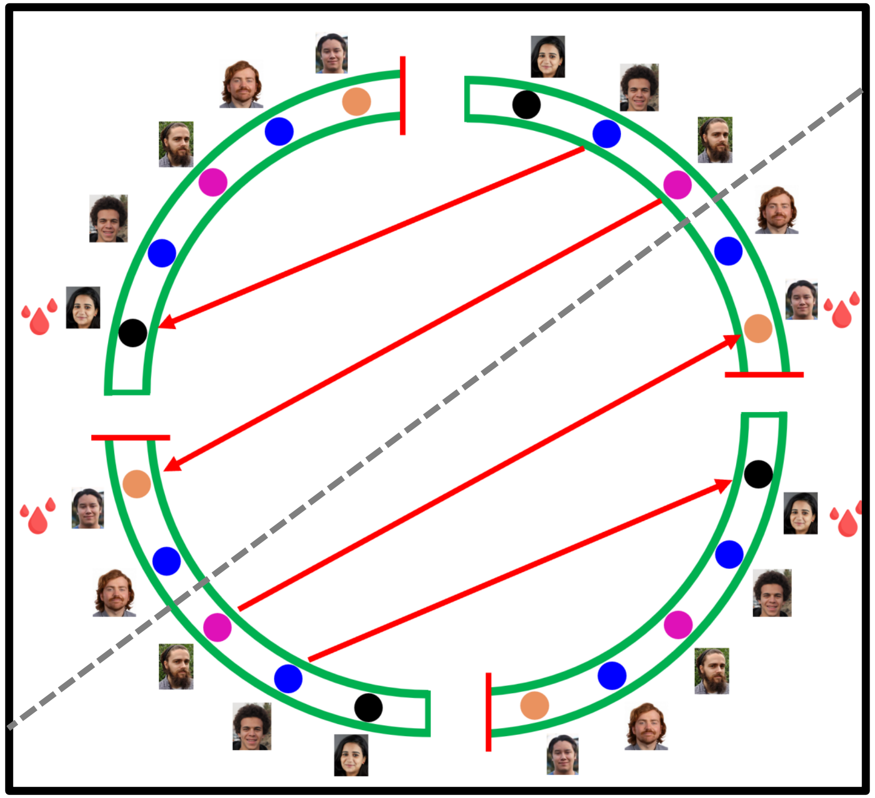


Rotate by 180 degrees

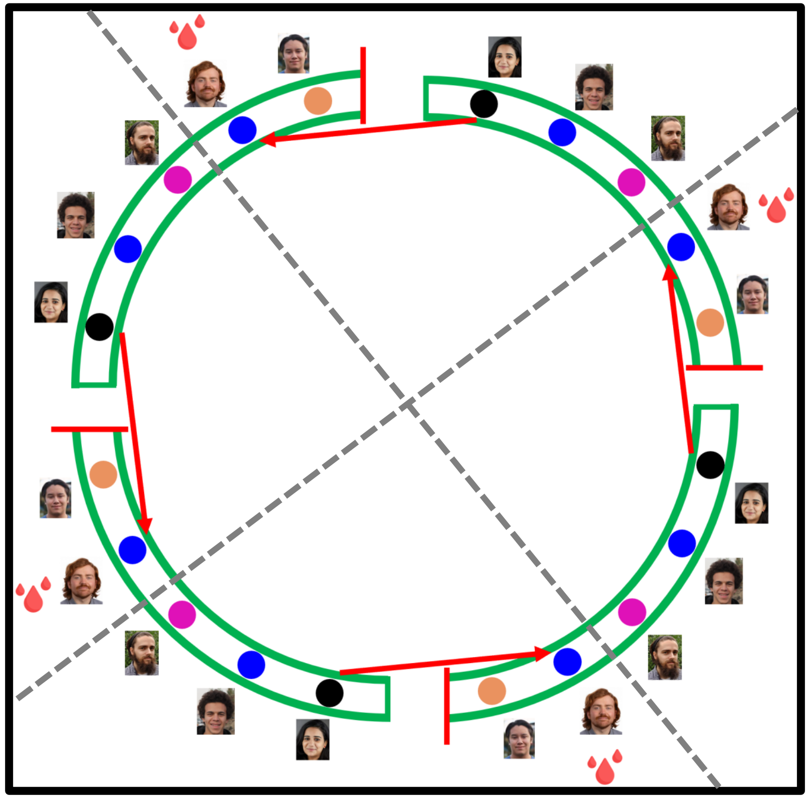


Let’s analyse this



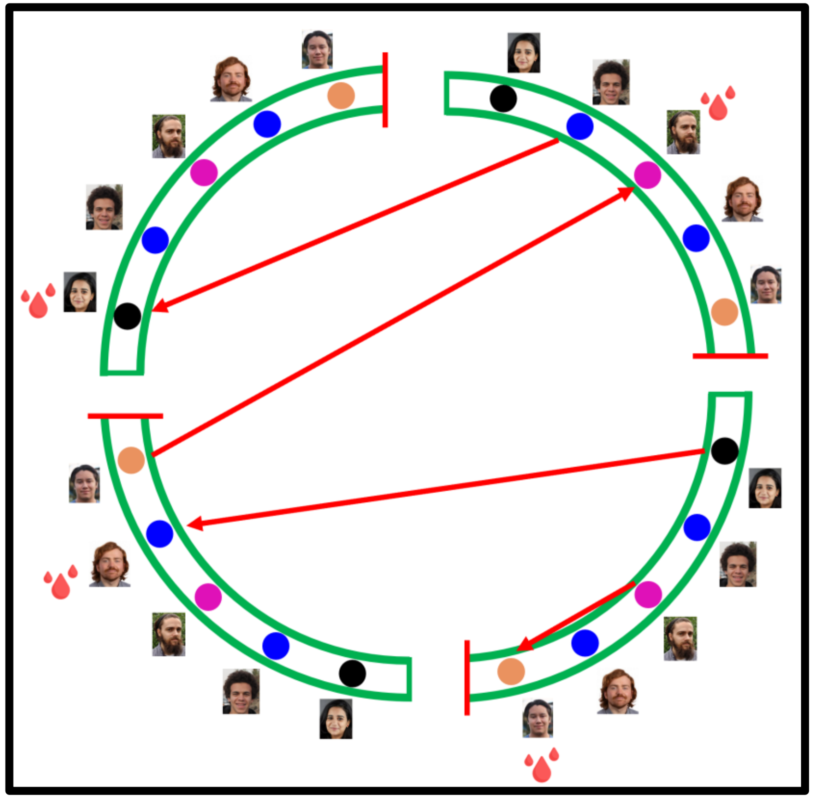


Rotate by 180 degrees

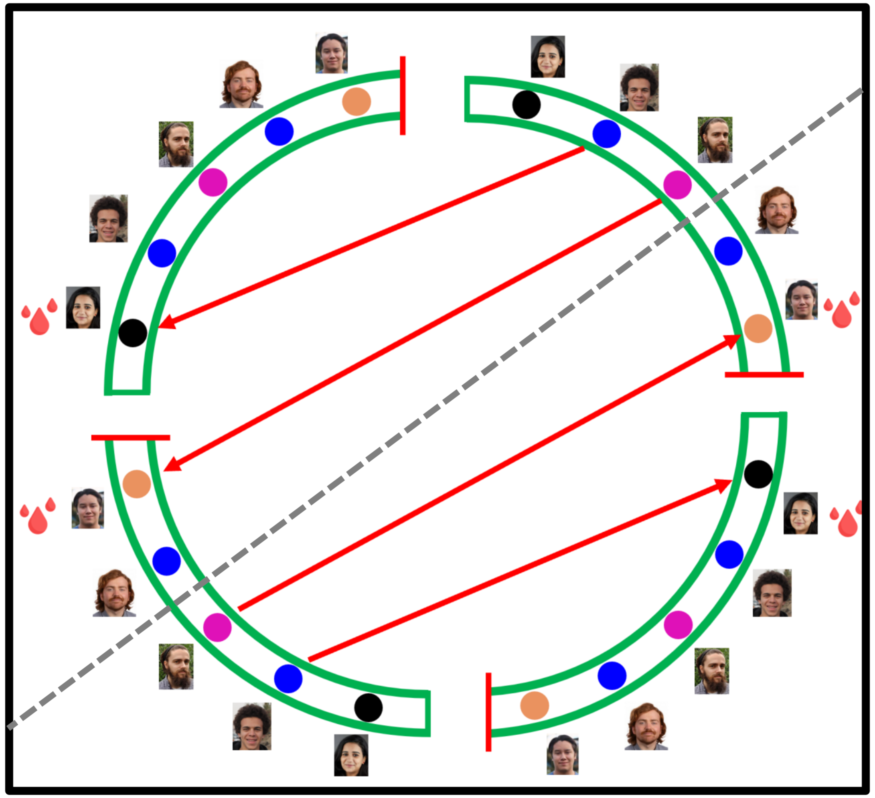


Rotate by 90 degrees

Let's analyse this

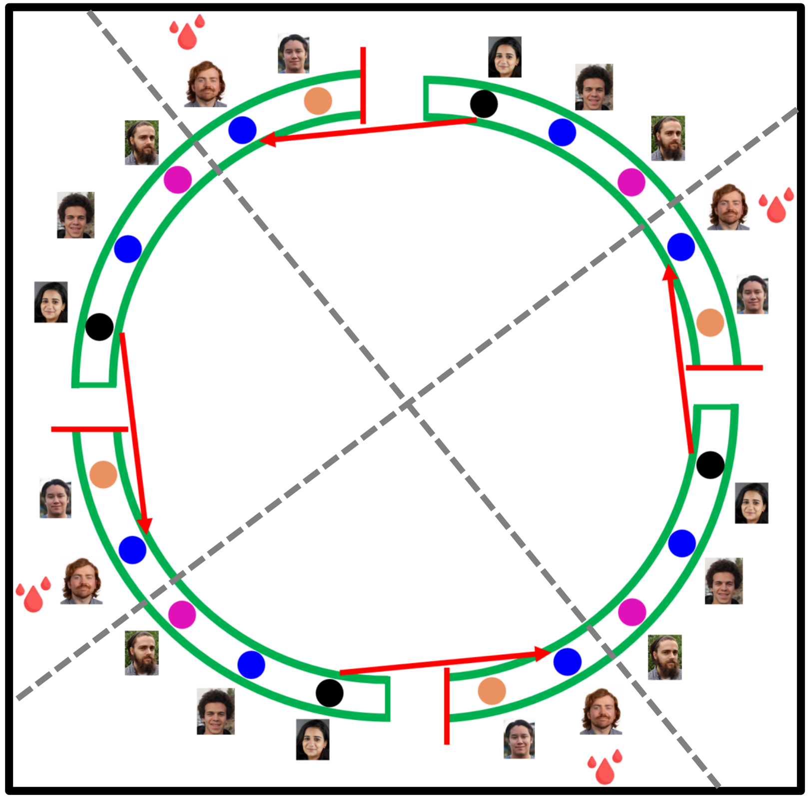


$R = 1$



Rotate by 180 degrees

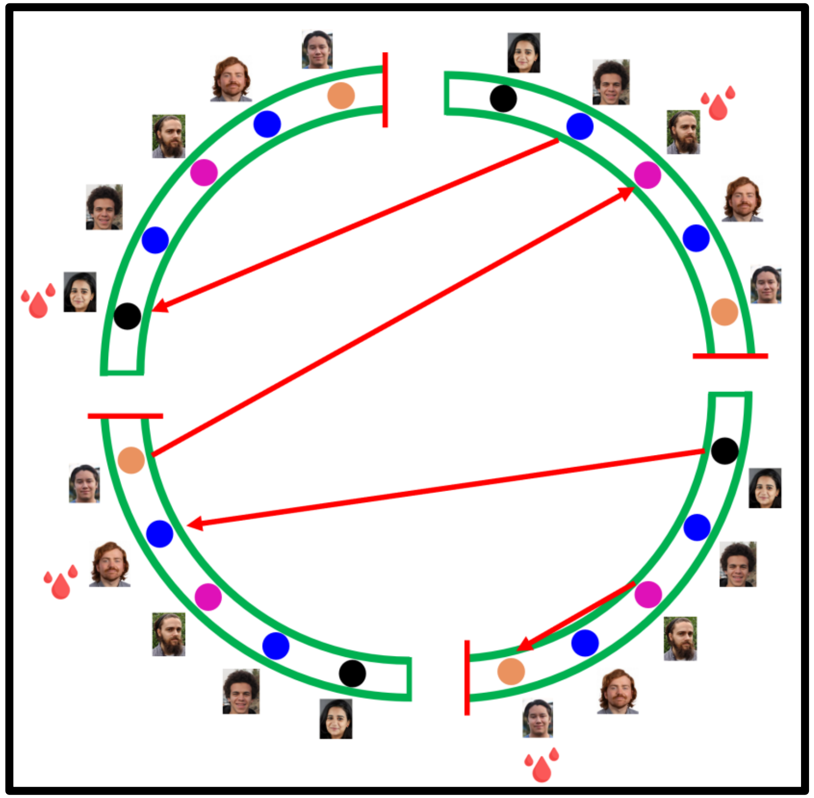
$R = 2$



Rotate by 90 degrees

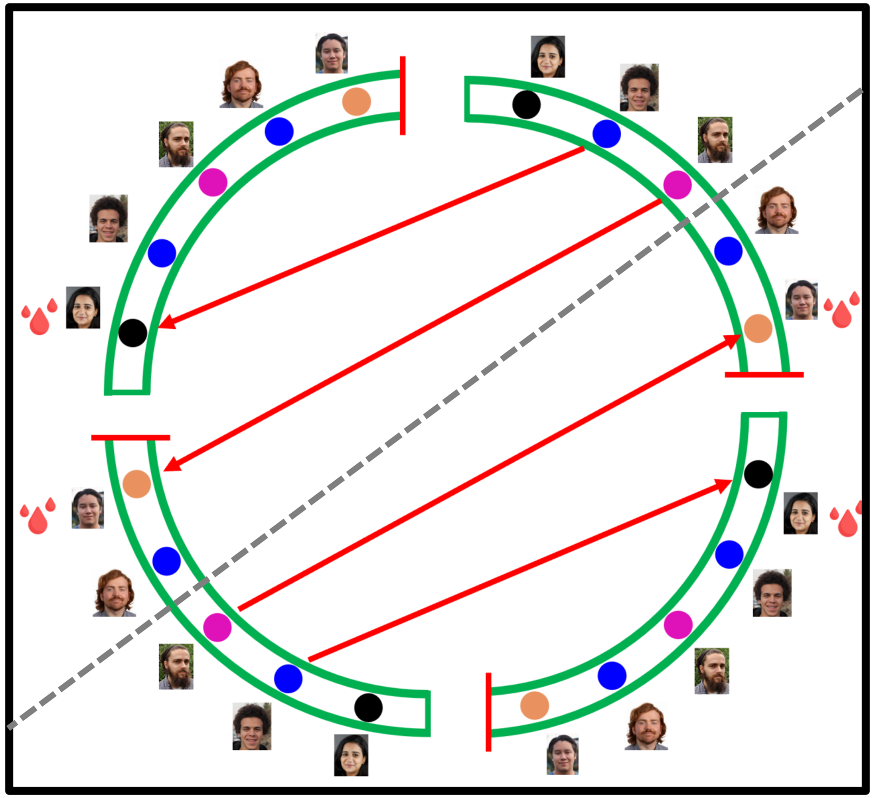
$R = 4$

Let's analyse this



$R = 1$

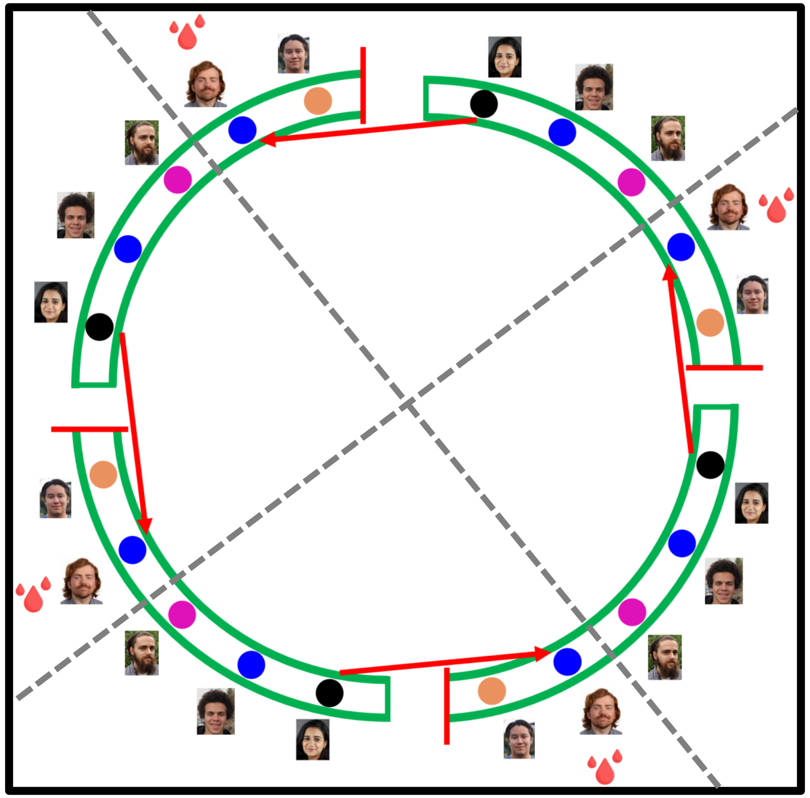
Doesn't penalize



Rotate by 180 degrees

$R = 2$

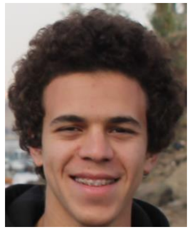
Penalize a little bit



Rotate by 90 degrees

$R = 4$

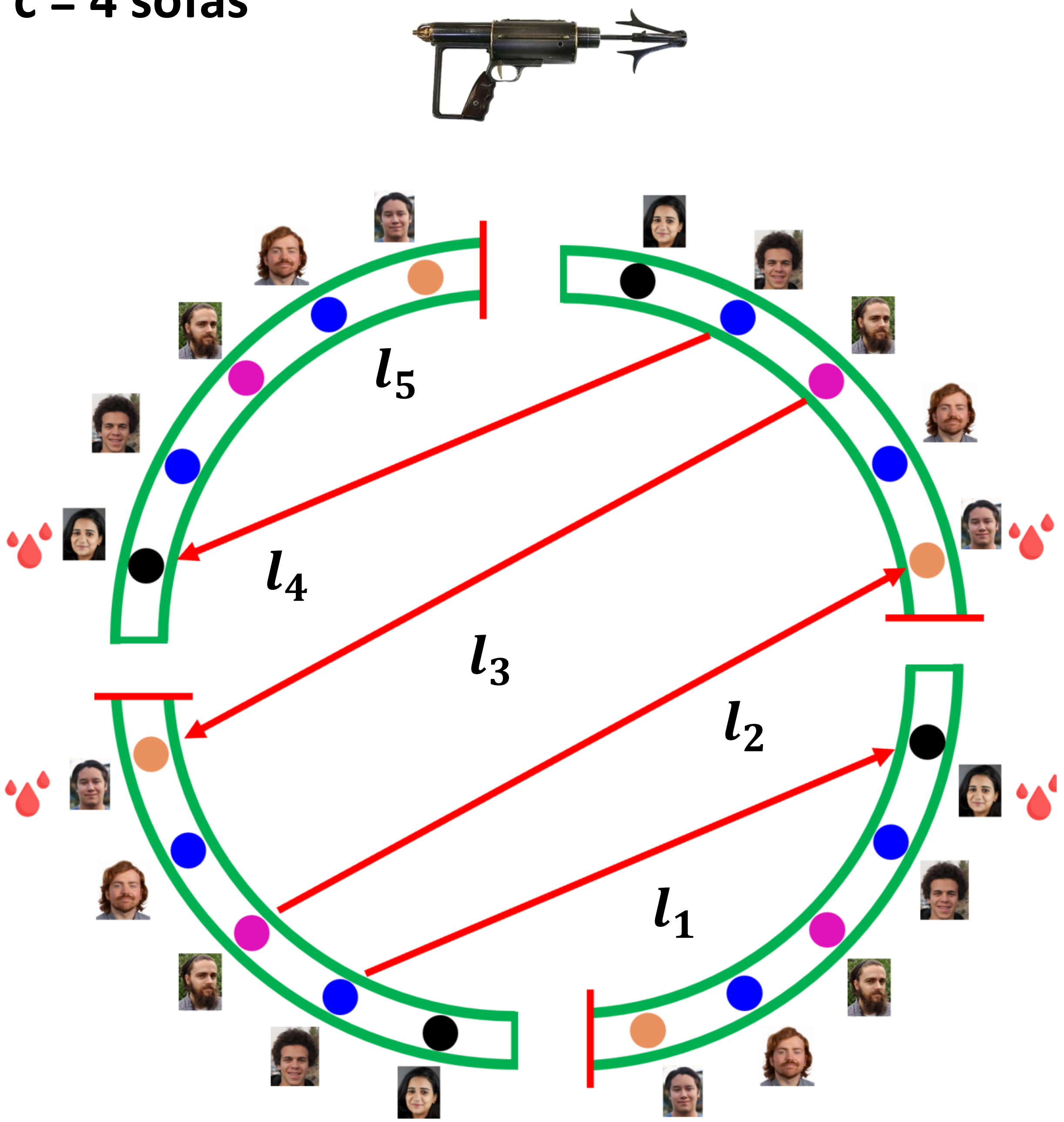
Penalize more



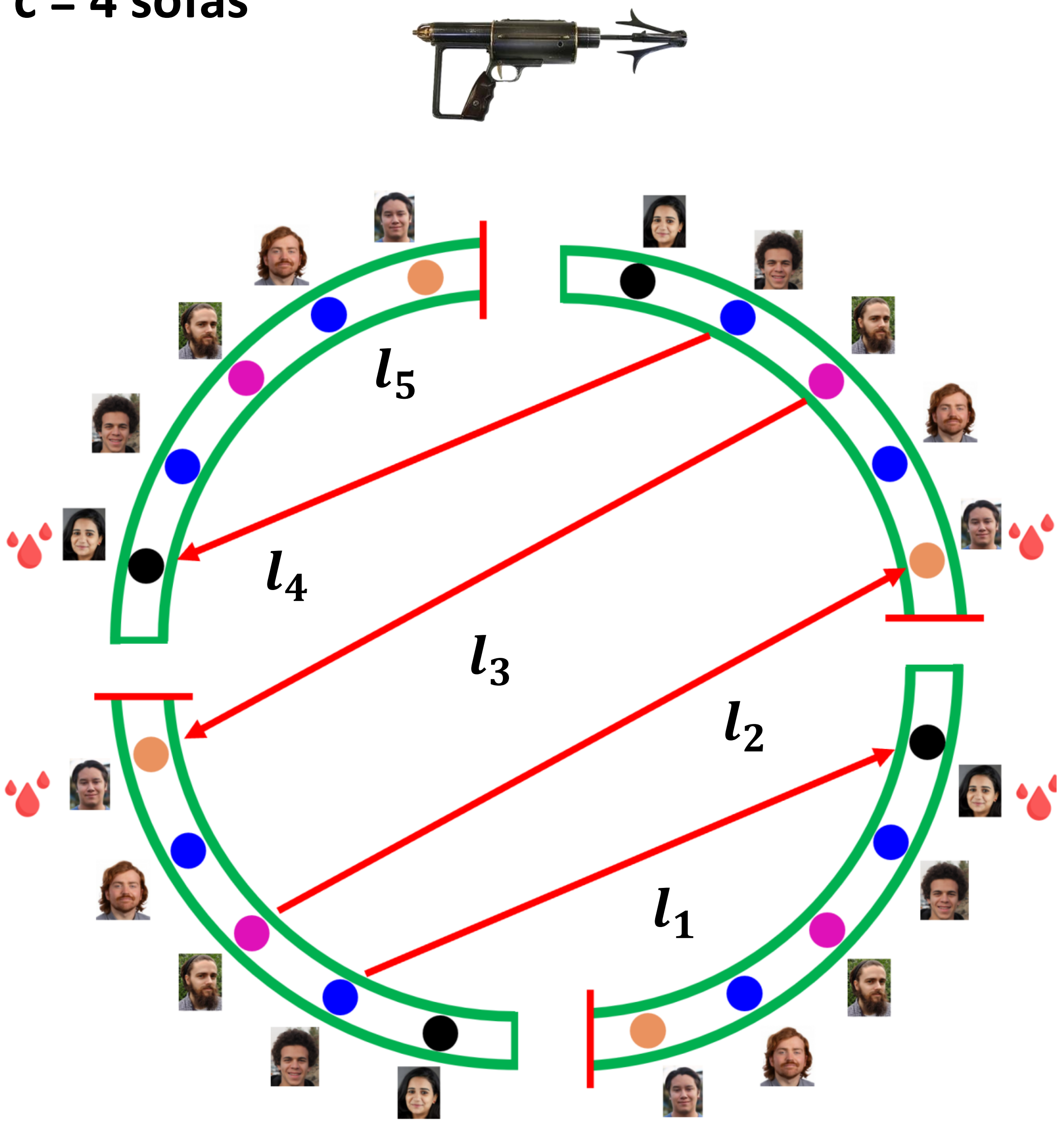
Ahmed's goal

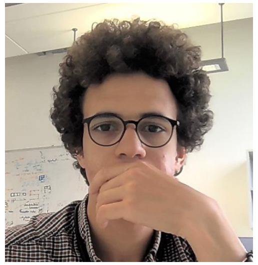
PI
Loves high quality blood
Loves mixed blood
Hates disconnectedness
Hates rotational symmetry

c = 4 sofas



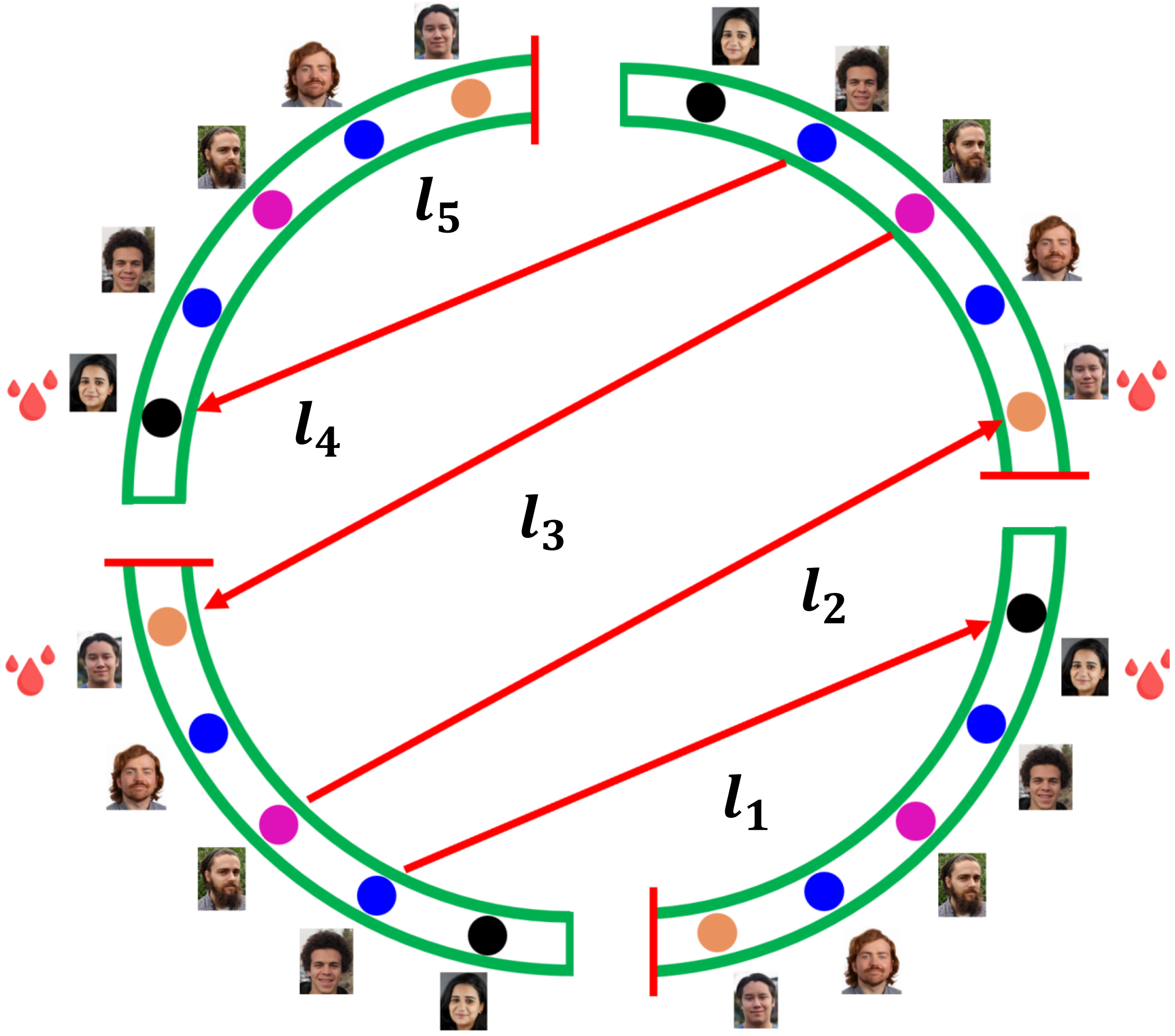
c = 4 sofas

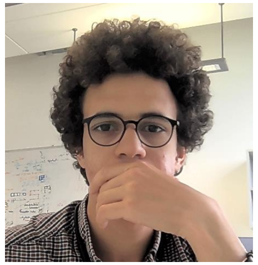




Some Criteria/Model ?

c = 4 sofas

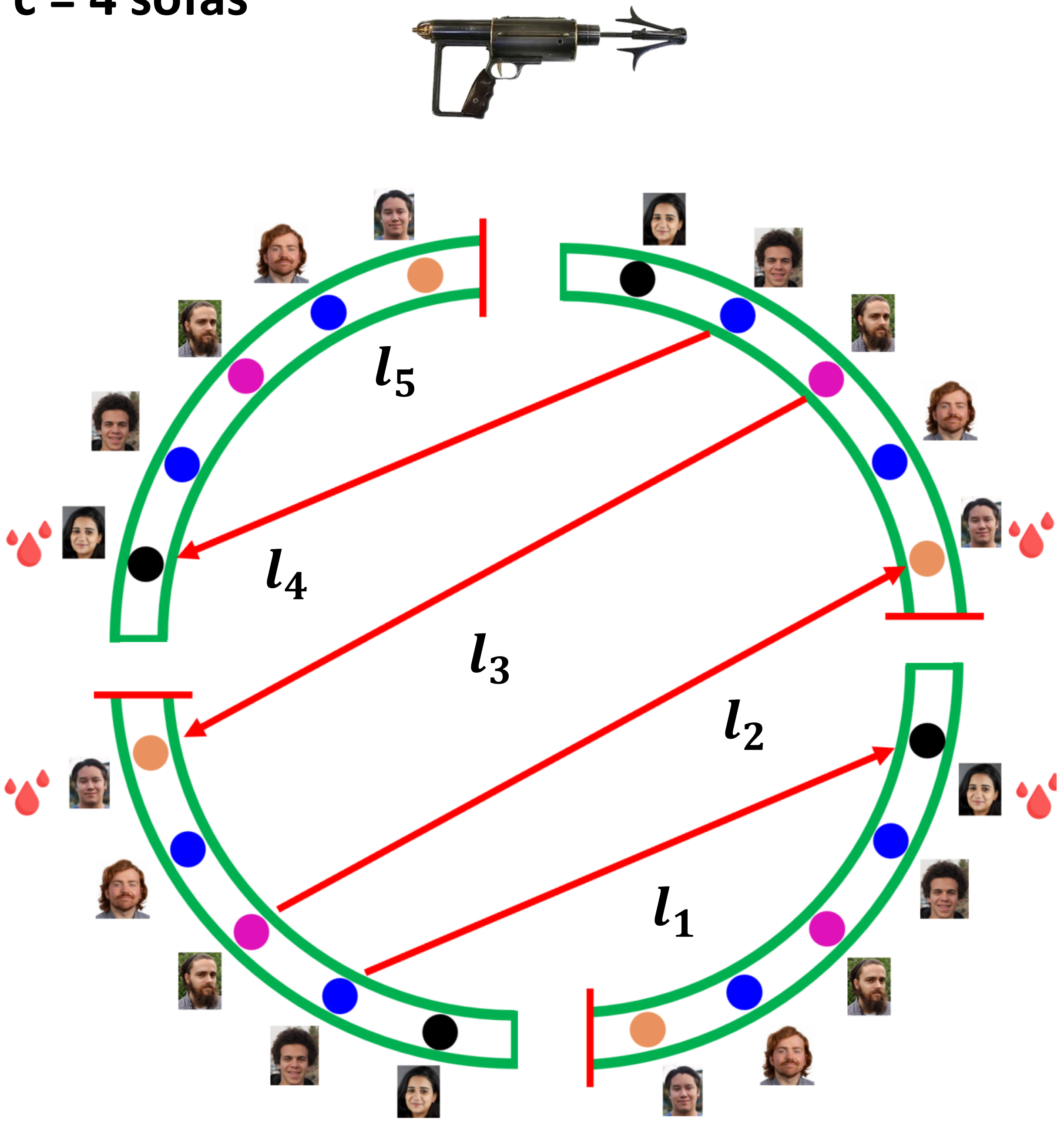


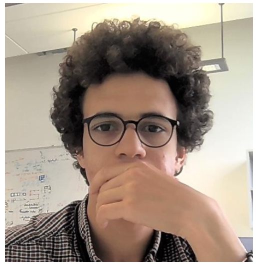


Some Criteria/Model ?

$$B(S) = \sum_{l} B(l) - (c-1)B^{\text{assoc}} - k_B T * \log R$$

c = 4 sofas





Some Criteria/Model ?

$$B(S) = \sum_{l} B(l) - (c-1)B^{\text{assoc}} - k_B T * \log R$$

$$\max_{S \in \Omega} B(S)$$

How to compute this fast?

We are done **Hamilton game**

Why

Why, Ahmed?

Hamilton game

First year

Daniel
Augustina
.
.
.

Second year

Ahmed
Andre
Paddy
Cormac
.
.

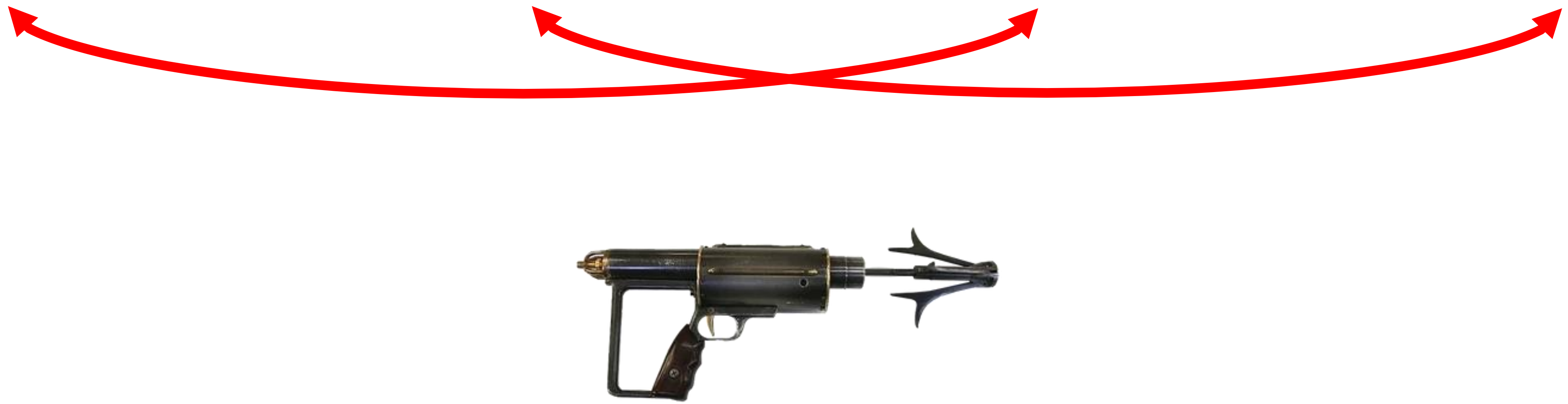
Third year

Dara
Solmaz
Oluwayomi
.
.
.

fourth year

Akash
Yc
Emma
Darshana
.
.

Hamilton game



Hamilton game

Hamilton game

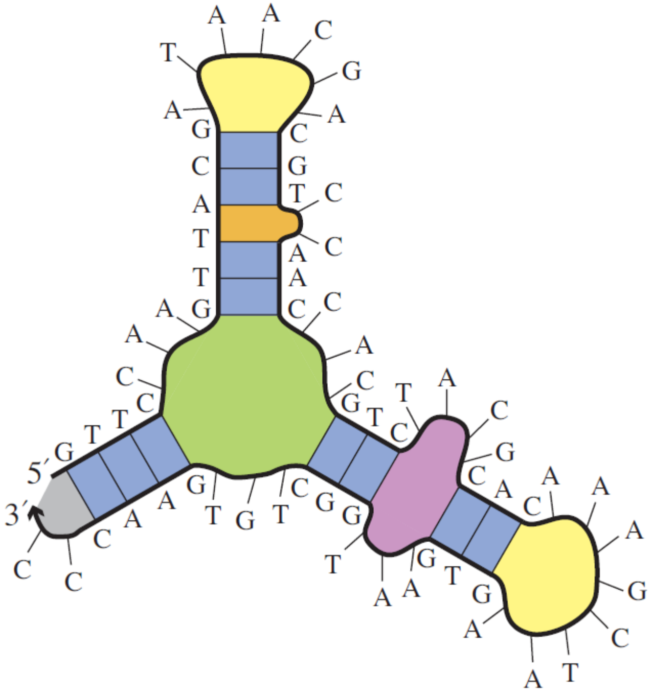
Chemical bonds

DNA secondary structures

Chemical bonds

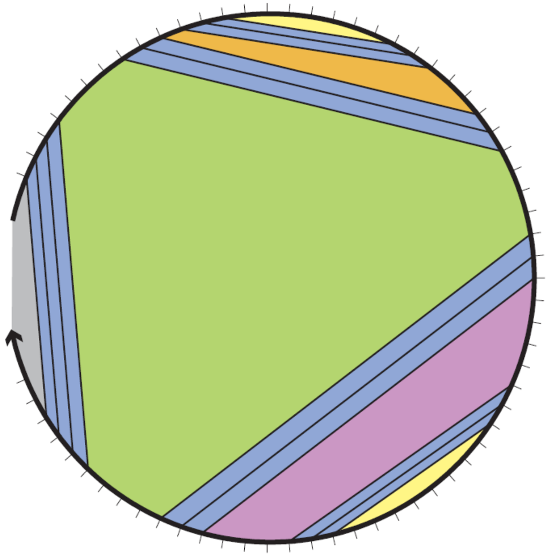
DNA secondary structure

Single stranded DNA



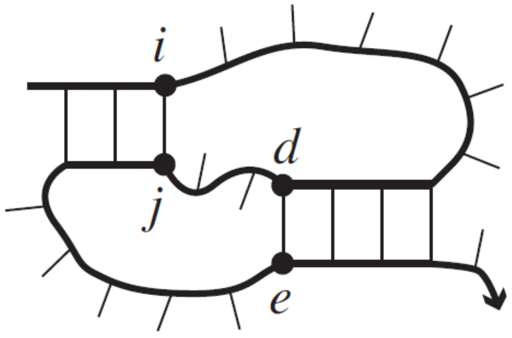
Secondary structure
=
A list of base pairs

pseudoknot-free

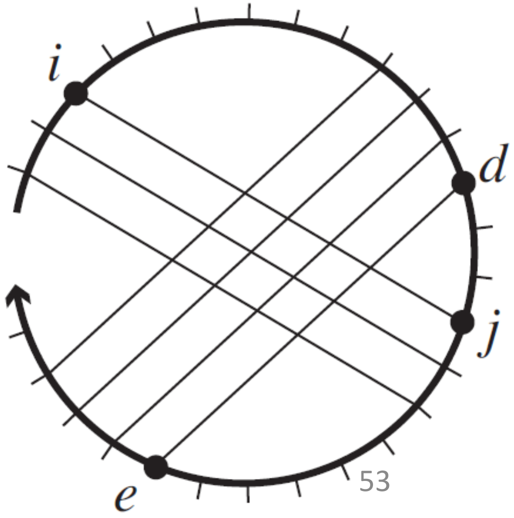


Polymer graph representation

NP – Hard

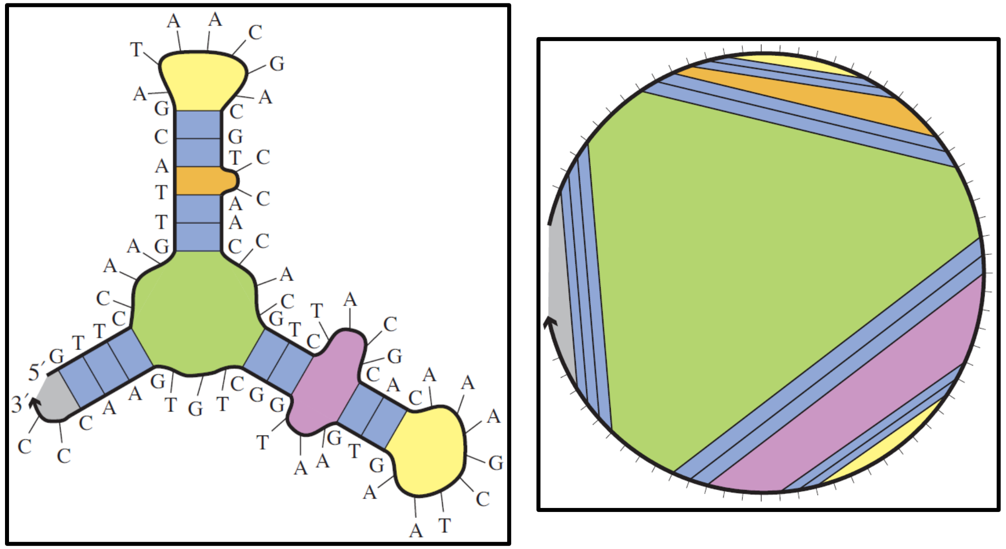


pseudoknotted

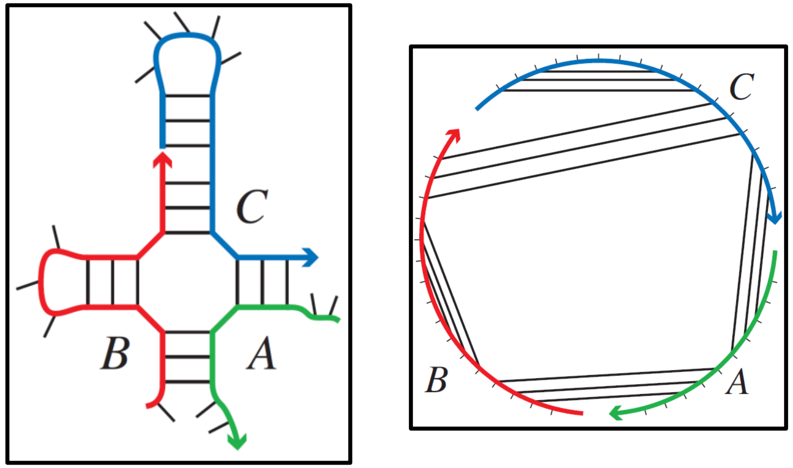


Energy models and Minimum Free Energy

Single stranded system

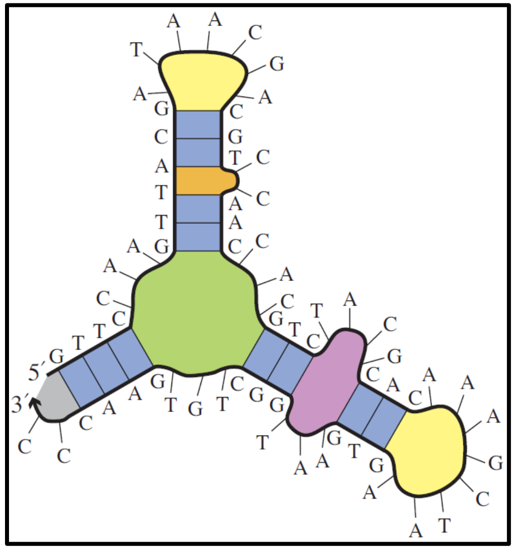


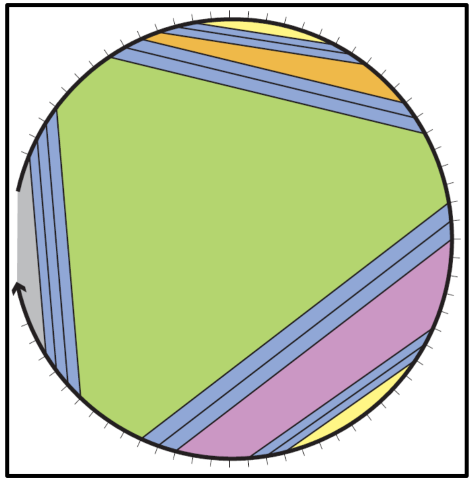
Multi stranded system of s strands



Energy models and Minimum Free Energy

Single stranded system



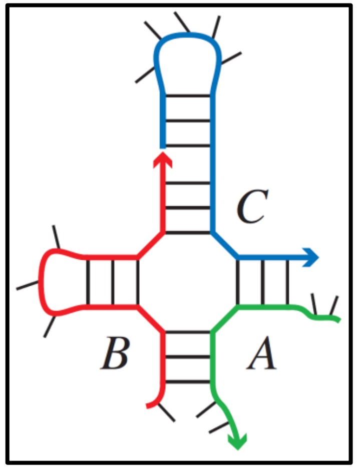


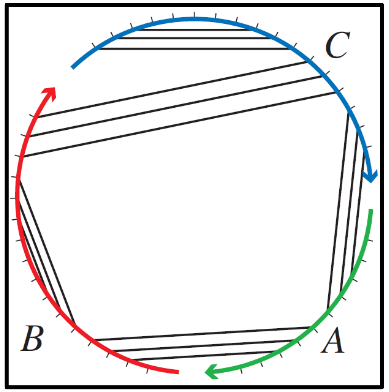
$$\Delta G(S)$$

Energy model

Capture the free energy of secondary structure

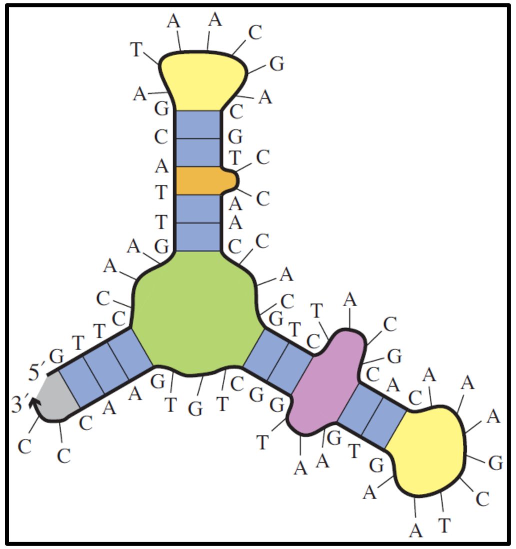
Multi stranded system of s strands

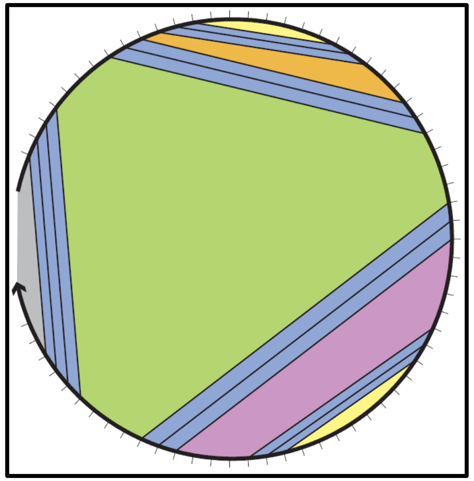




Energy models and Minimum Free Energy

Single stranded system



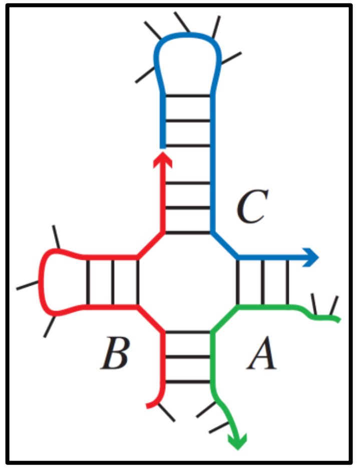


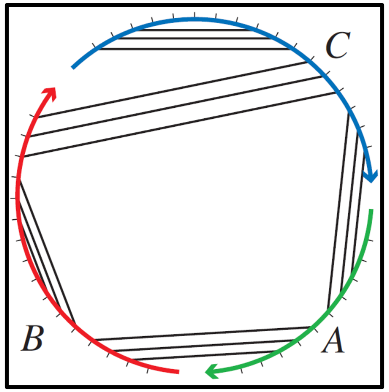
$\Delta G(S)$

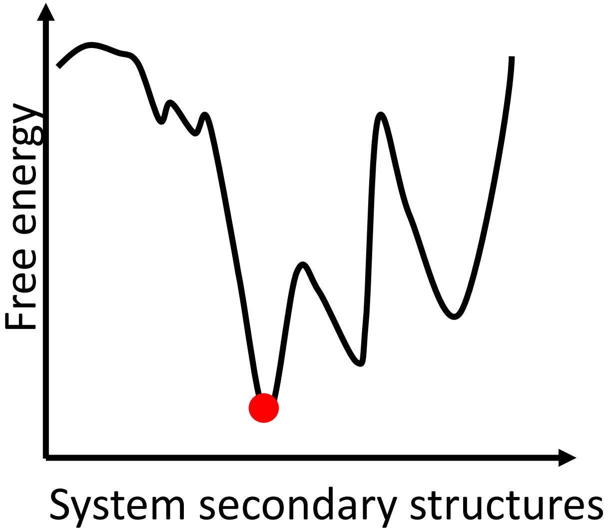
Energy model

Capture the free energy of secondary structure

Multi stranded system of s strands

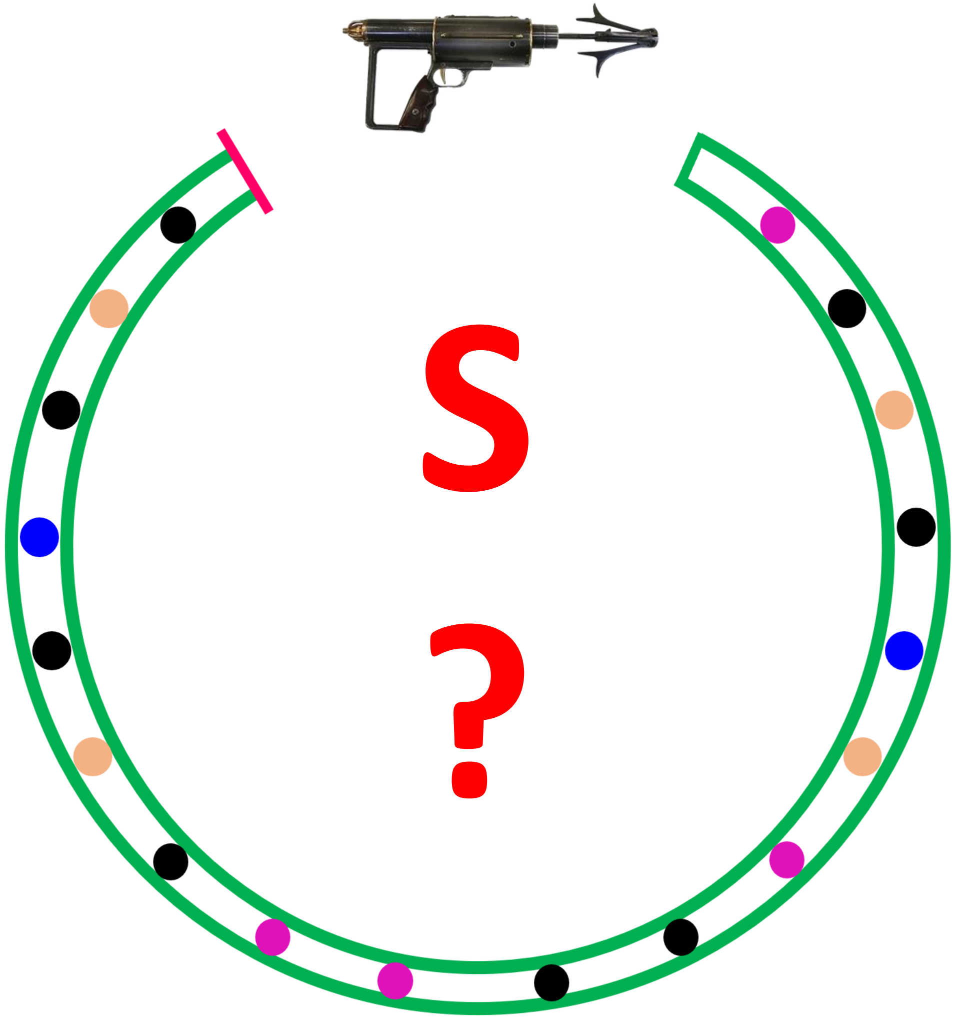






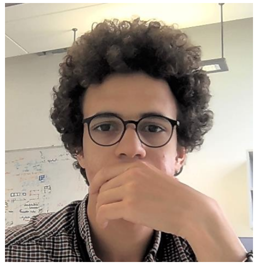
$$\text{MFE} = \min_{S \in \Omega} \Delta G(S)$$

Minimum Free Energy



That is so cool!

1



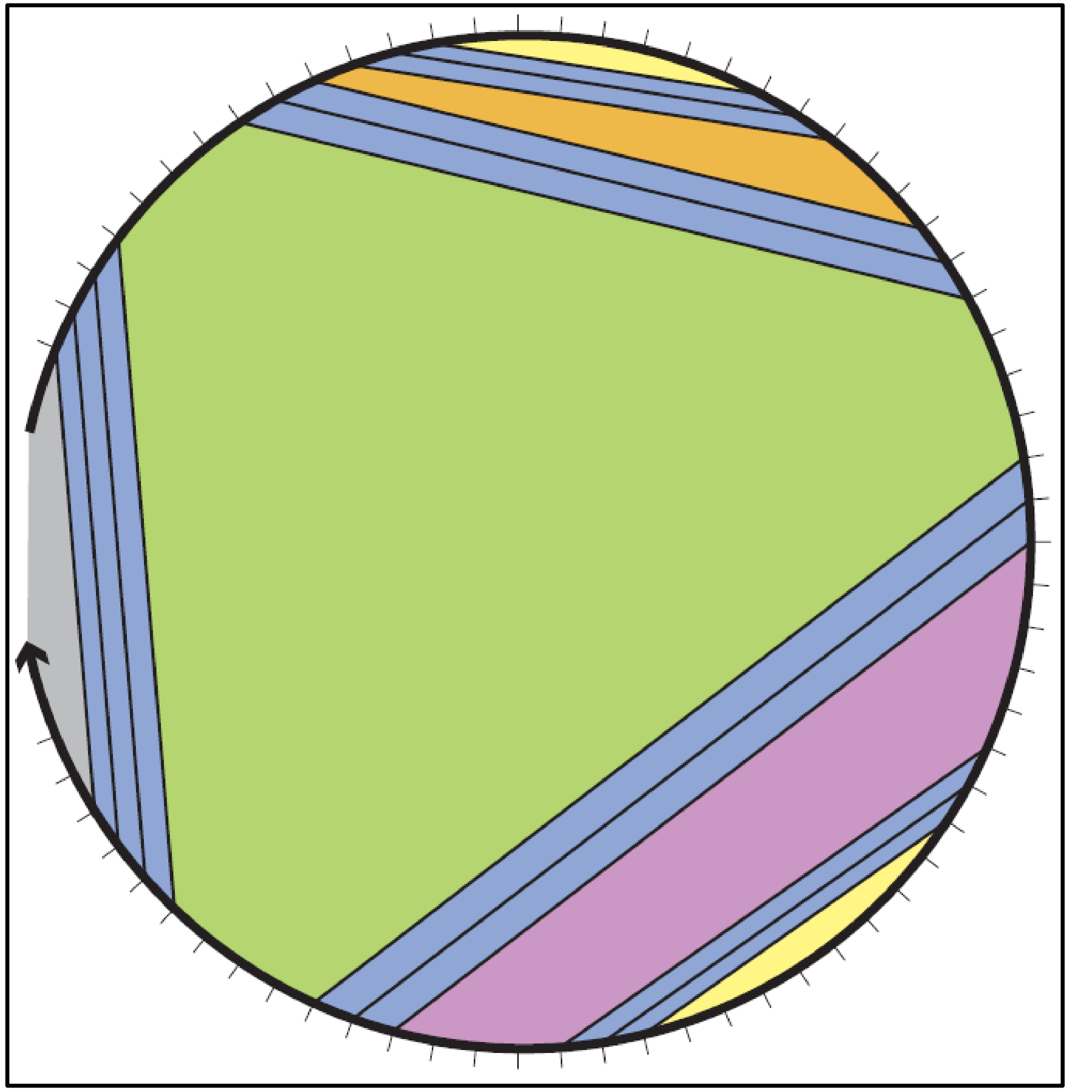
Some Criteria/Model ?

$$B(S) = \#\text{killed PhDs}$$

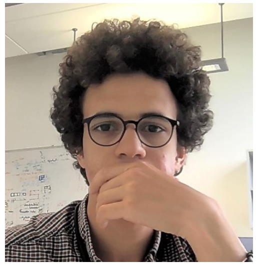
$$\max_{S \in \Omega} B(S)$$

Ω is the set of all possible structures that respect the game rules

How to compute this fast?



1



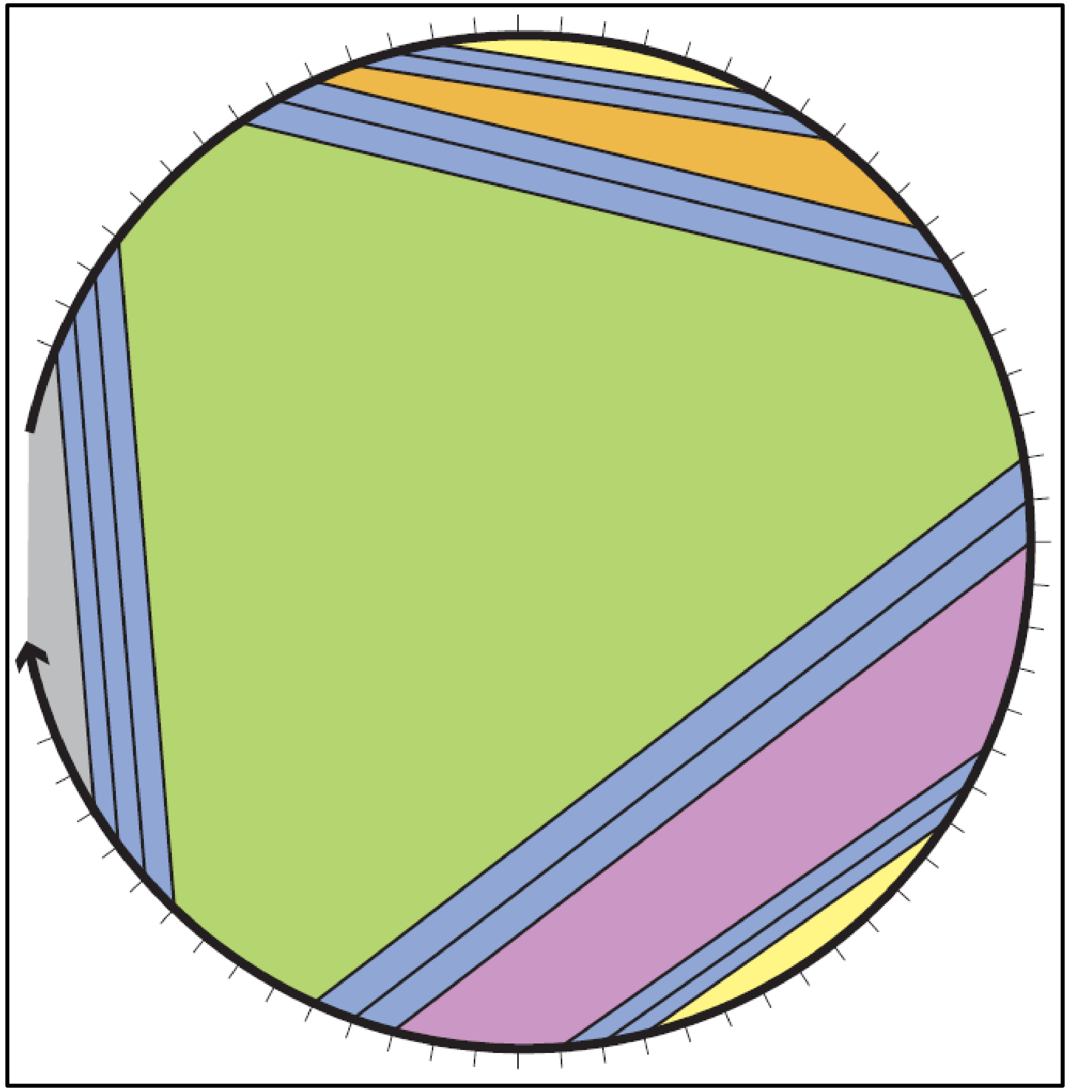
Some Criteria/Model ?

$$\Delta G(S) = -\#\text{base pairs}$$

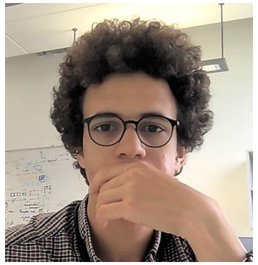
$$\min_{S \in \Omega} \Delta G(S)$$

Ω is the set of all possible structures that respect the game rules

How to compute this fast?



1



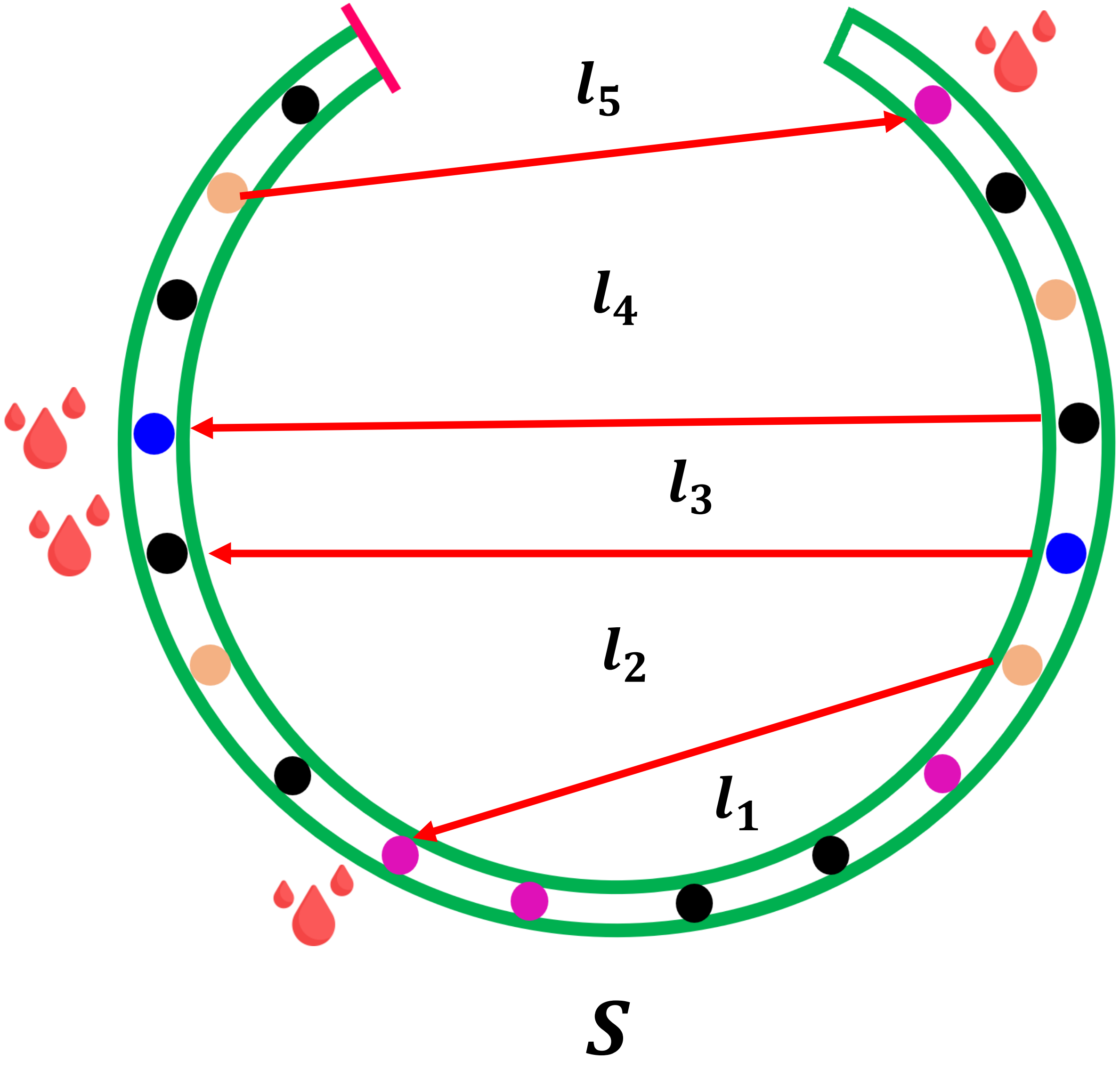
Some Criteria/Model?

$$\Delta G(S) = -\#\text{base pairs}$$

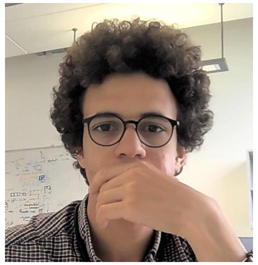
$$\min_{S \in \Omega} \Delta G(S)$$

Ω is the set of all possible structures that respect the game rules

How to compute this fast? **Yes**



2

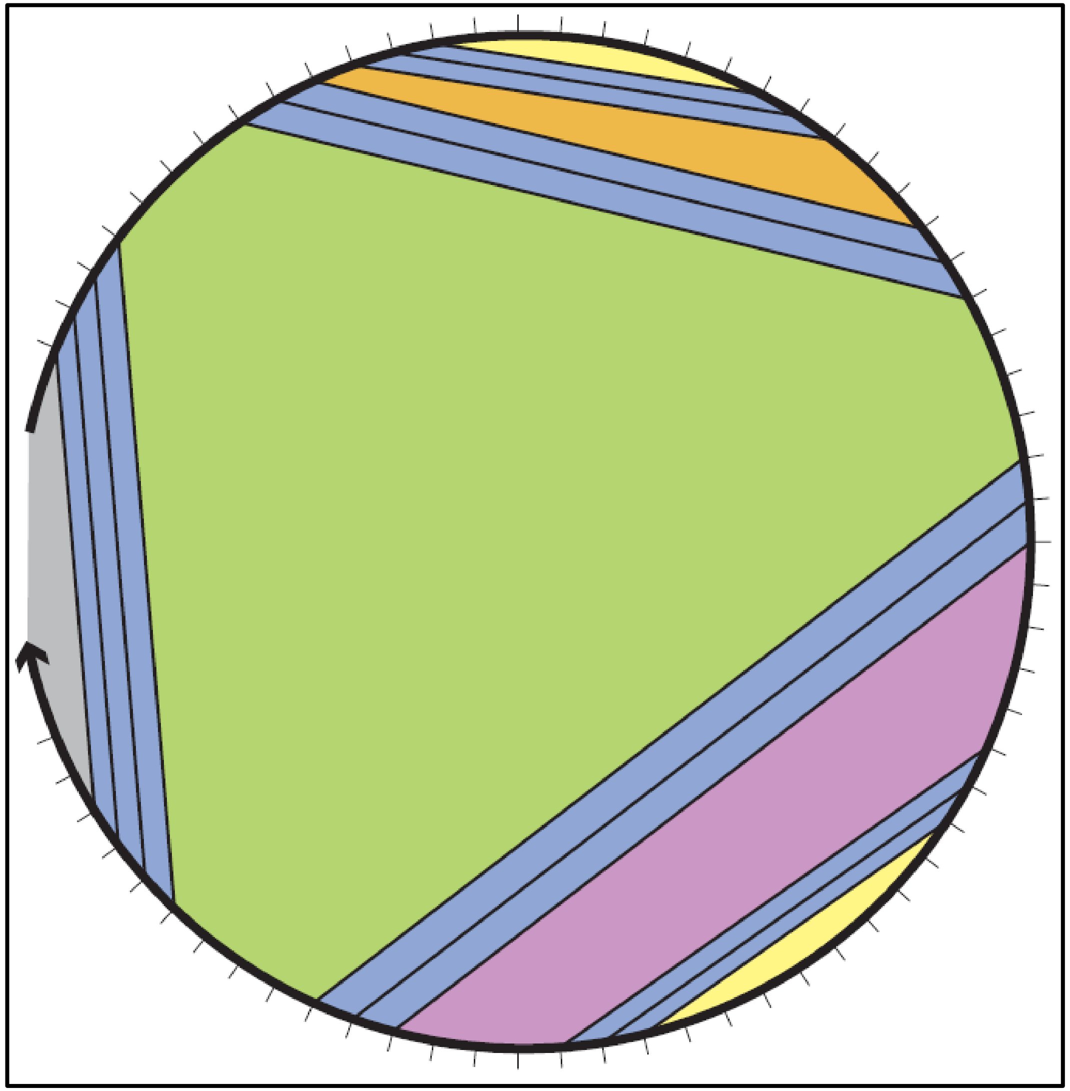


Some Criteria/Model ?

$$B(S) = \sum_{l} B(l)$$

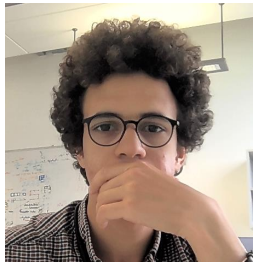
$$\max_{S \in \Omega} B(S)$$

How to compute this fast?



S

2

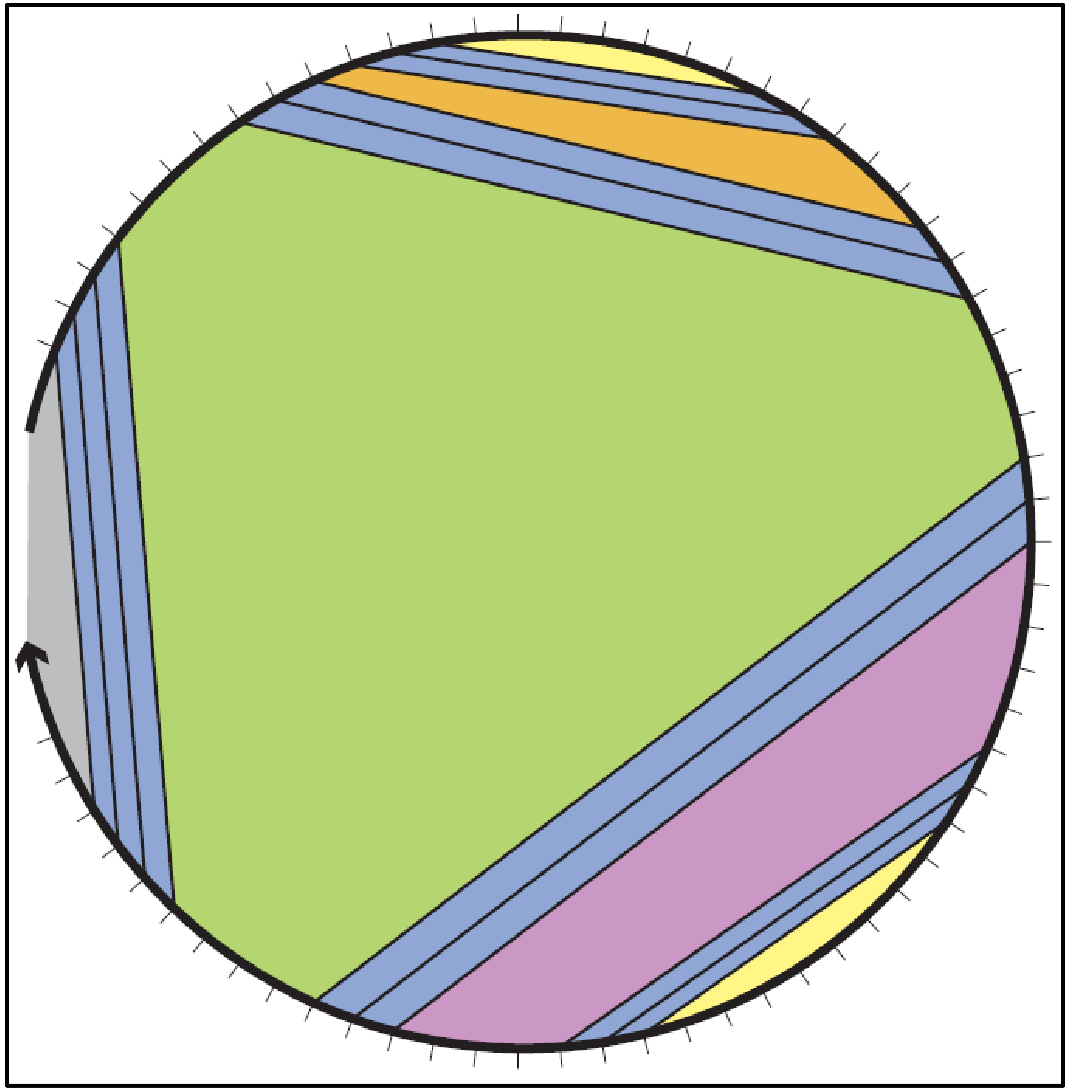


Some Criteria/Model ?

$$\Delta G(S) = \sum_{l} \Delta G(l)$$

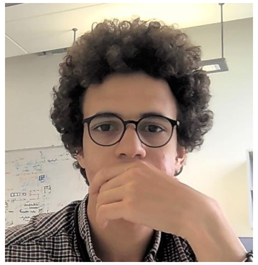
$$\min_{S \in \Omega} \Delta G(S)$$

How to compute this fast?



S

2



Some Criteria/Model ?

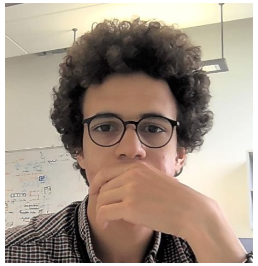
$$\Delta G(S) = \sum_{l} \Delta G(l)$$

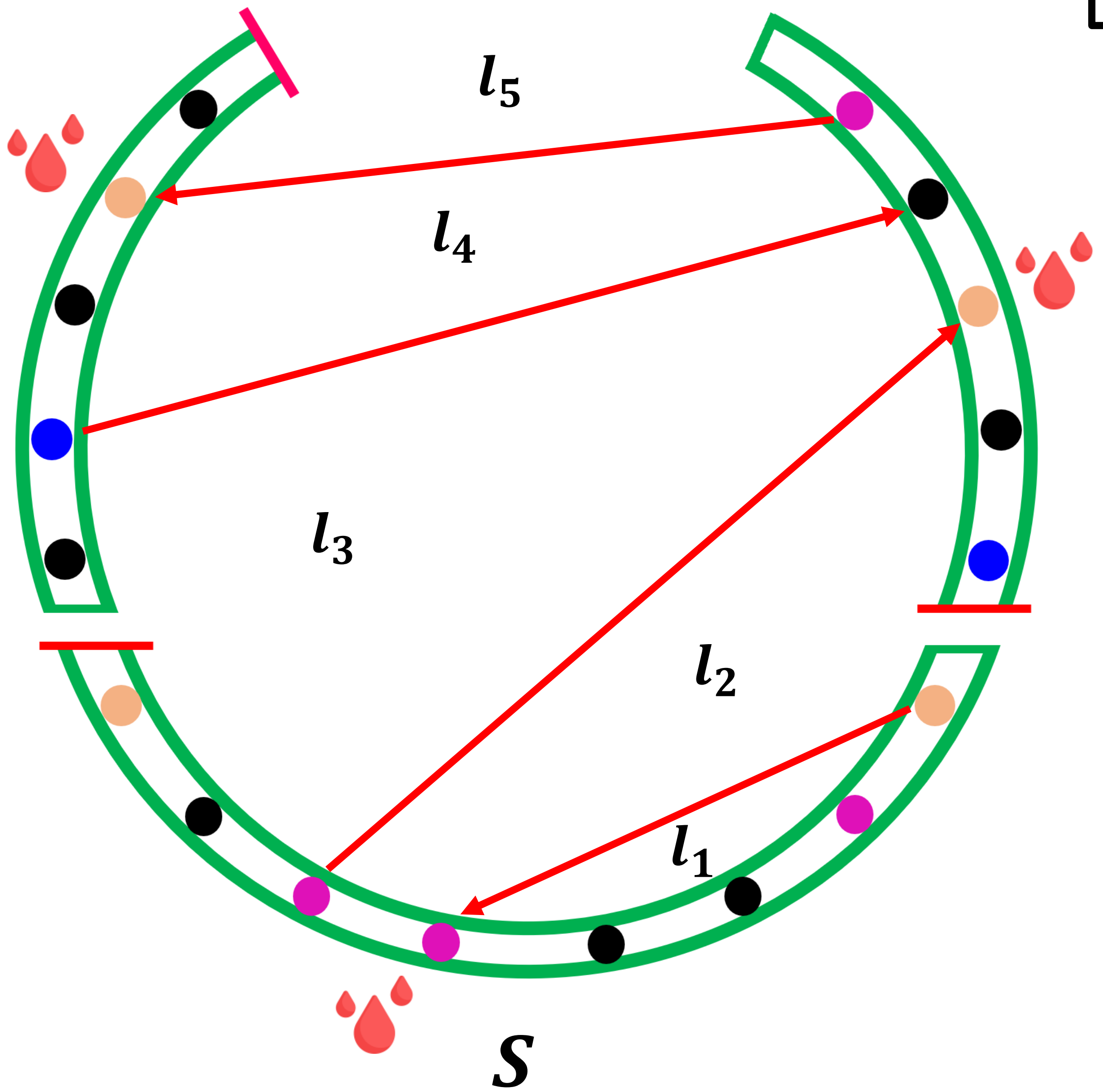
$$\min_{S \in \Omega} \Delta G(S)$$

How to compute this fast? Yes

c = 3 sofas

3





Some Criteria/Model ?

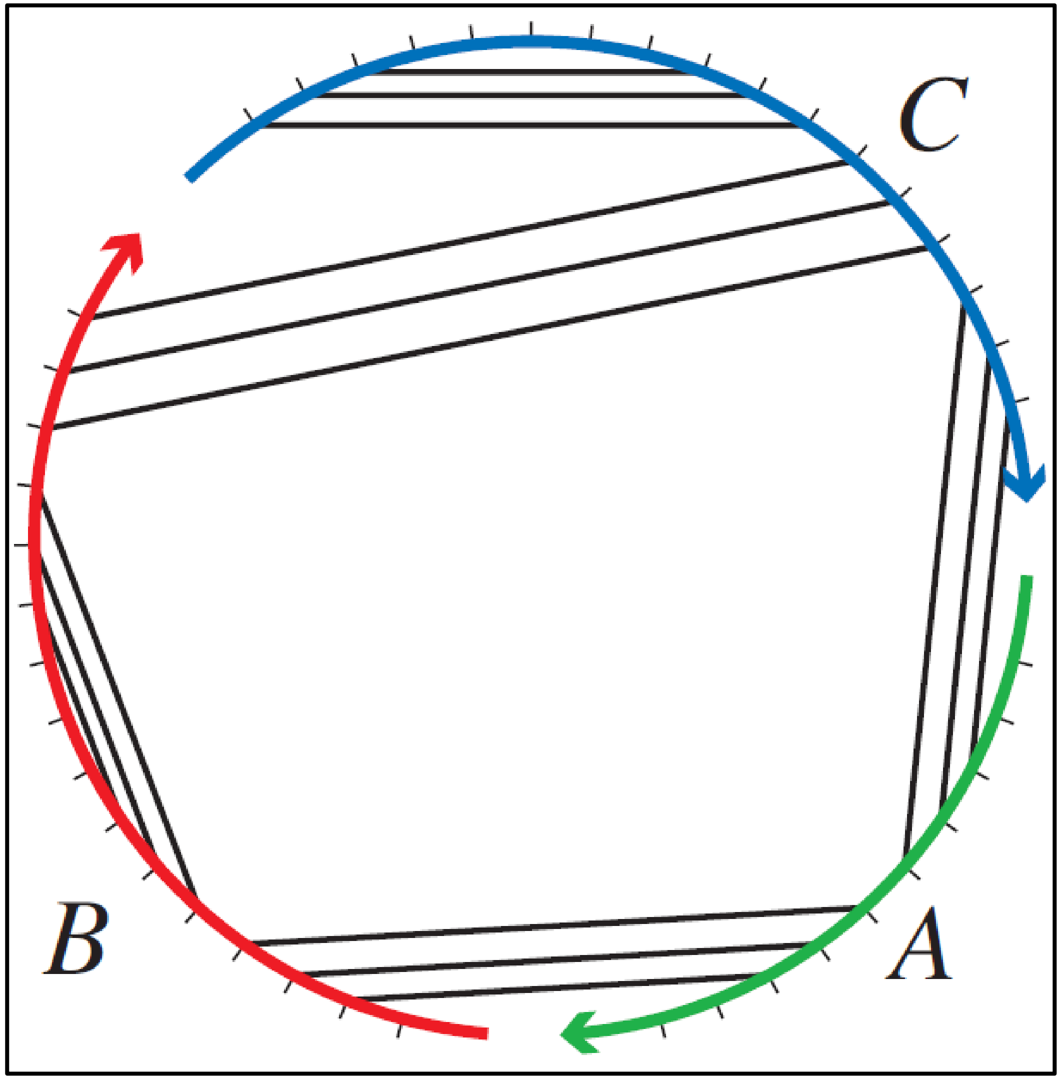
$$B(S) = \sum_{l} B(l) - (c-1)\, B^{\text{assoc}}$$

$$\max_{S \in \Omega} B(S)$$

Ω: the set of all connected structures that respect the game rules

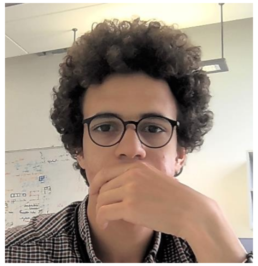
How to compute this fast?

c = 3 strands



S

3



Some Criteria/Model ?

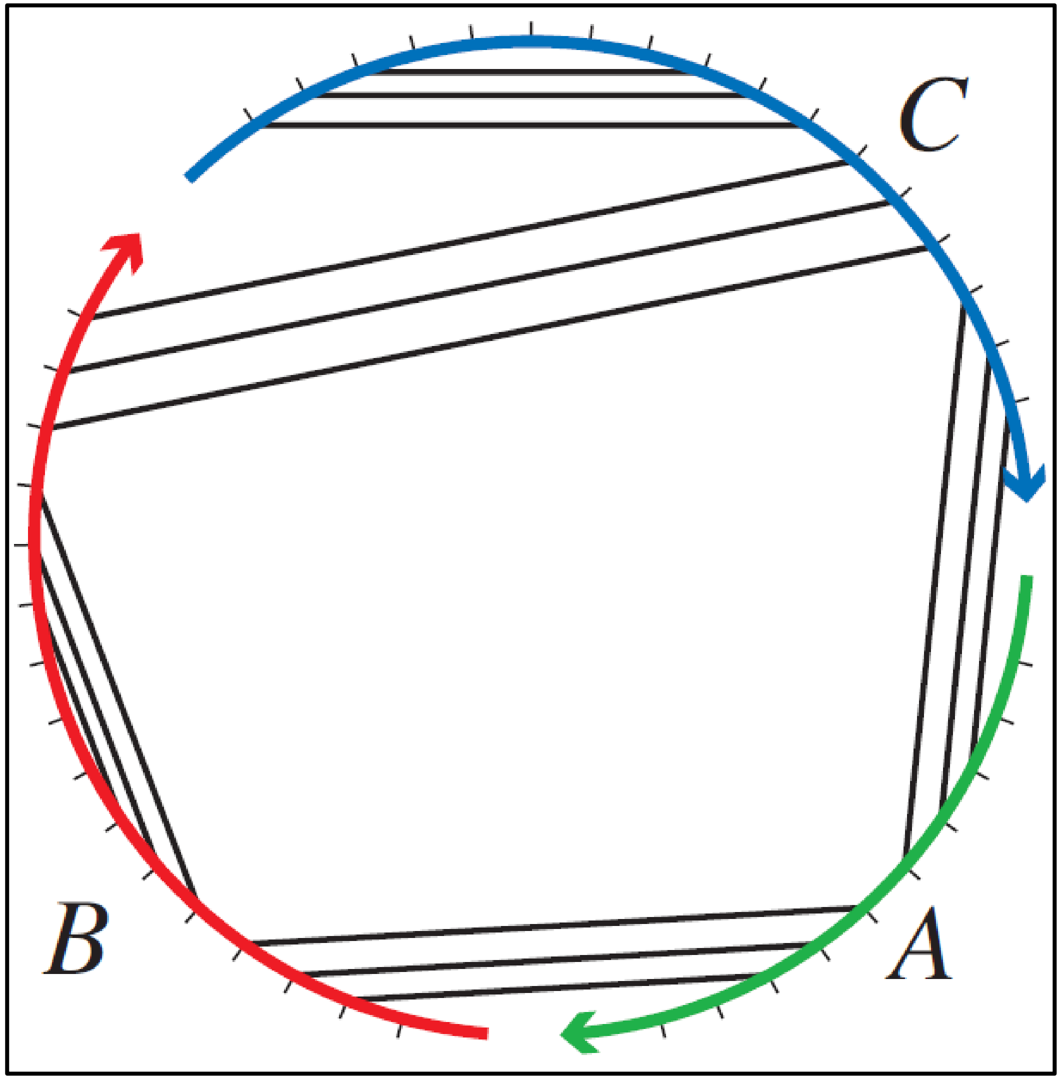
$$\Delta G(S) = \sum_{l} \Delta G(l) + (c-1)\,\Delta G^{\text{assoc}}$$

$$\min_{S \in \Omega} \Delta G(S)$$

Ω: the set of all connected structures that respect the game rules

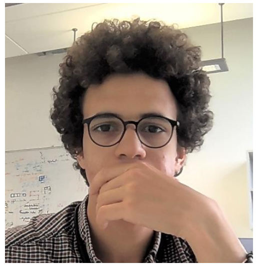
How to compute this fast?

c = 3 strands



S

3



Some Criteria/Model ?

$$\Delta G(S) = \sum_{l} \Delta G(l) + (c-1)\,\Delta G^{\mathrm{assoc}}$$

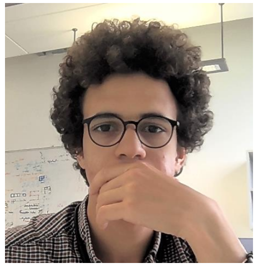
$$\min_{S\in\Omega} \Delta G(S)$$

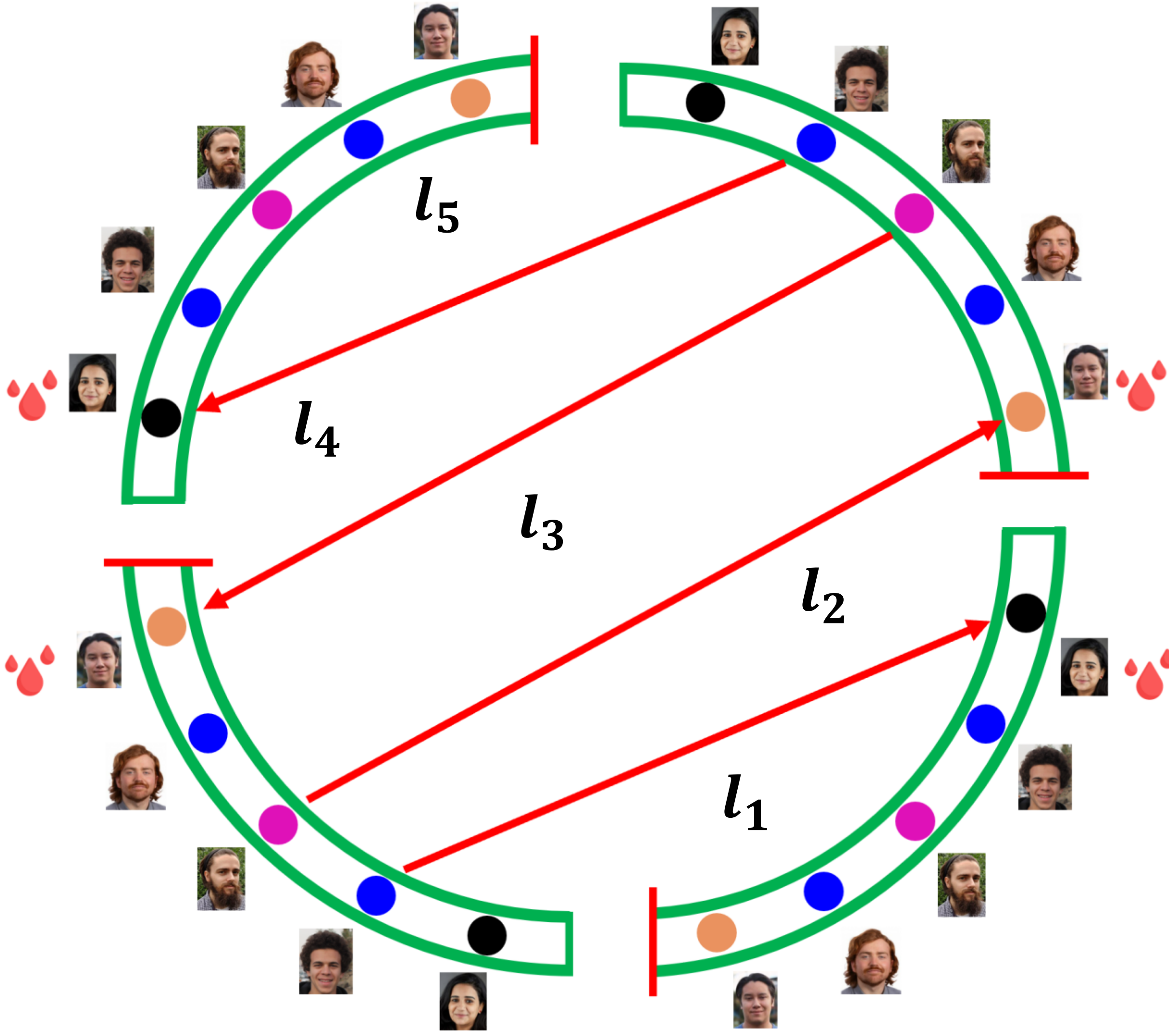
Ω: the set of all connected structures that respect the game rules

How to compute this fast? Yes

c = 4 sofas

4





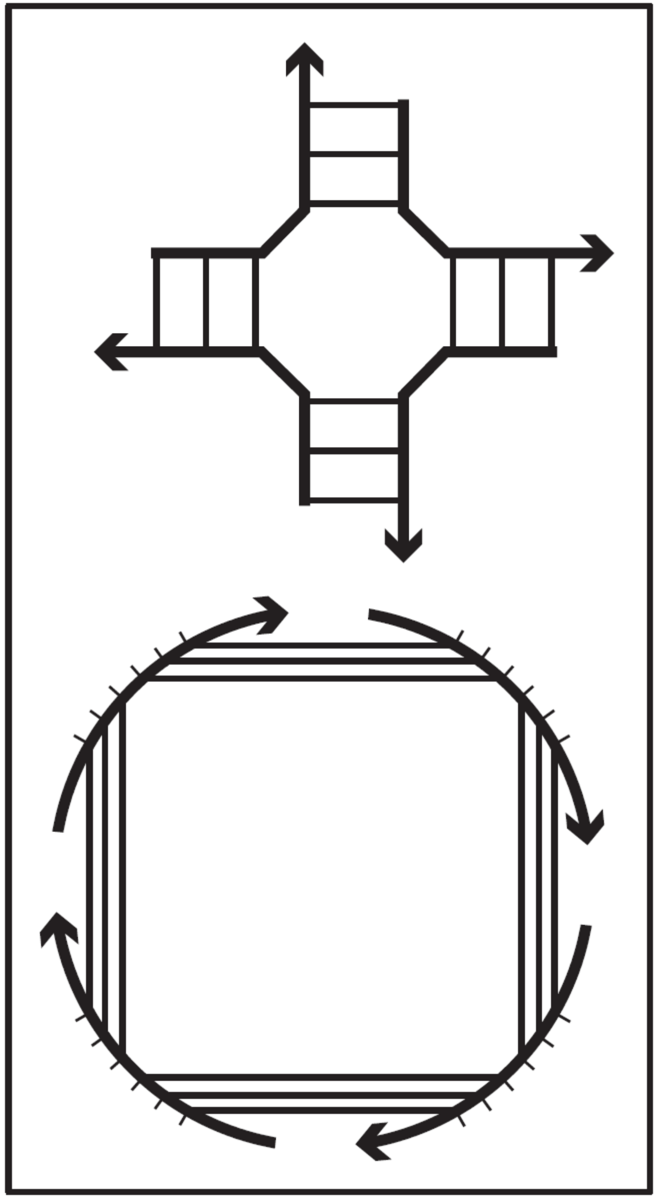
Some Criteria/Model ?

$$B(S) = \sum_{l} B(l) - (c-1)B^{\text{assoc}} - k_B T * \log R$$

$$\max_{S \in \Omega} B(S)$$

How to compute this fast?

c = 4 strands



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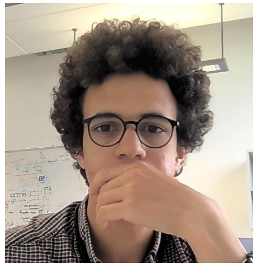


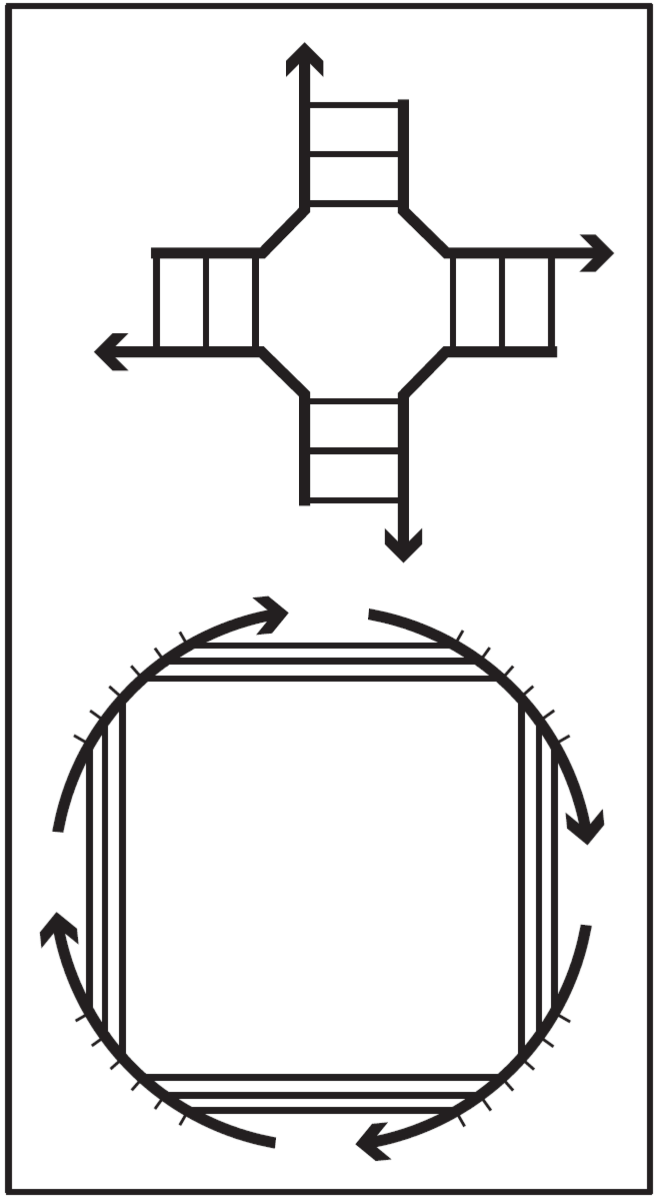
Some Criteria/Model ?

$$\Delta G(S) = \sum_{l} \Delta G(l) + (c-1)\Delta G^{\text{assoc}} + k_B T * \log R$$

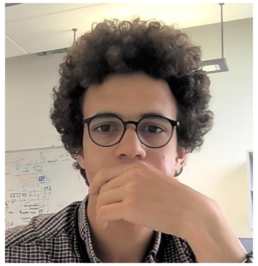
$$\min_{S \in \Omega} \Delta G(S)$$

How to compute this fast?

c = 4 strands



4



Some Criteria/Model ?

$$\Delta G(S) = \sum_{l} \Delta \mathrm{G}(l) + (c-1)\Delta G^{\mathrm{assoc}} + k_B T * \log R$$

$$\min_{S \in \Omega} \Delta G(S)$$

How to compute this fast?

No, till now

Free energy   Loop energy   Entropic association cost   Symmetry penalty

$$\Delta G(S) = \sum_{l \in S} \Delta G(l) + (c-1) * \Delta G^{\text{assoc}} + k_B T * \log R$$

− + +

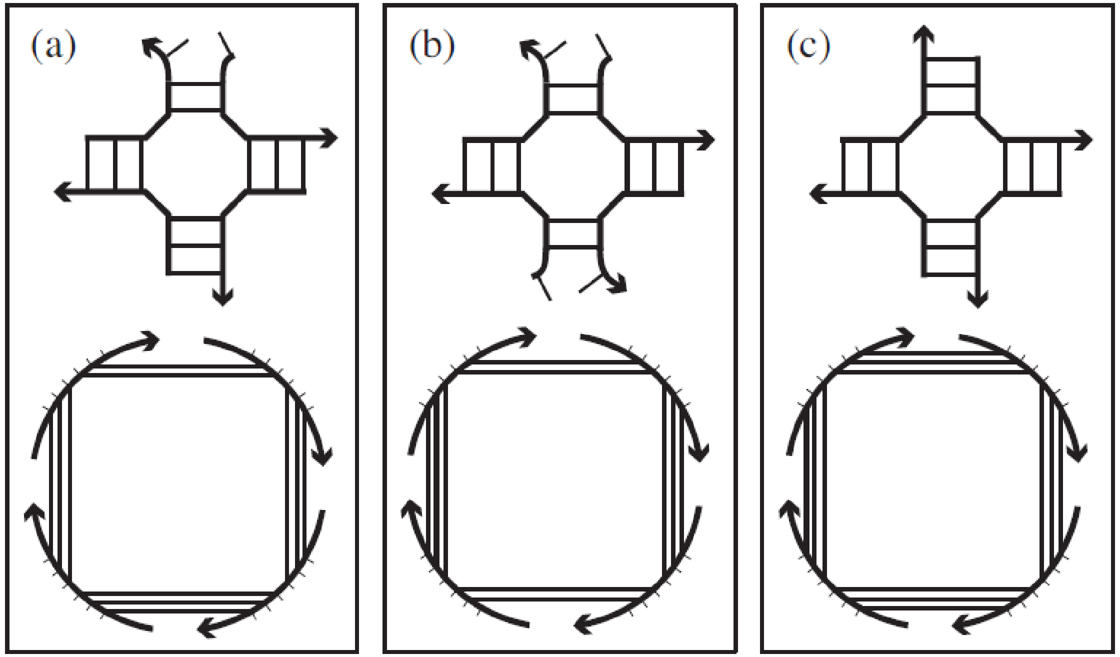


Fig. 2.2 *Sample secondary structures and polymer graphs for a complex of four indistinguishable strands.* (a) *1-fold (i.e., no) rotational symmetry.* (b) *2-fold rotational symmetry.* (c) *4-fold rotational symmetry.*

Computational complexity of Minimum Free Energy algorithms

Level	Input Type	MFE
1	Single Strand (Maximum matching)	$O(N^3)$
2	Single Strand (Loop model)	$O(N^3)$
3	Multiple **unique** Strands, Bounded ($\leq$ c)	$O(N^3(\mathrm{c}-1)!)$
4	Multiple Strands, Bounded ($\leq$ c)	?

N bases, c strands

Computational complexity of Minimum Free Energy algorithms

Level	Input Type	MFE
1	Single Strand (Maximum matching)	$O(N^3)$
2	Single Strand (Loop model)	$O(N^3)$
3	Multiple **unique** Strands, Bounded ($\leq$ c)	$O(N^3(c-1)!)$
4	Multiple Strands, Bounded ($\leq$ c)	?

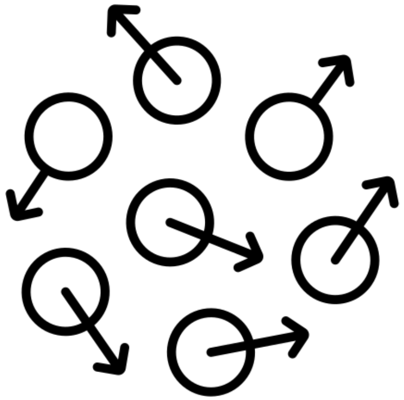
N bases, c strands

Open problem for $\approx$ 20 years

Why symmetry makes that difference?

Why symmetry makes that difference?

Entropy



$$\Delta G$$

Free energy

ΔG

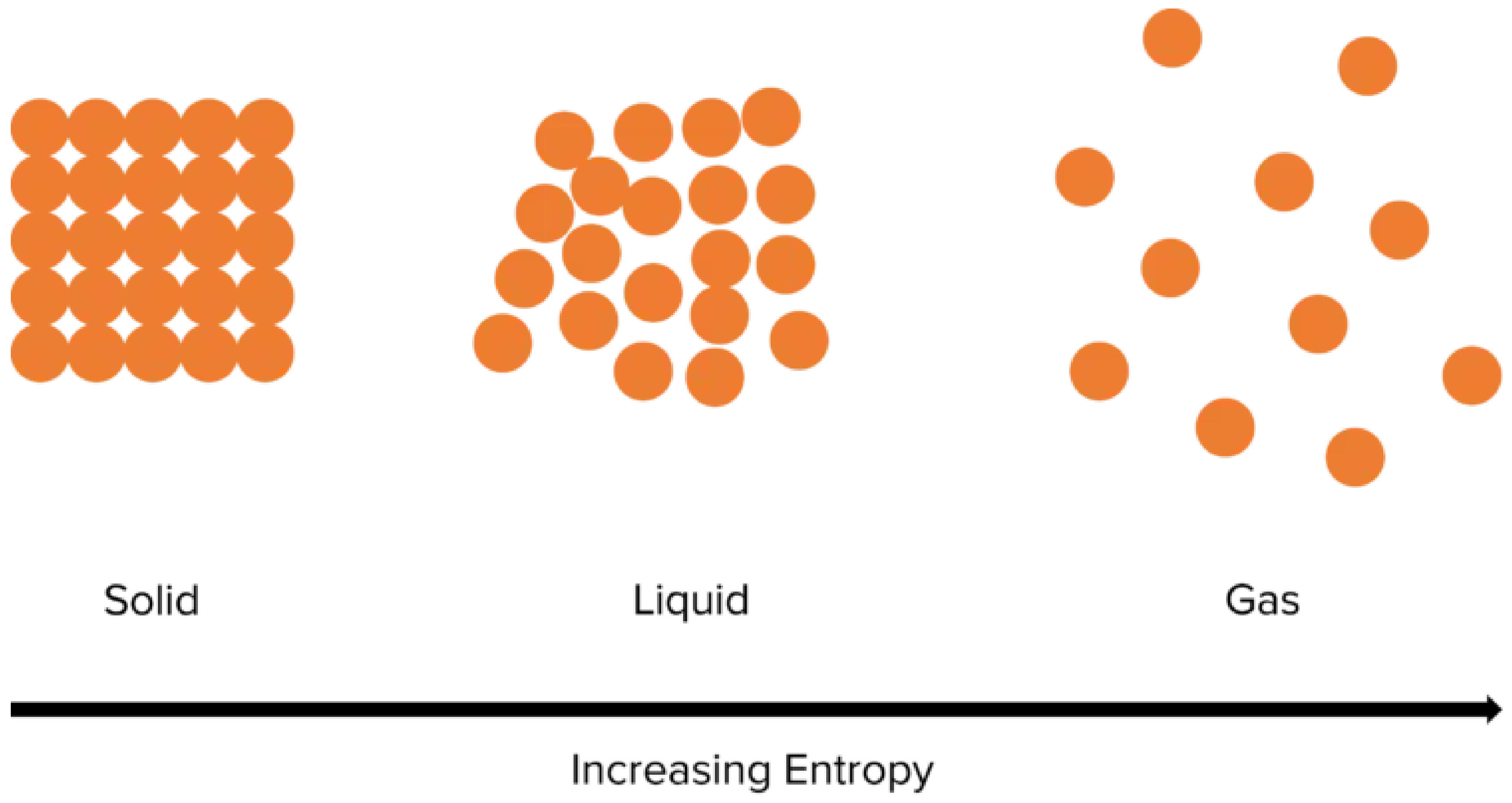
Free energy

Enthalpy

H

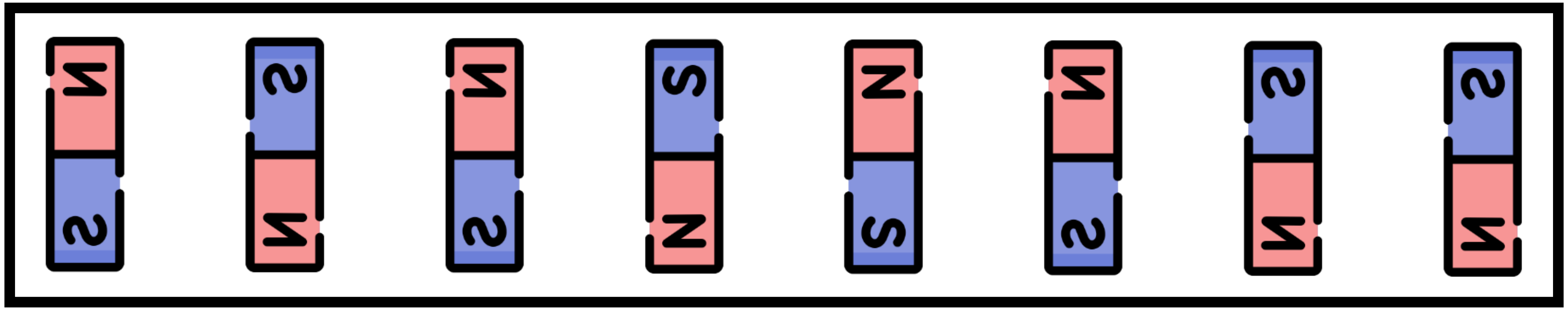
Entropy

S


Solid
Liquid
Gas
Increasing Entropy

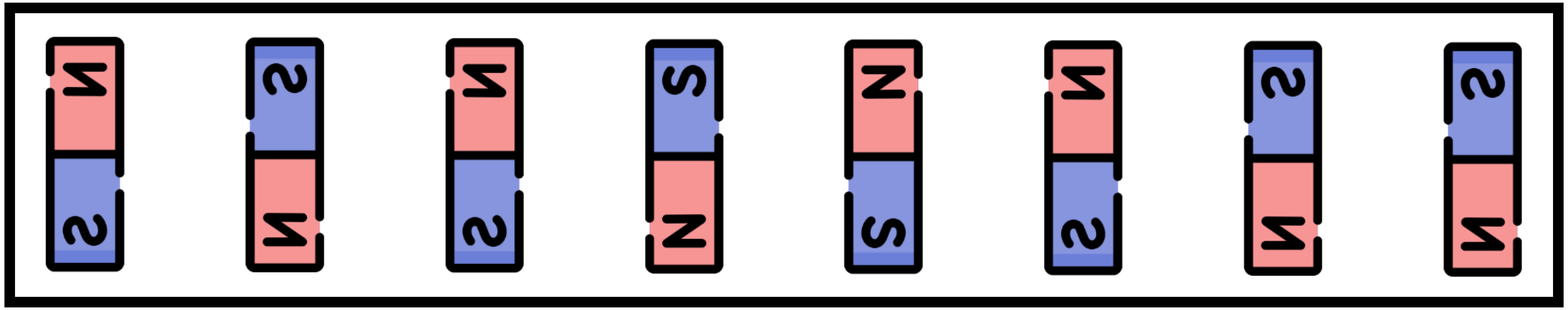
$$S = k_B \log \Pi$$

N



$$S = k_B \log \Pi$$

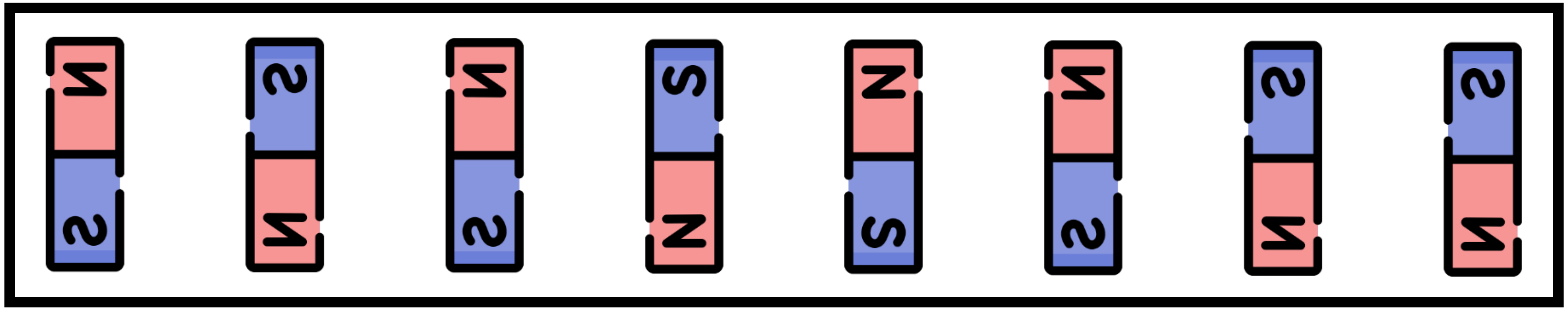
N



The total number of states of the N magnets is $\Pi = 2^N$

$$S = k_B \log \Pi$$

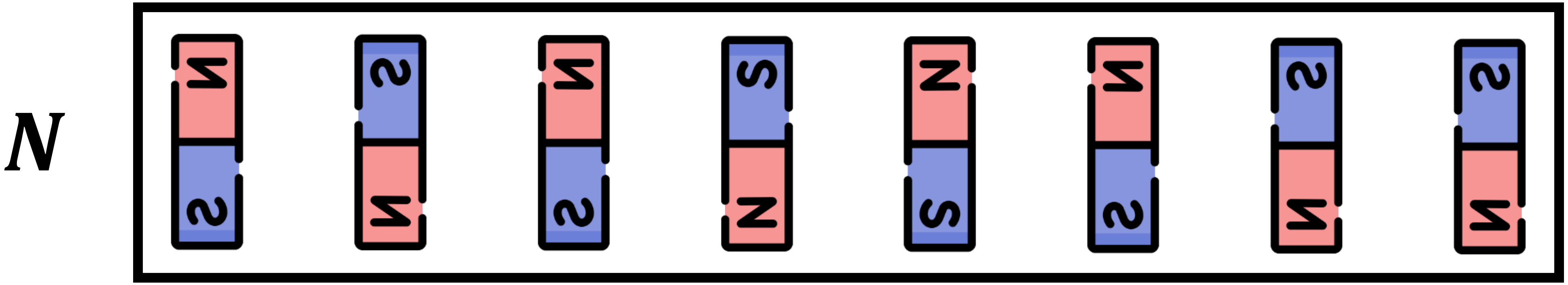
N



The total number of states of the N magnets is $\Pi = 2^N$

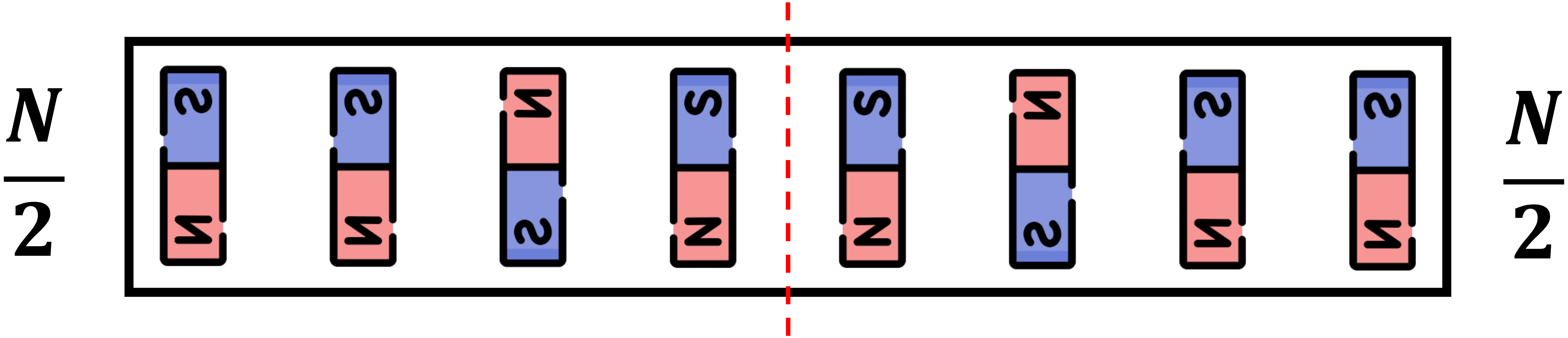
$$S = k_B N \log 2$$

$$S = k_B \log \Pi$$



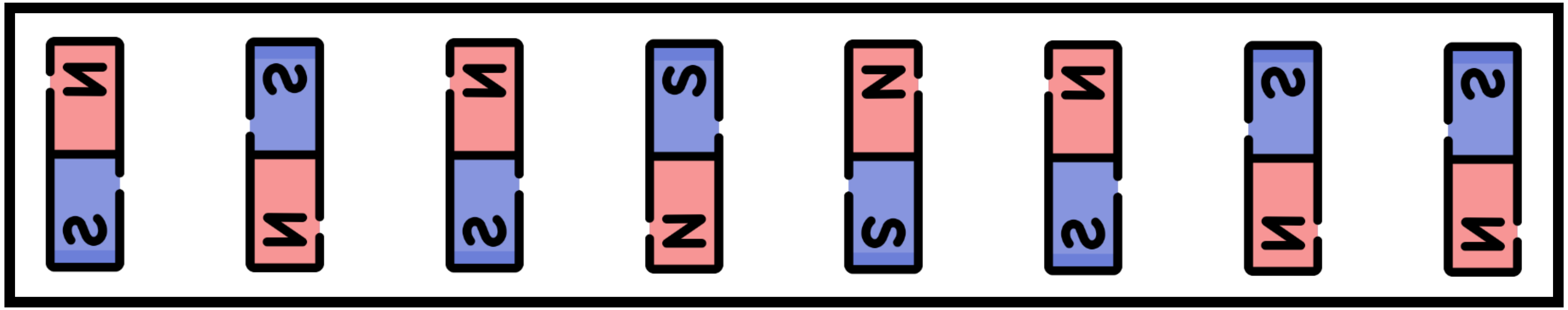
The total number of states of the N magnets is $\Pi = 2^N$

$$S = k_B N \log 2$$



$$S = k_B \log \Pi$$

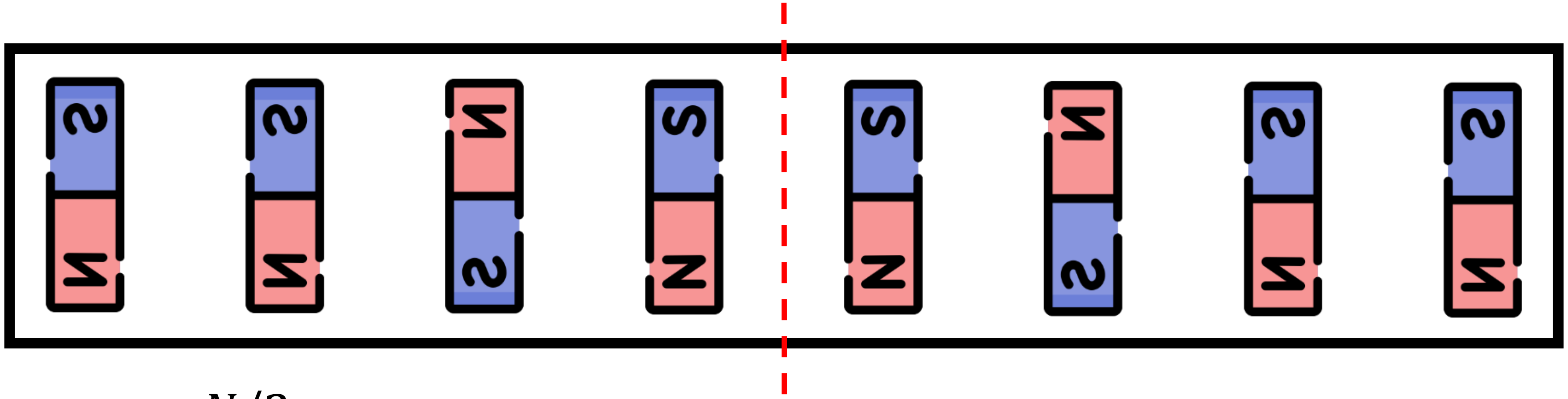
$\boldsymbol{N}$



The total number of states of the N magnets is $\Pi = 2^N$

$$S = k_B N \log 2$$

$\boldsymbol{\frac{N}{2}}$

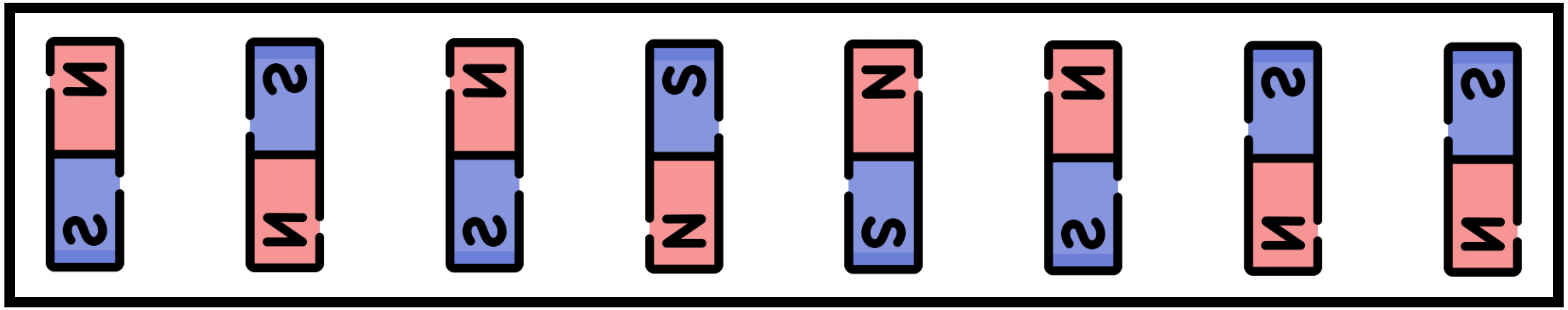


$\boldsymbol{\frac{N}{2}}$

$\Pi = 2^{N/2}$

$$S = k_B \log \Pi$$

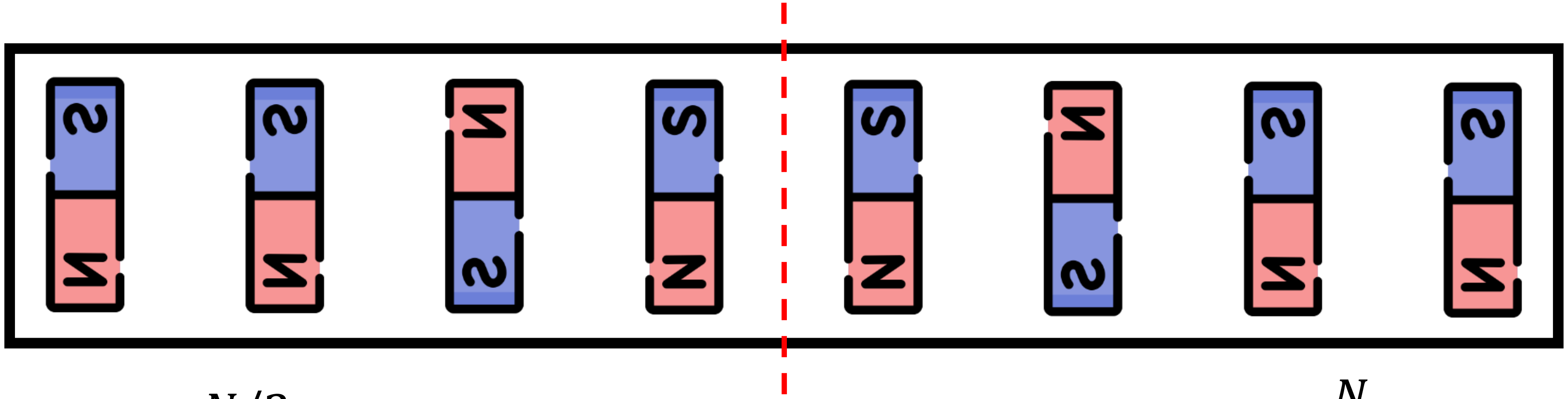
$\boldsymbol{N}$



The total number of states of the N magnets is $\Pi = 2^N$

$$S = k_B N \log 2$$

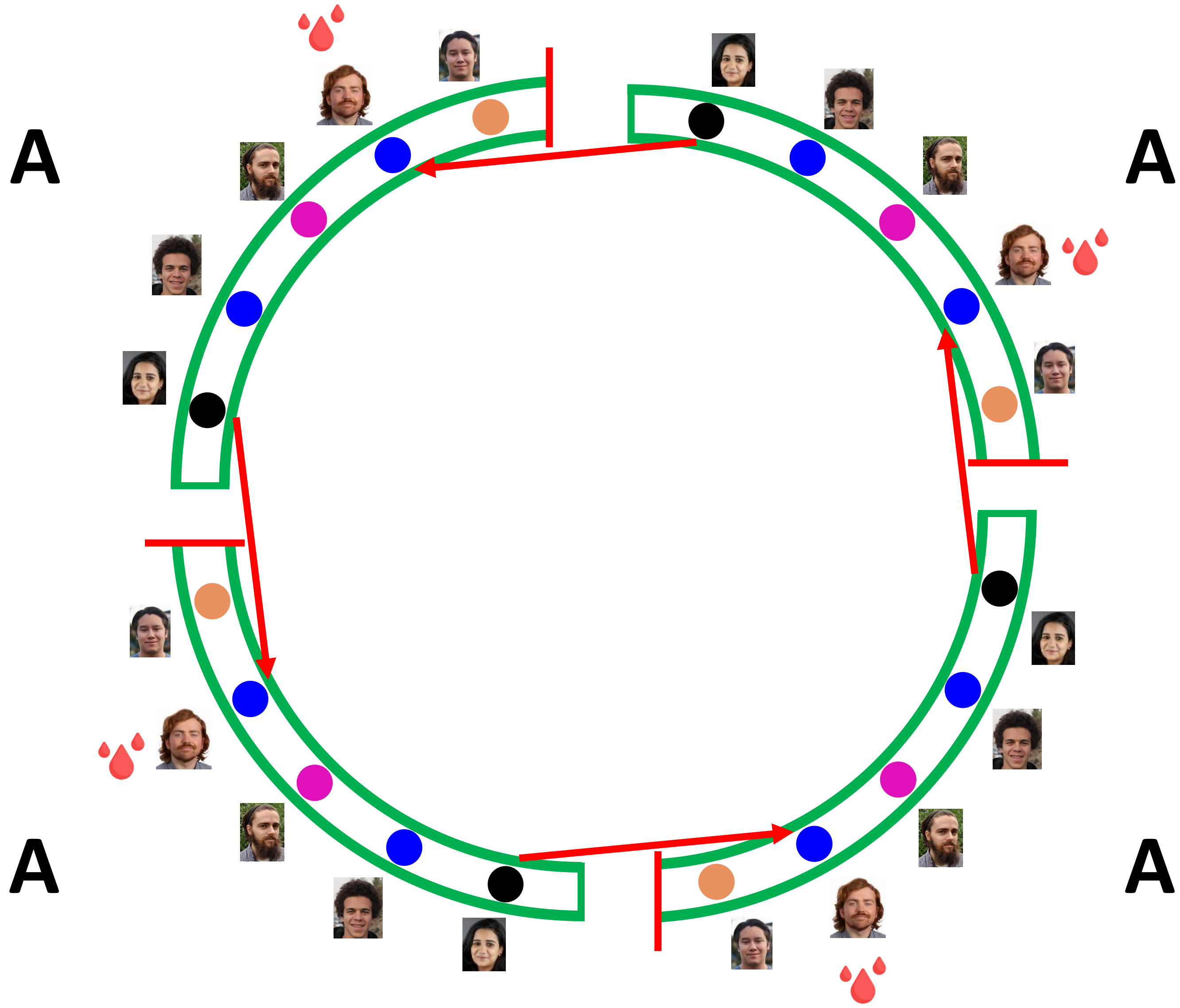
$\boldsymbol{\frac{N}{2}}$



$\boldsymbol{\frac{N}{2}}$

$\Pi = 2^{N/2}$ → $S = k_B \frac{N}{2} N \log 2$

c = 4 sofas



That is ugh ugh!

Free energy — Loop energy — Entropic association cost — Symmetry penalty

$$\Delta G(S) = \sum_{l \in S} \Delta G(l) + (c-1) * \Delta G^{\text{assoc}} + k_B T * \log R$$

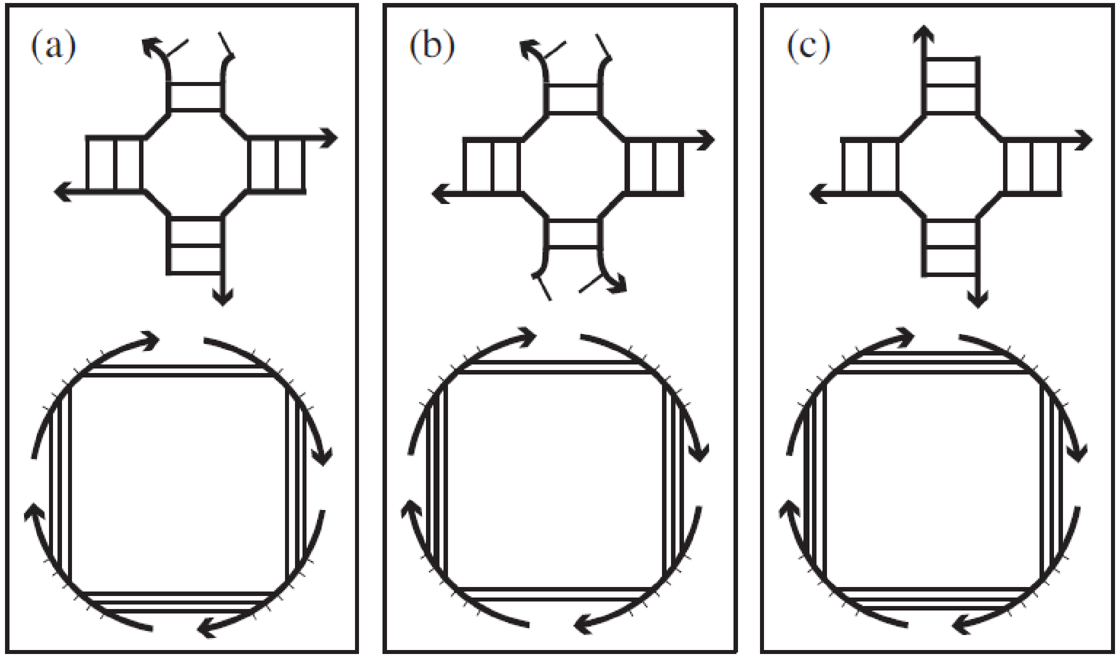


Fig. 2.2 *Sample secondary structures and polymer graphs for a complex of four indistinguishable strands.* (a) *1-fold (i.e., no) rotational symmetry.* (b) *2-fold rotational symmetry.* (c) *4-fold rotational symmetry.*

Why is this difficult?

Computational complexity of Minimum Free Energy algorithms

Level	Input Type	MFE
1	Single Strand (Maximum matching)	$O(N^3)$
2	Single Strand (Loop model)	$O(N^3)$
3	Multiple **unique** Strands, Bounded ($\leq$ c)	$O(N^3(\mathrm{c}-1)!)$
4	Multiple Strands, Bounded ($\leq$ c)	?

N bases, c strands

Computational complexity of Minimum Free Energy algorithms

Level	Input Type	MFE
1	Single Strand (Maximum matching)	$O(N^3)$
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N bases, c strands

All of these are dynamic programming algorithms

Computational complexity of Minimum Free Energy algorithms

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3	Multiple **unique** Strands, Bounded $(\leq \mathrm{c})$	$O(N^3(\mathrm{c}-1)!)$
4	Multiple Strands, Bounded $(\leq \mathrm{c})$	?

N bases, c strands

All of these are dynamic programming algorithms

Subproblems → **Big problem**

Level	Input Type	MFE
1	Single Strand (Maximum matching)	$O(N^3)$
2	Single Strand (Loop model)	$O(N^3)$
3	Multiple **unique** Strands, Bounded ($\leq c$)	$O\left(N^3(c-1)!\right)$
4	Multiple Strands, Bounded ($\leq c$)	?

N bases, c strands

All of these are dynamic programming algorithms

Subproblems → **Big problem**

Level	Input Type	MFE
1	Single Strand (Maximum matching)	$O(N^3)$
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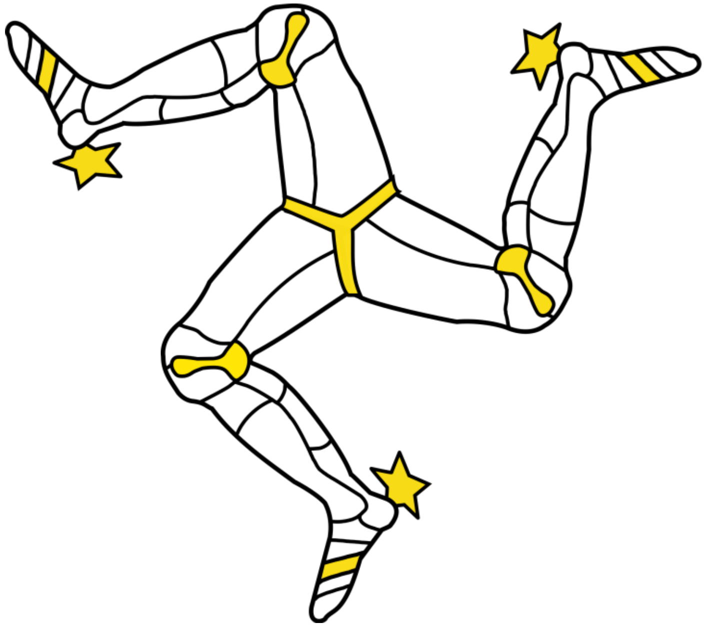
4	Multiple Strands, Bounded ($\leq$ c)	?

N bases, c strands

All of these are dynamic programming algorithms

Subprograms → **Big problem**



Level	Input Type	MFE
1	Single Strand (Maximum matching)	$O(N^3)$
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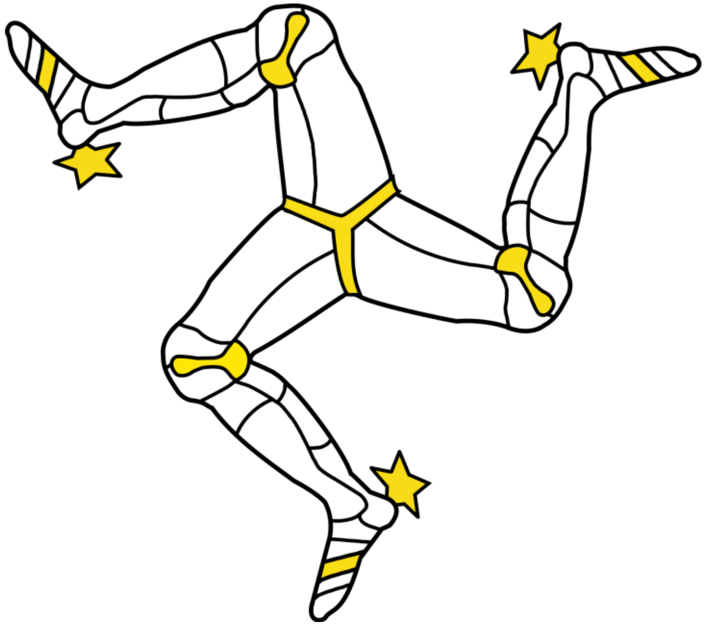
3	Multiple **unique** Strands, Bounded ($\leq$ c)	$O\left(N^3(c-1)!\right)$
4	Multiple Strands, Bounded ($\leq$ c)	?

N bases, c strands

All of these are **dynamic programming** algorithms

Subprogblems → **Big problem**



Global property

Level	Input Type	MFE
1	Single Strand (Maximum matching)	$O(N^3)$
2	Single Strand (Loop model)	$O(N^3)$
3	Multiple unique Strands, Bounded ($\leq$ c)	$O(N^3(c-1)!)$
4	Multiple Strands, Bounded ($\leq$ c)	?

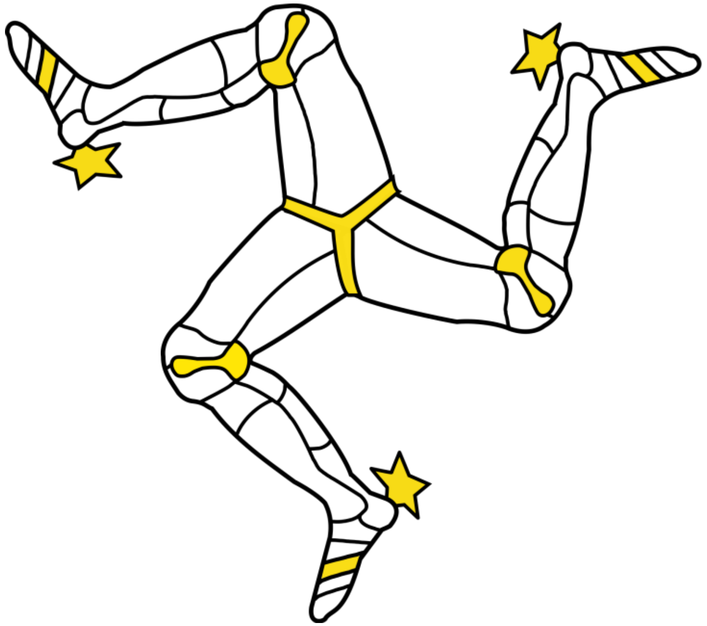
N bases, c strands

All of these are dynamic programming algorithms

Subproblems → Big problem

↓

Local point of view



Global property

Level	Input Type	MFE
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4	Multiple Strands, Bounded ($\leq$ c)	?

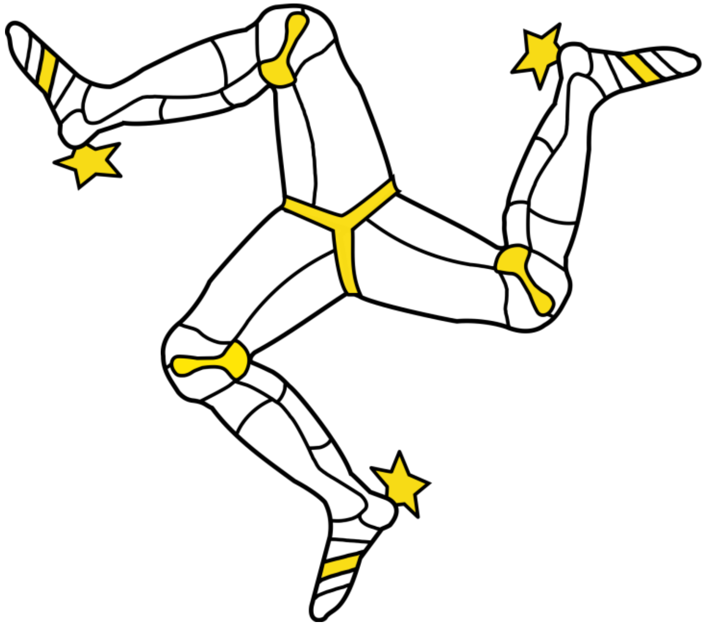
N bases, c strands

All of these are dynamic programming algorithms

Subprojects → Big problem

↓

Local point of view → ? → Global property



Computational complexity of Minimum Free Energy algorithms

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4	Multiple Strands, Bounded ($\leq$ c)	?

N bases, c strands

$$B(S) = \sum_{l} B(l) - (c-1)\, B^{\mathrm{assoc}}$$

Computational complexity of Minimum Free Energy algorithms

Level	Input Type	MFE
1	Single Strand (Maximum matching)	$O(N^3)$
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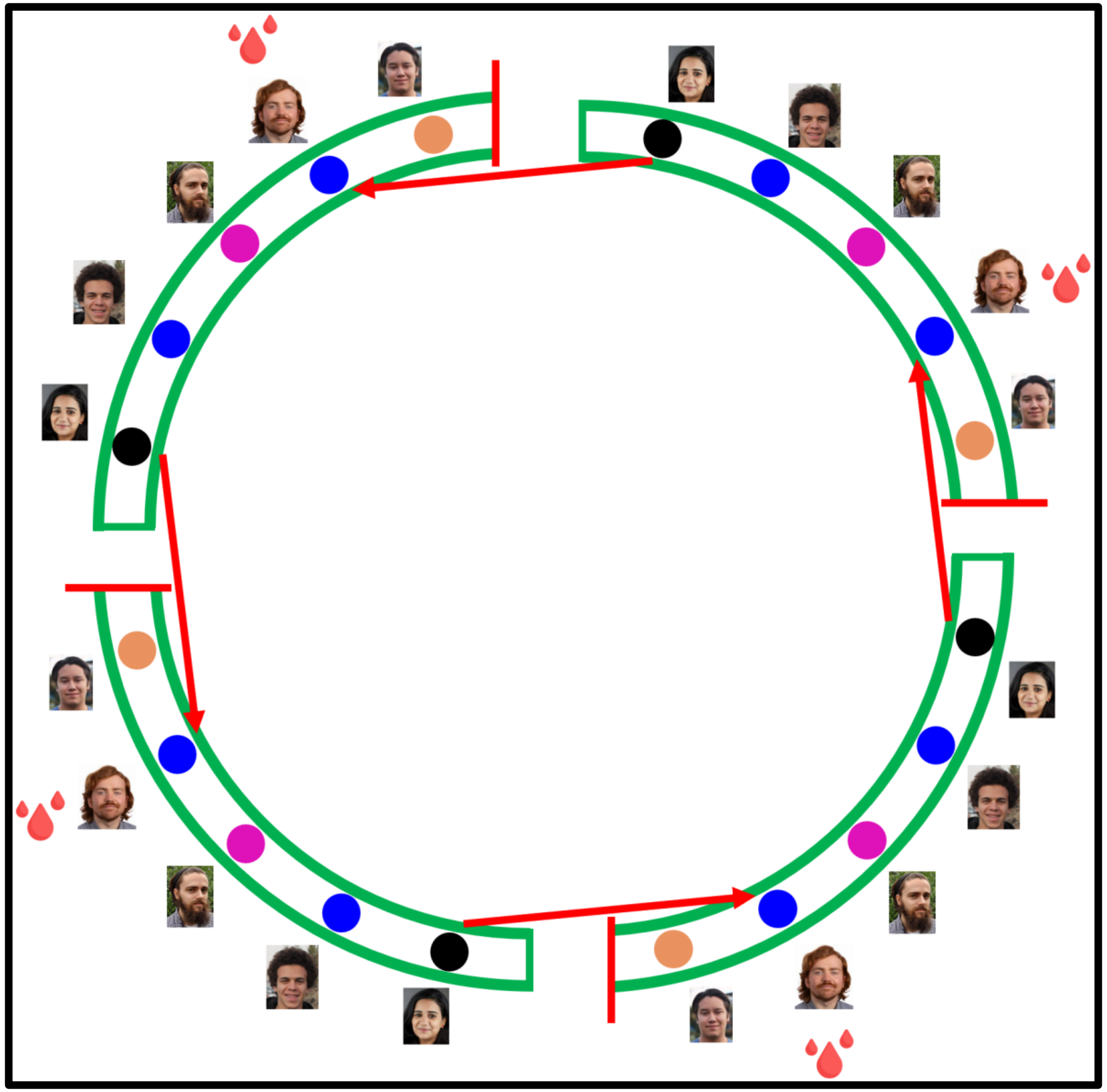
4	Multiple Strands, Bounded ($\leq$ c)	?

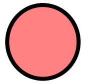
N bases, c strands

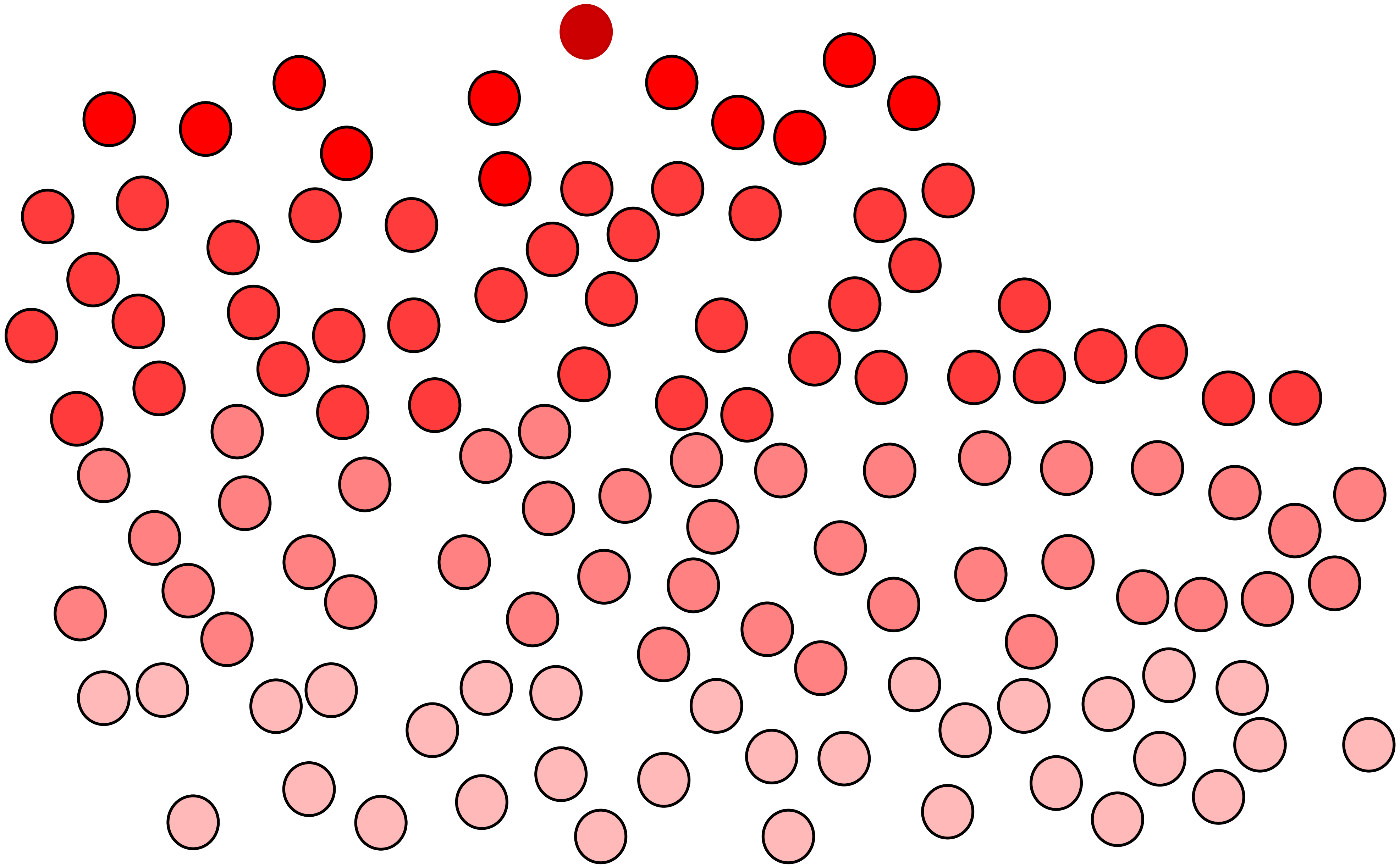
$$B(S) = \sum_l B(l) - (c-1)\, B^{\text{assoc}}$$

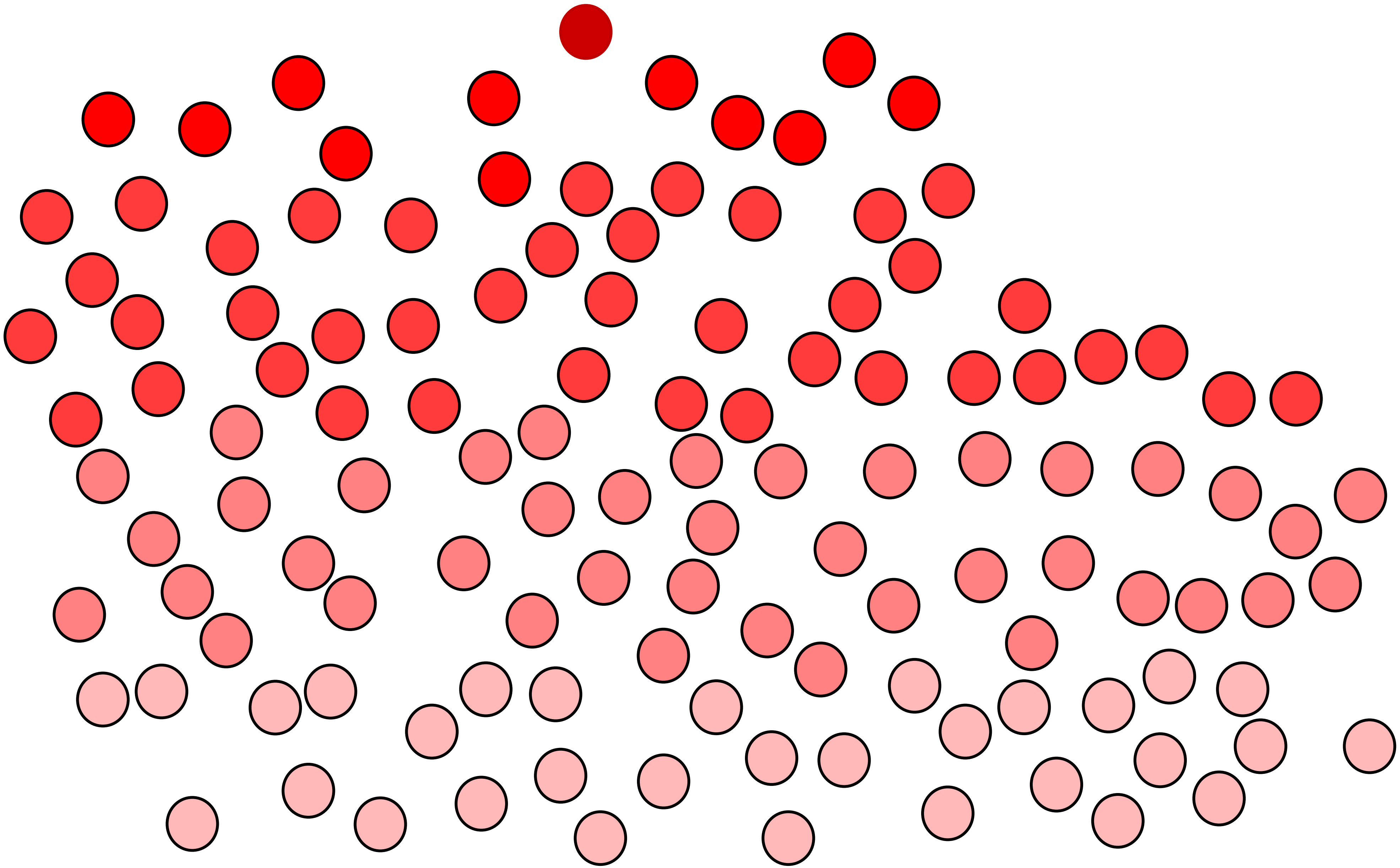
$$B(S) = \sum_l B(l) - (c-1) B^{\text{assoc}} - \boldsymbol{k_B T * \log R}$$

Let's ignore the symmetry for a while

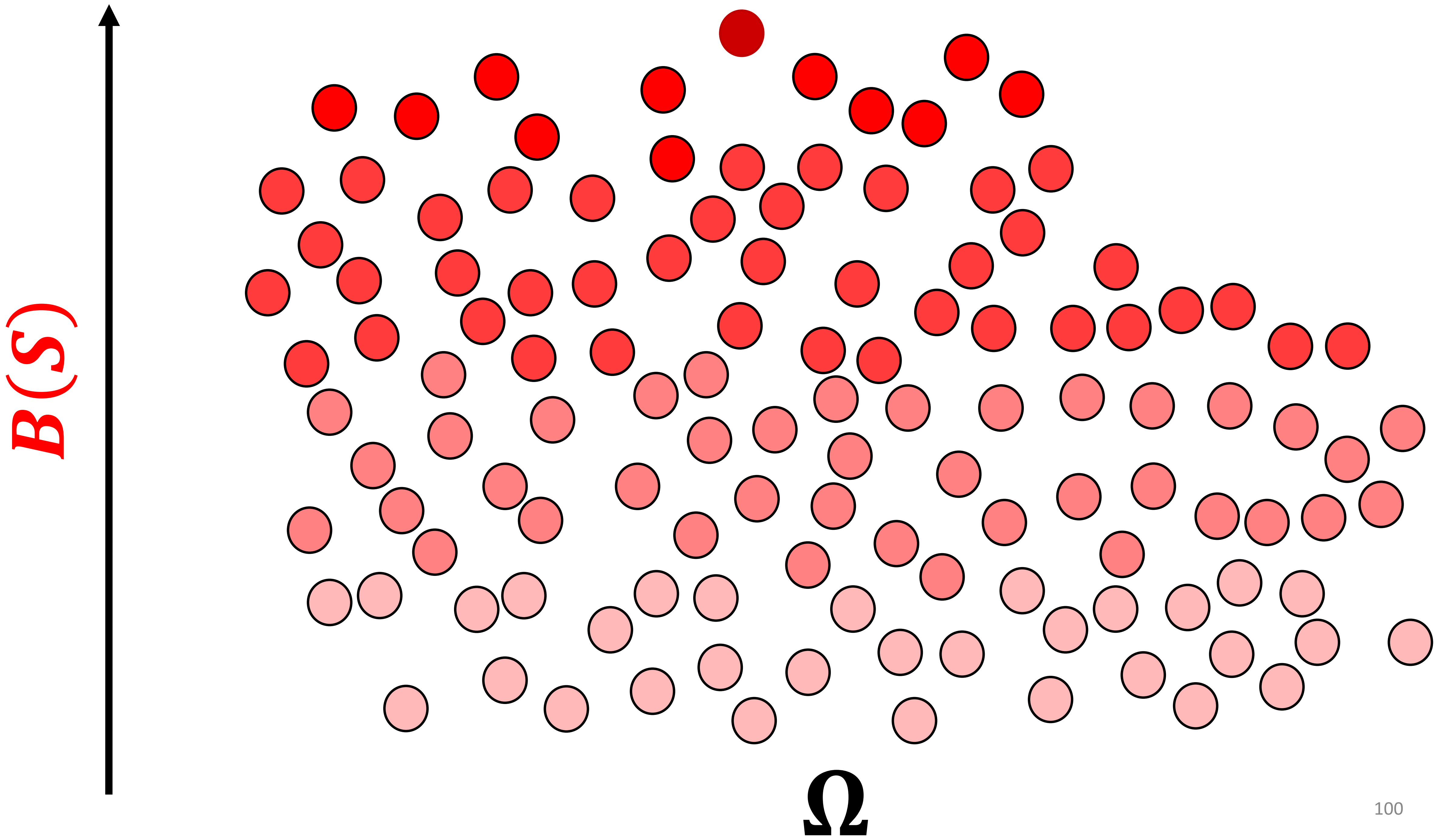


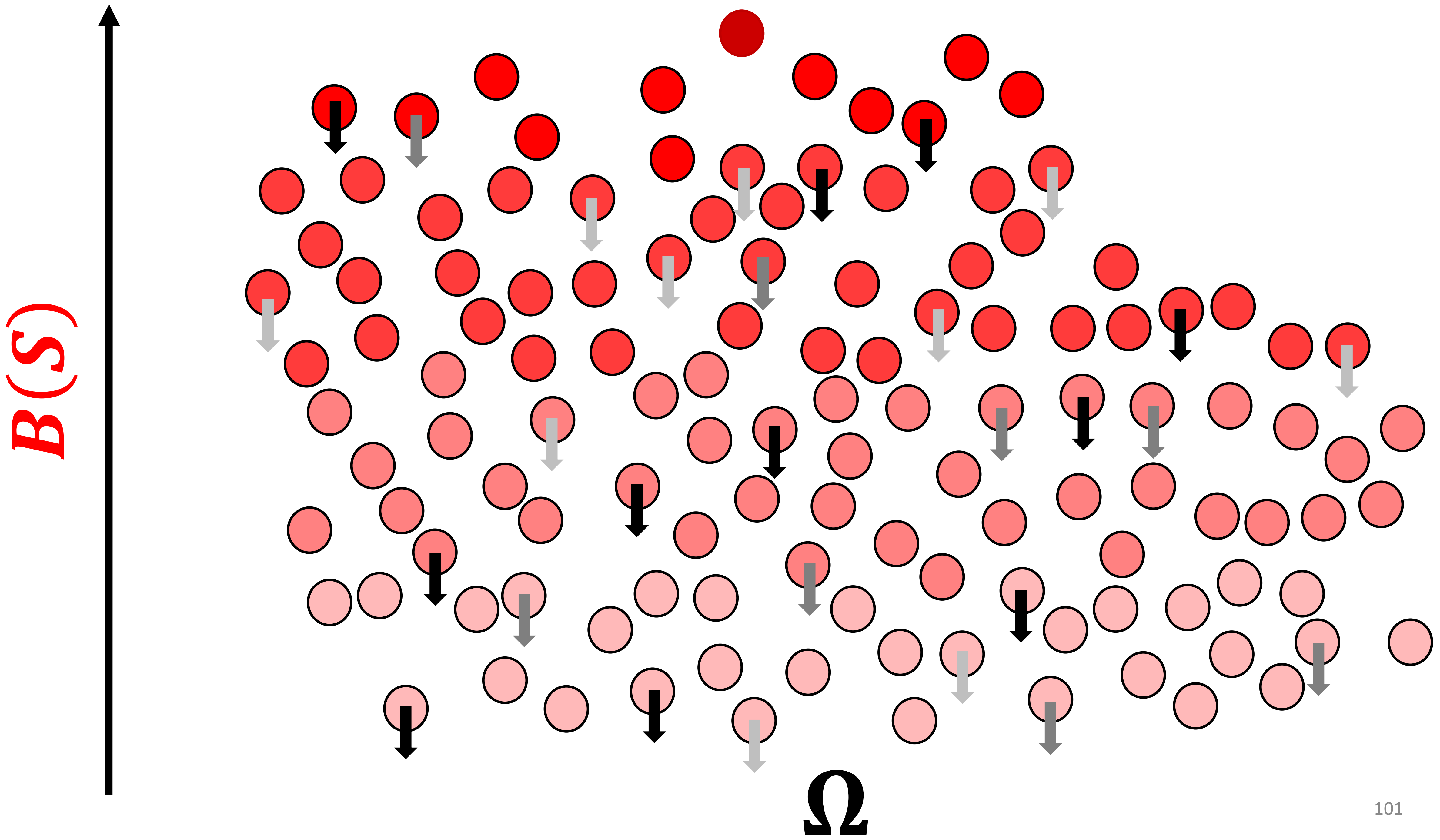


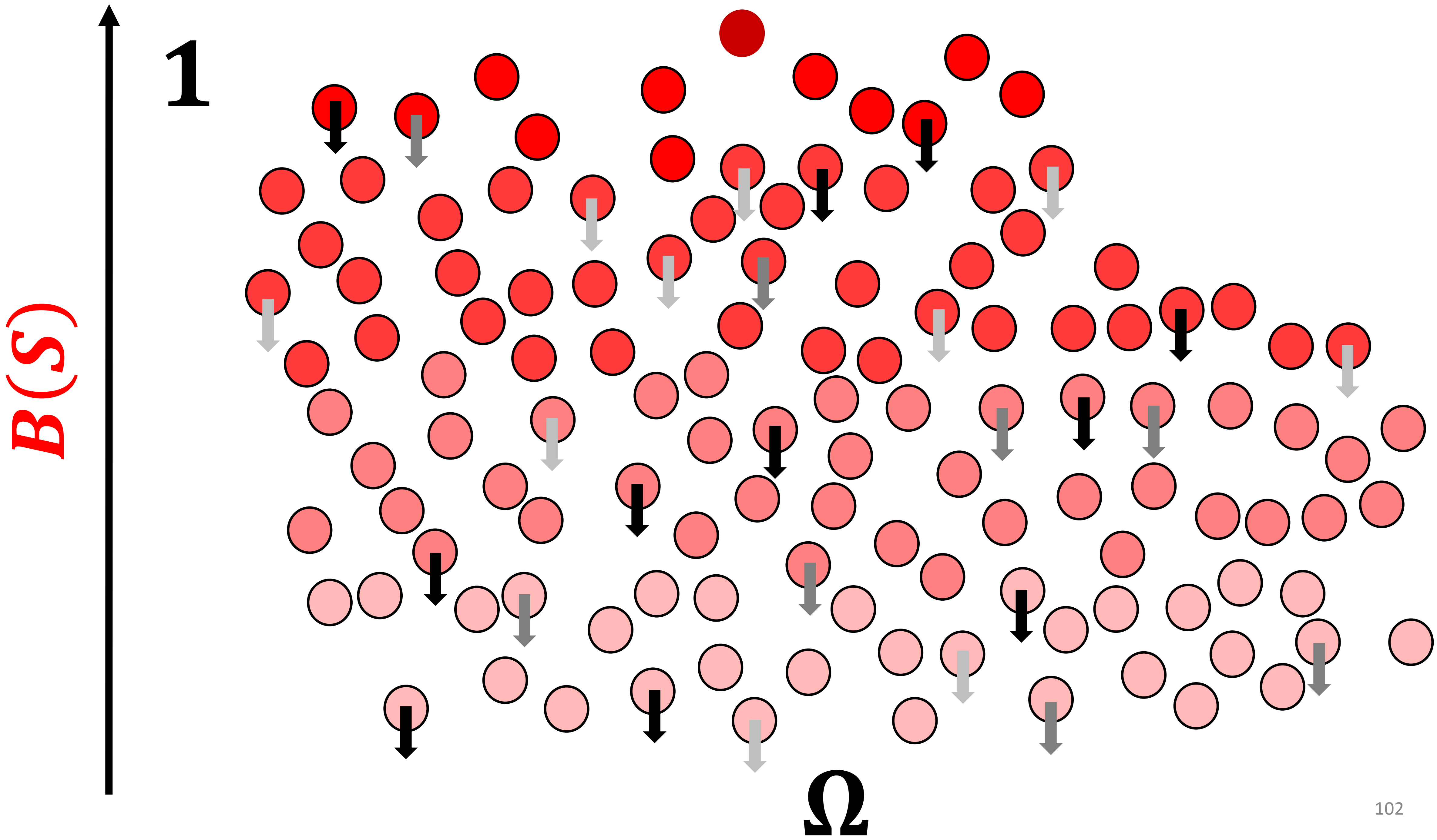


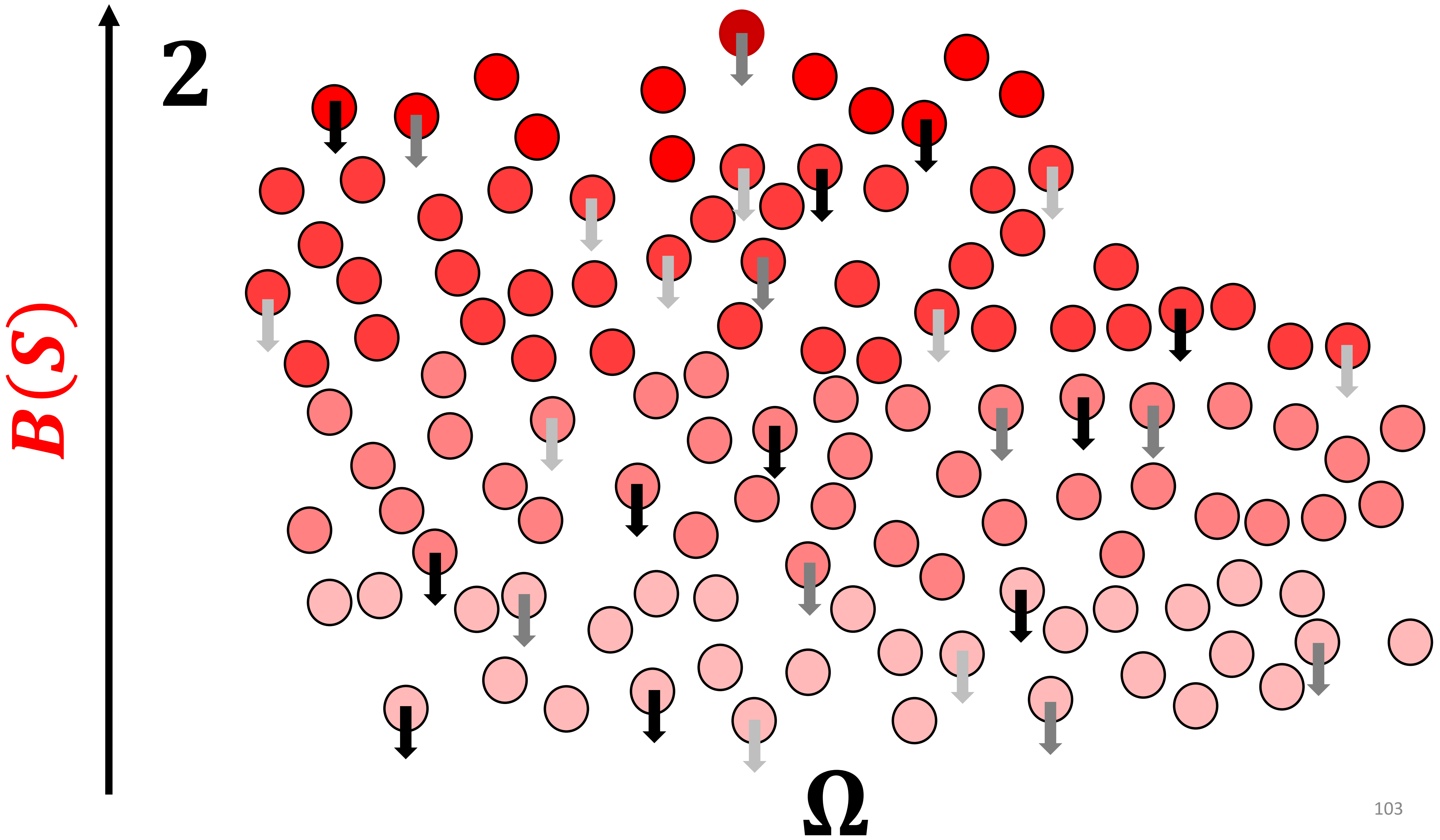


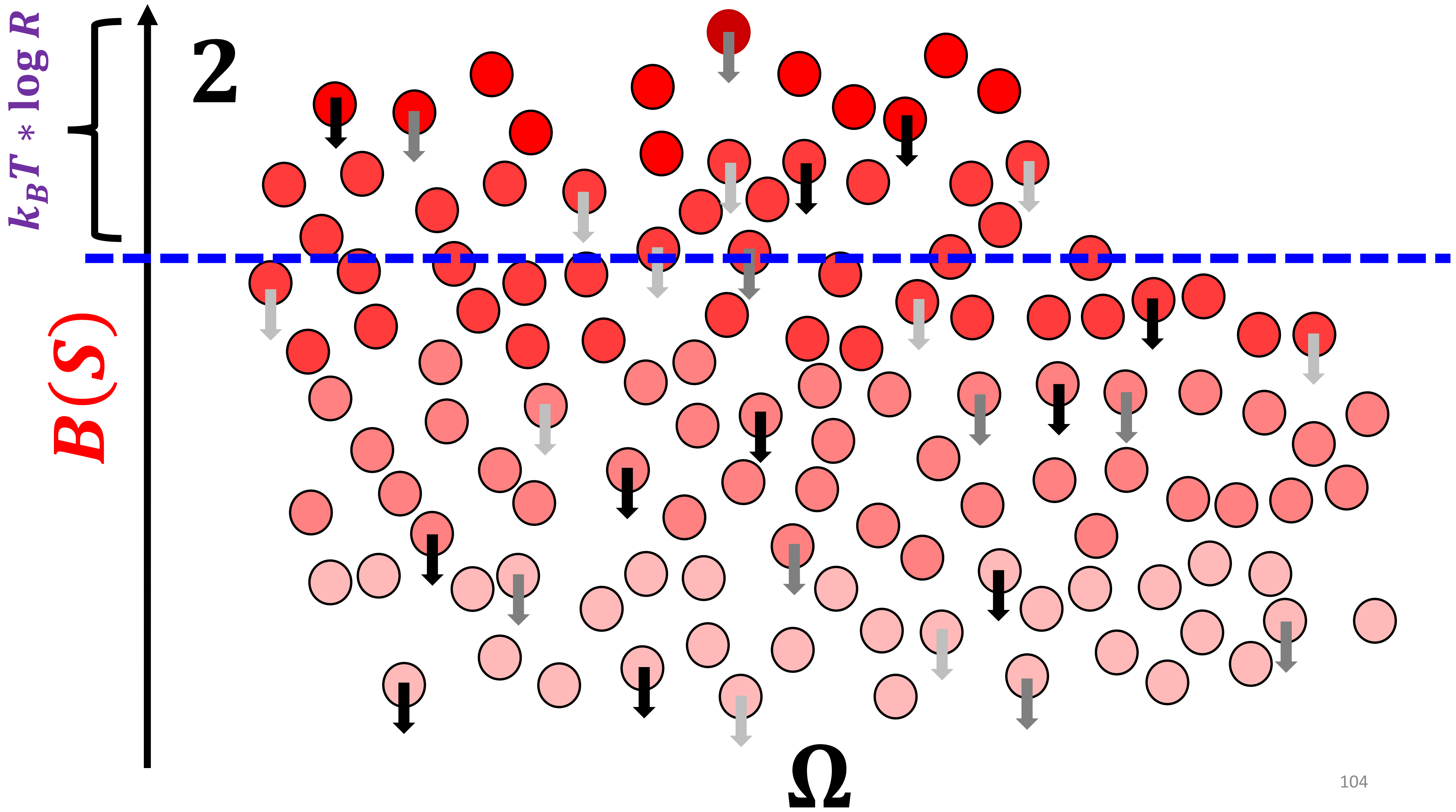
Ω

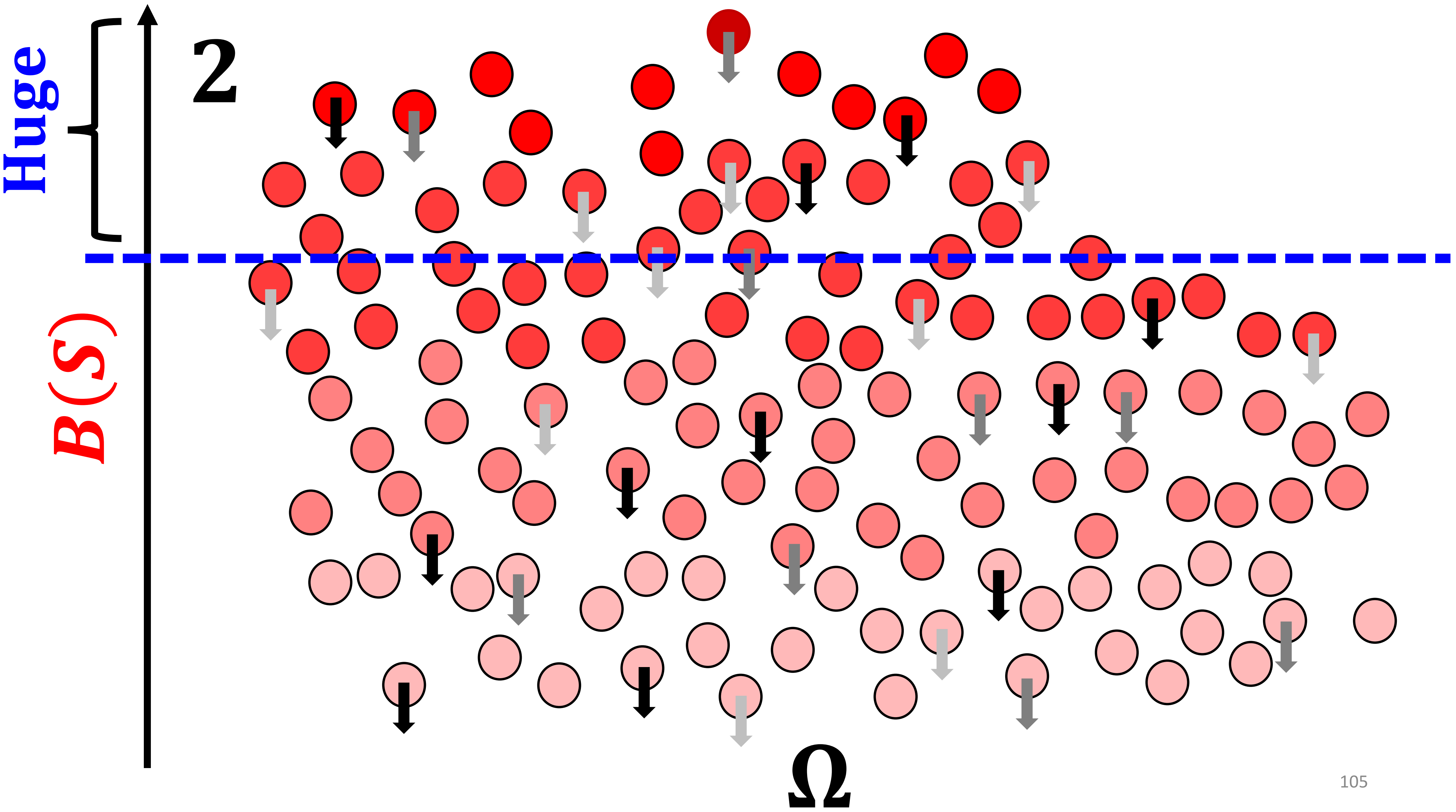

B(S)
Ω


B(S)
Ω


1
B(S)
Ω


B(S)
2
Ω


$k_B T * \log R$
2
$B(S)$
Ω

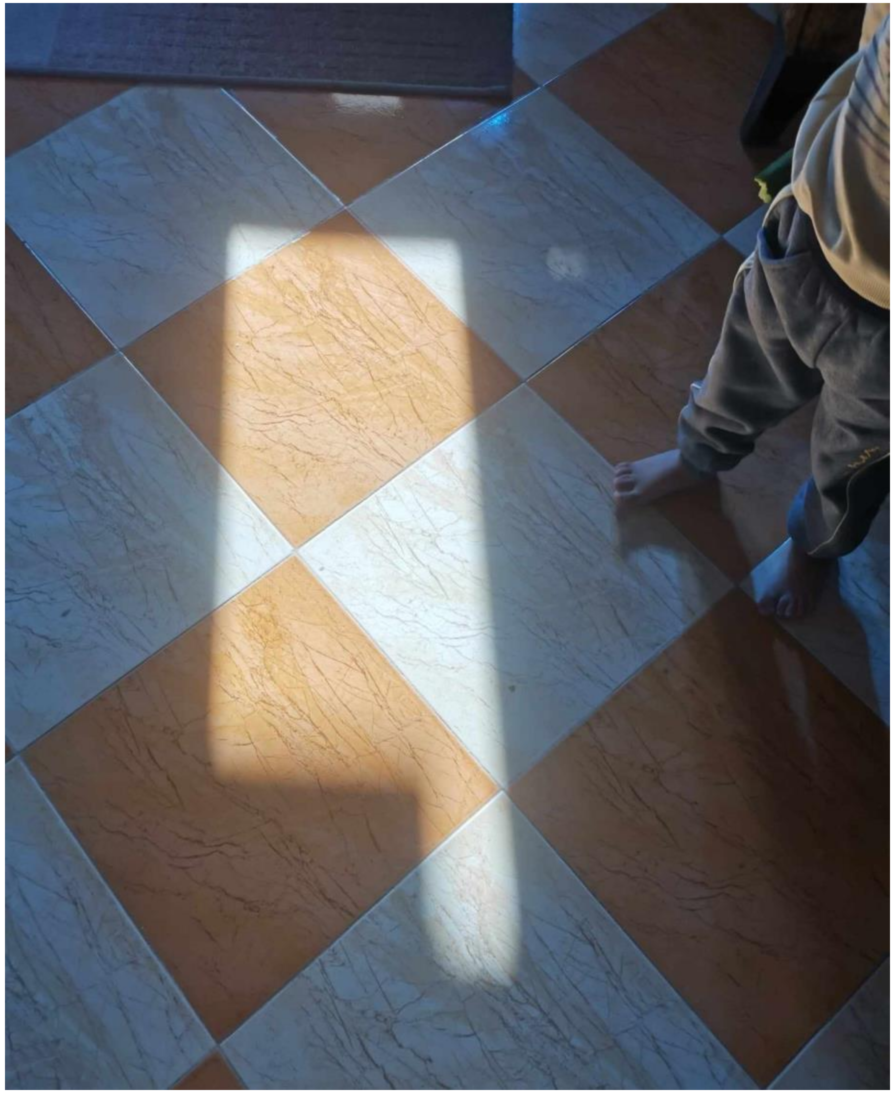

Huge
2
B(S)
Ω

Is there any hope?

TAKE A BREAK

Yasso


BelFone
Digital CH 1
Zone 1
TX: 410.97500
RX: 410.97500
Menu
SMS



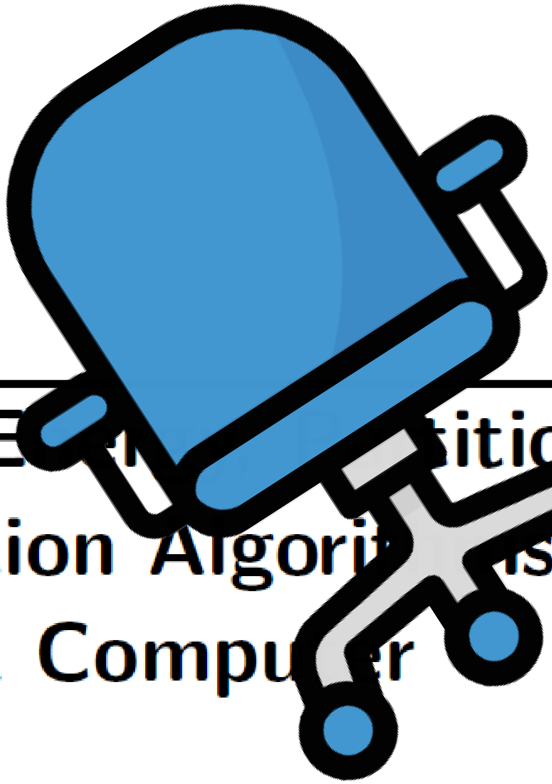
Last summer, we went to Japan

Minimum Free Energy, Partition Function and Kinetics Simulation Algorithms for a Multistranded Scaffolded DNA Computer

Ahmed Shalaby
Hamilton Institute, Department of Computer Science, Maynooth University, Ireland

Chris Thachuk
Paul G. Allen School of Computer Science & Engineering, University of Washington, Seattle, WA, USA

Damien Woods
Hamilton Institute, Department of Computer Science, Maynooth University, Ireland



Minimum Free E ition Function and Kinetics Simulation Algori s a Multistranded Scaffolded DNA Compu er

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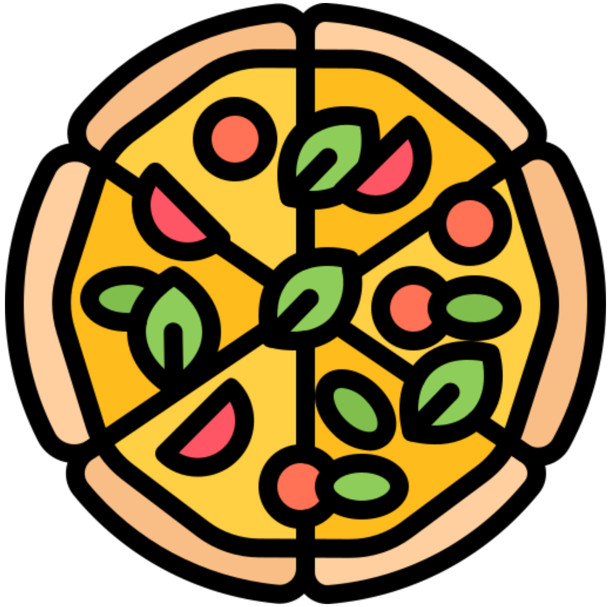
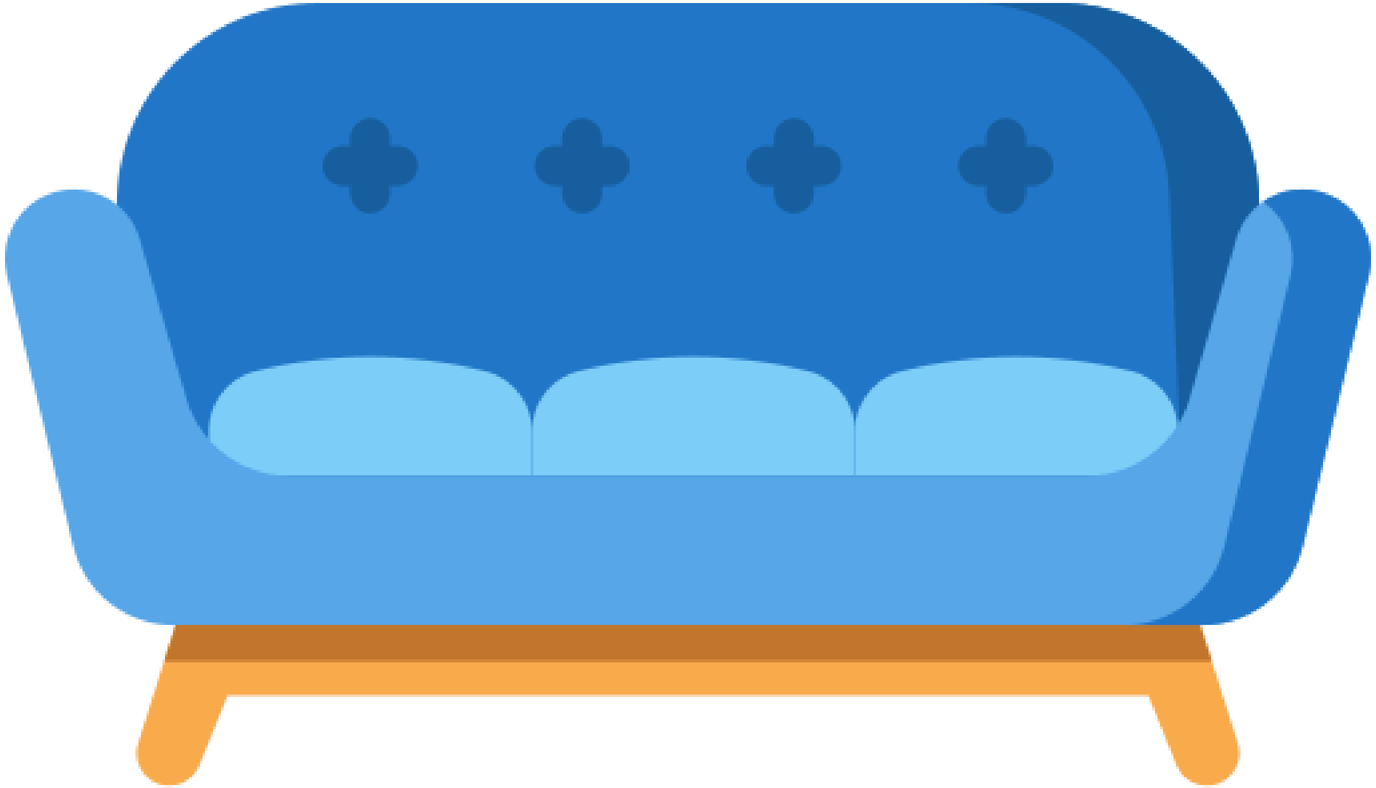
太平山
高清水
高清水
両関
北鹿
月桂冠
月桂冠
月桂冠
白雪
白雪
白雪
千福
浦霞
八海山
鶴齢
菊水
黄桜
黄桜
ZAKU
菊美人
司牡丹

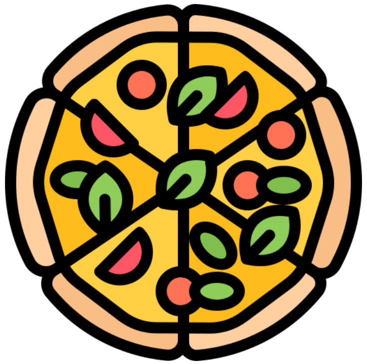
白雪
月桂冠
高清水
両関
北鹿
菊水
黄桜
司牡丹
酔鯨
ZAKU

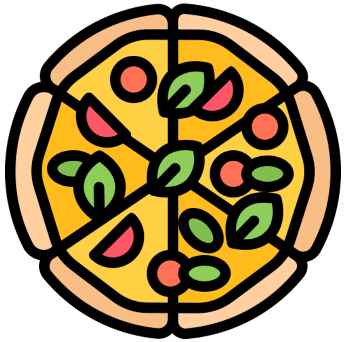
Welcome home

Yasso loves

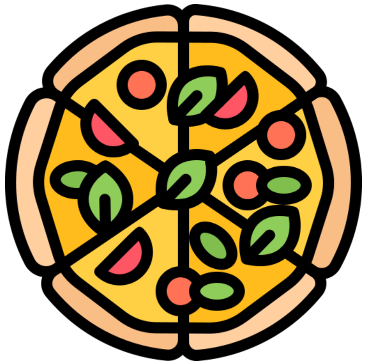






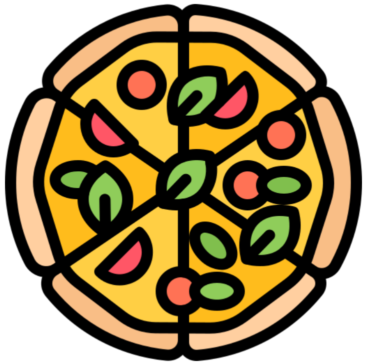


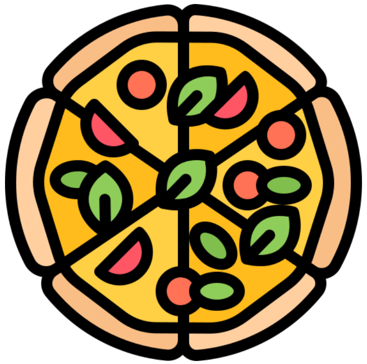


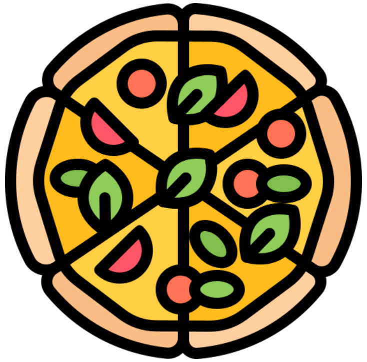


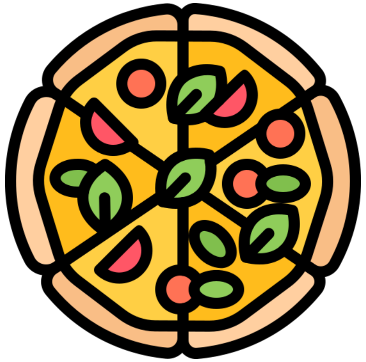


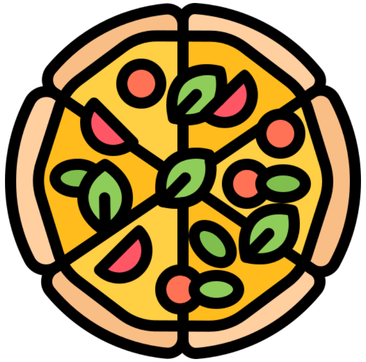




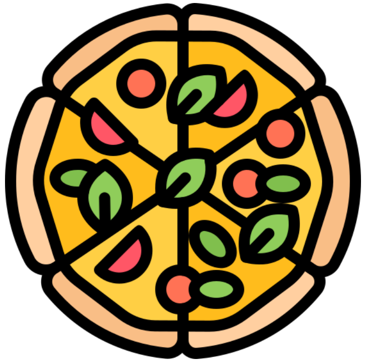




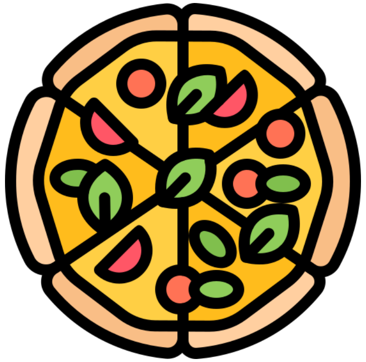


كله تمام يا خالو أحمد!

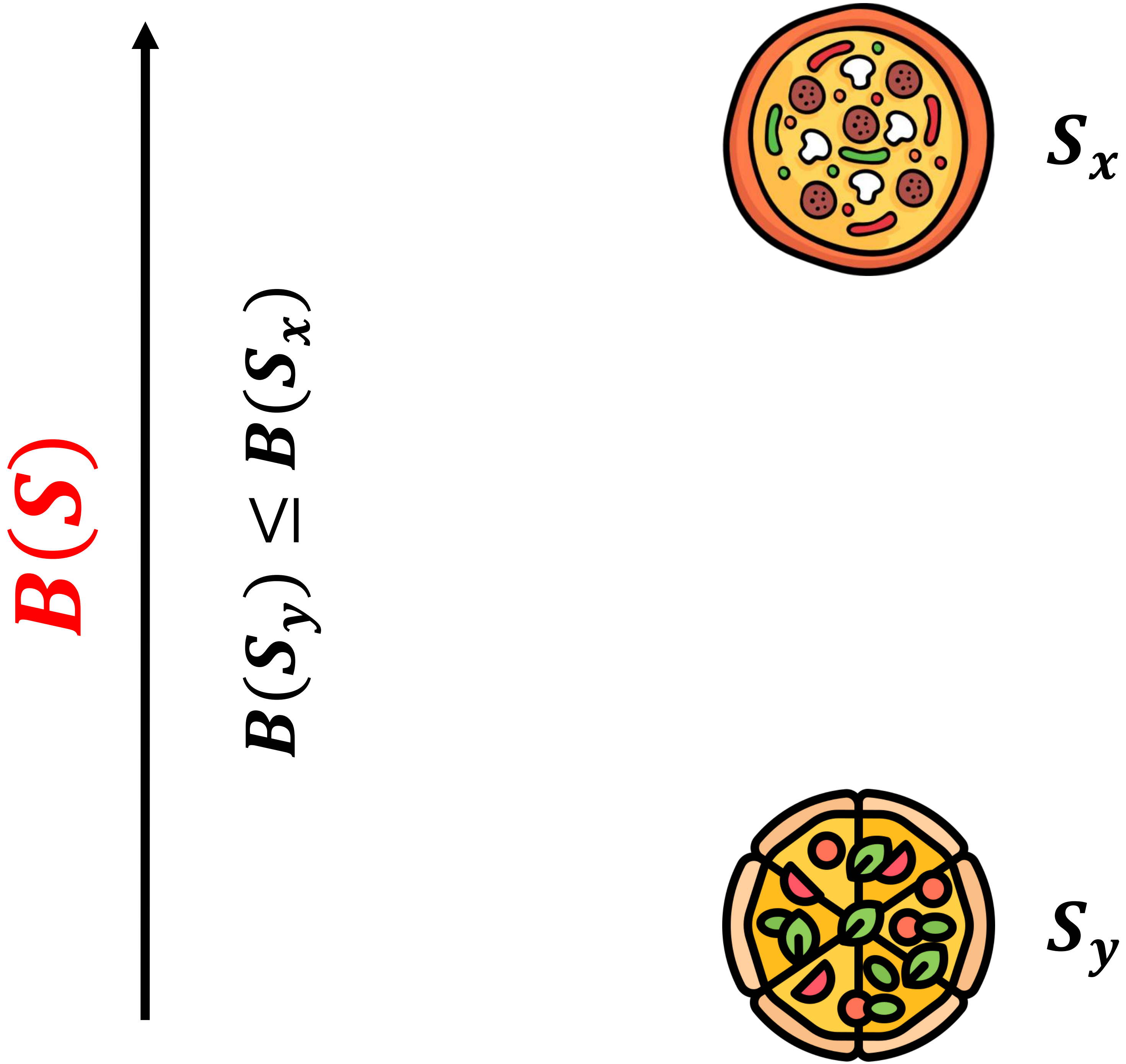
كله تمام يا خالو أحمد!



S_x



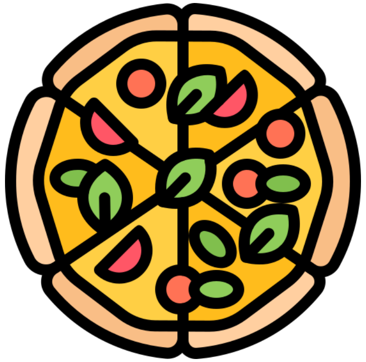
S_y


$B(S)$
$B(S_y) \leq B(S_x)$
S_x
S_y

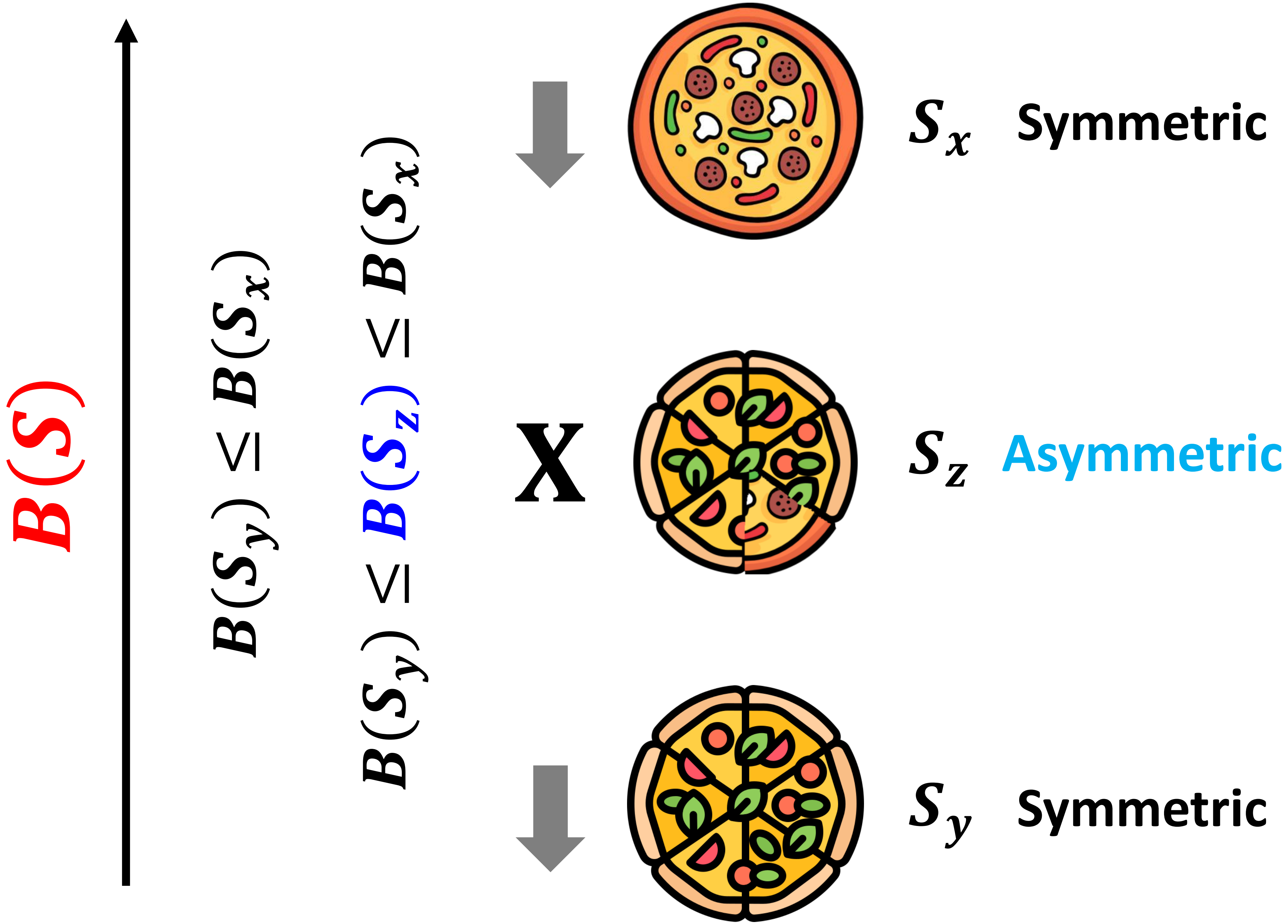
$B(S)$

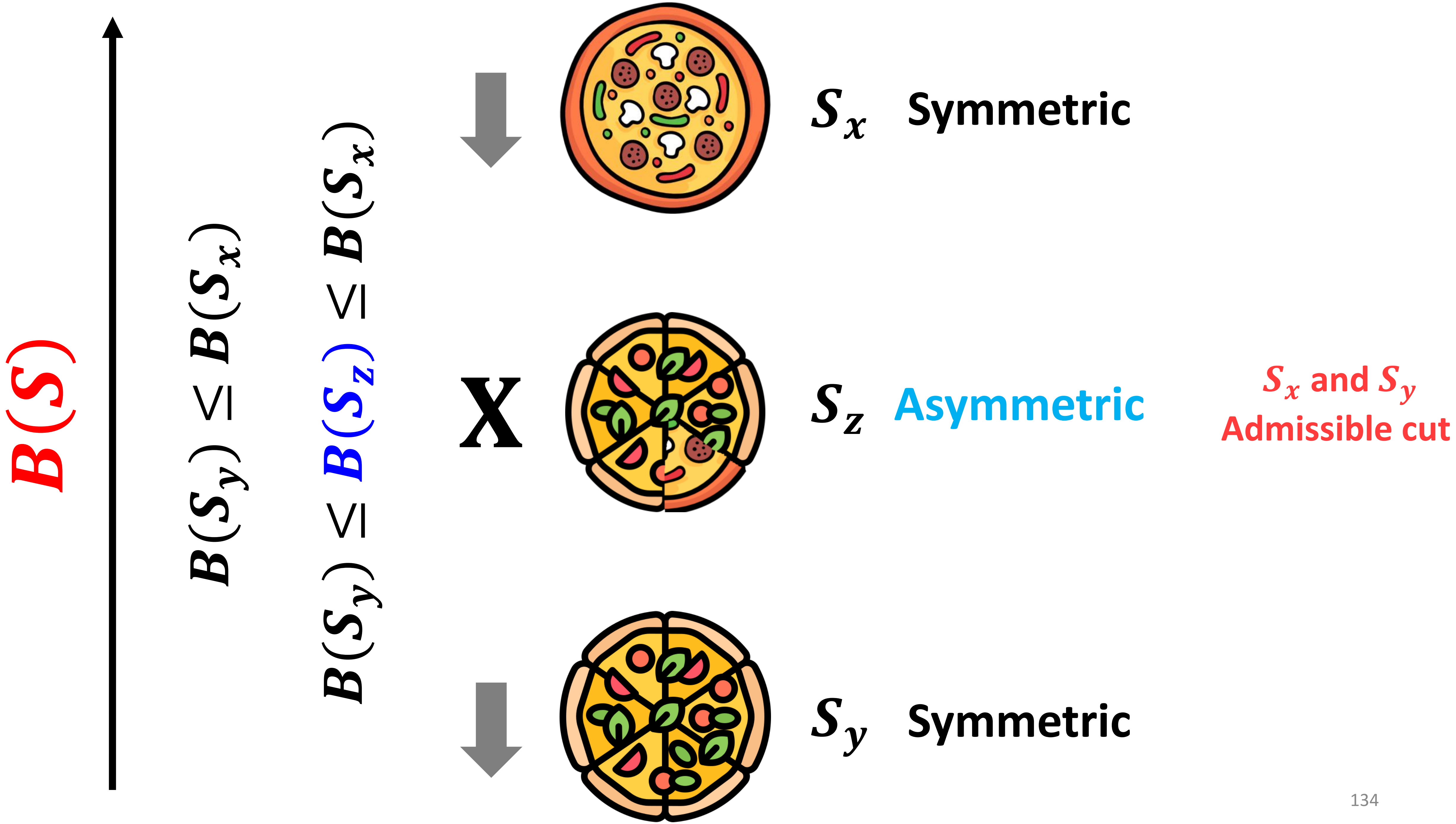
$B(S_y) \le B(S_x)$

S_x **Symmetric**



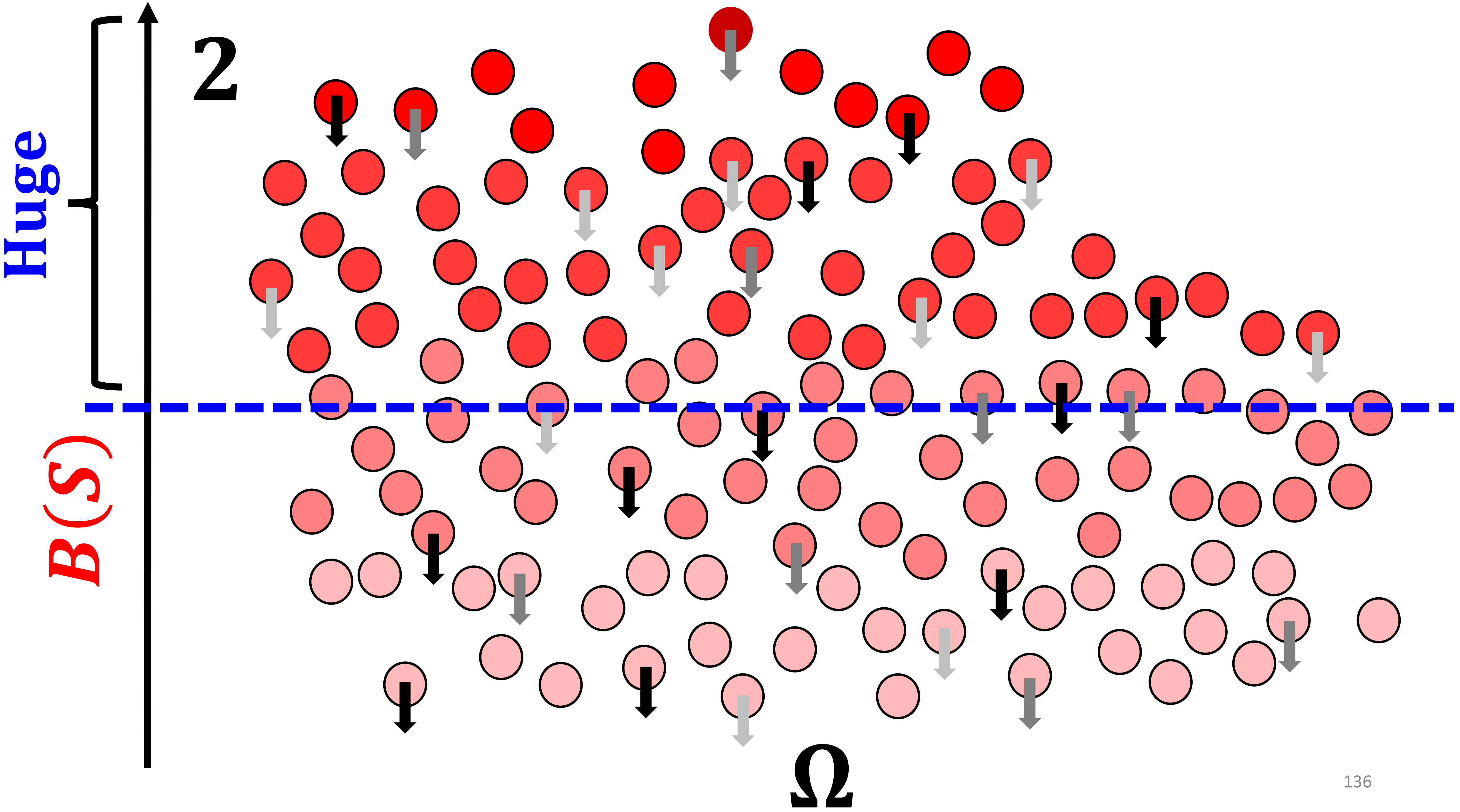
S_y **Symmetric**


$B(S)$
$B(S_y) \leq B(S_x)$
$B(S_y) \leq B(S_z) \leq B(S_x)$
X
S_x Symmetric
S_z Asymmetric
S_y Symmetric

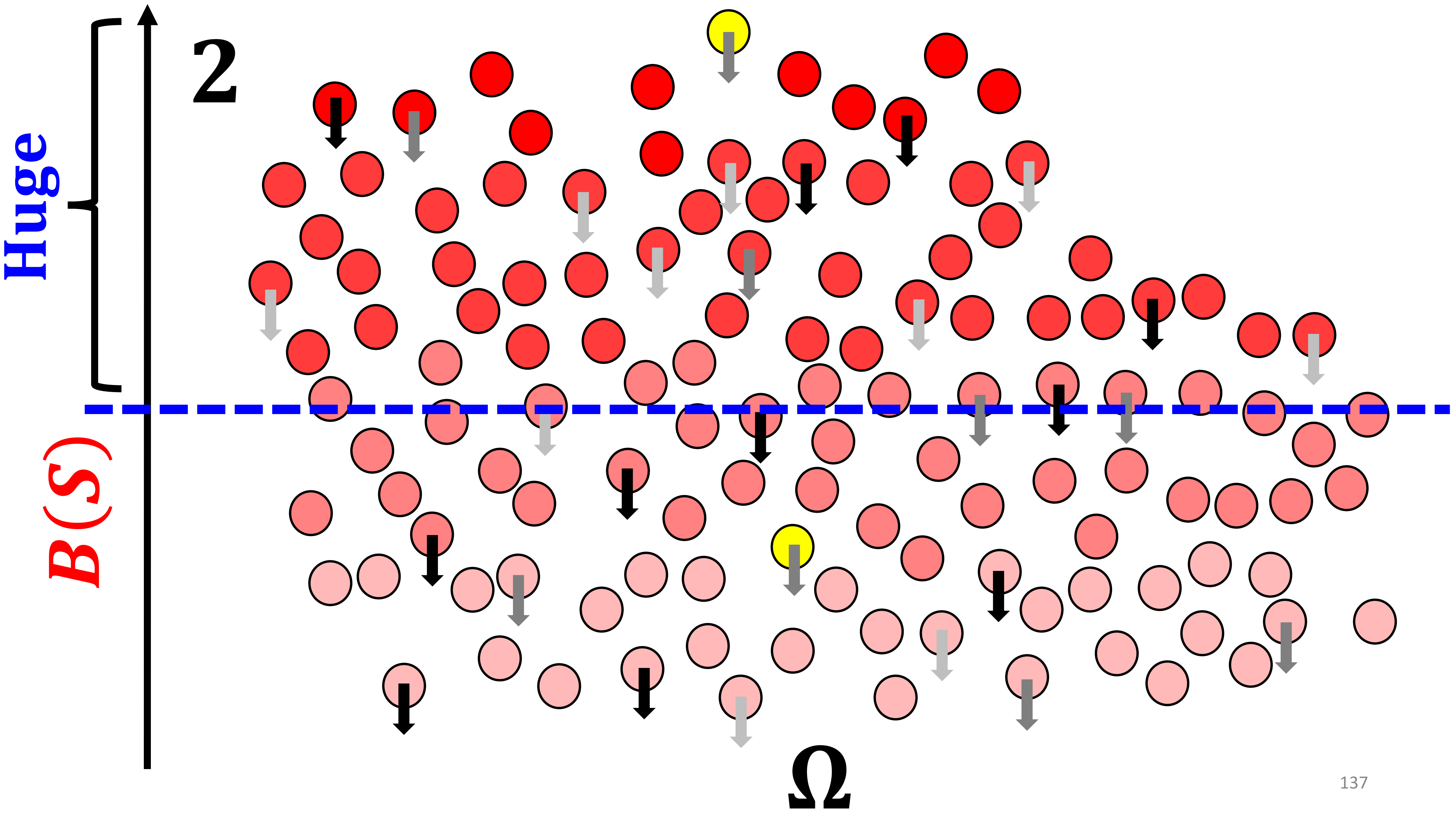

$B(S)$
$B(S_y) \leq B(S_x)$
$B(S_y) \leq B(S_z) \leq B(S_x)$
X
S_x Symmetric
S_z Asymmetric
S_y Symmetric
S_x and S_y
Admissible cut

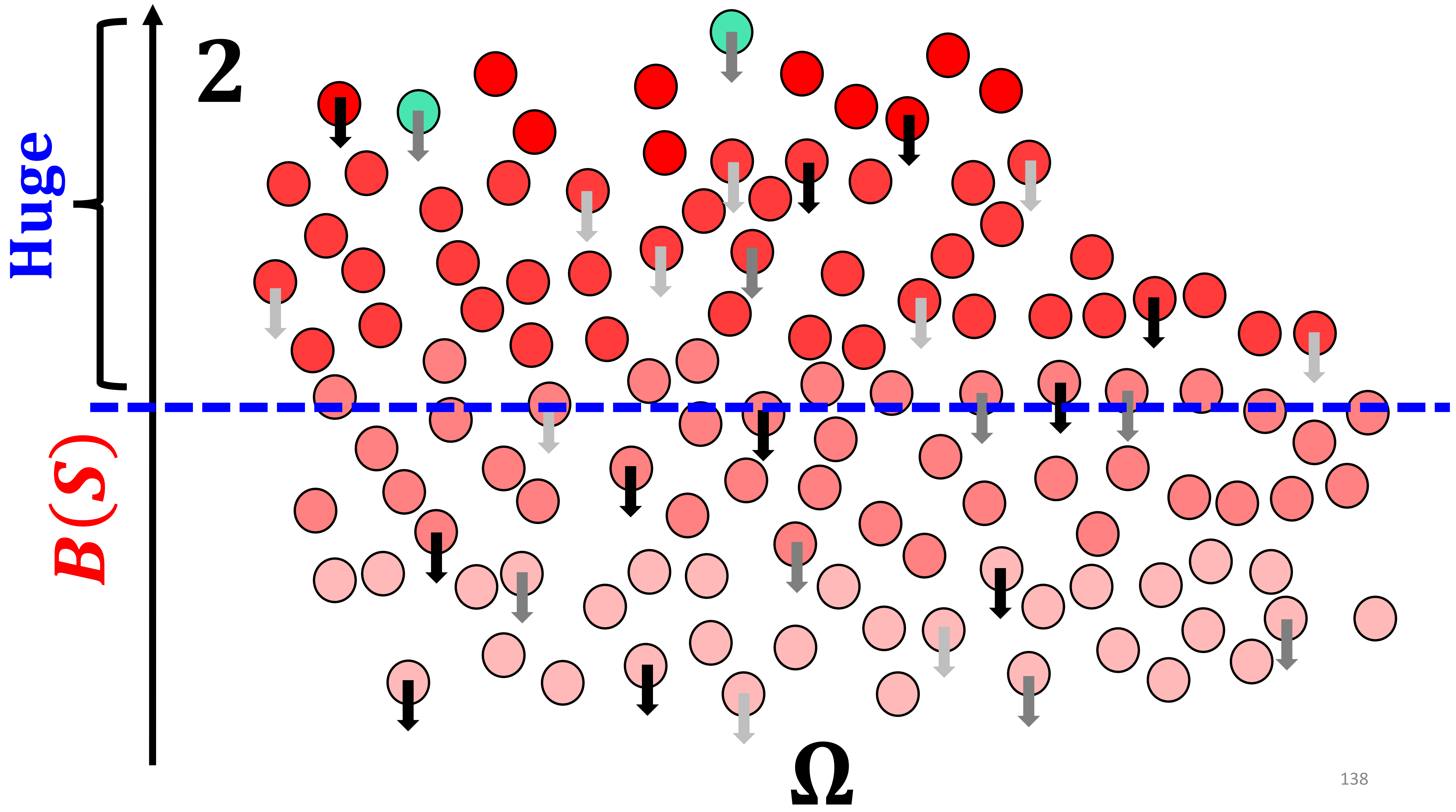
The sandwich theorem of secondary structures

Does this solve the problem?

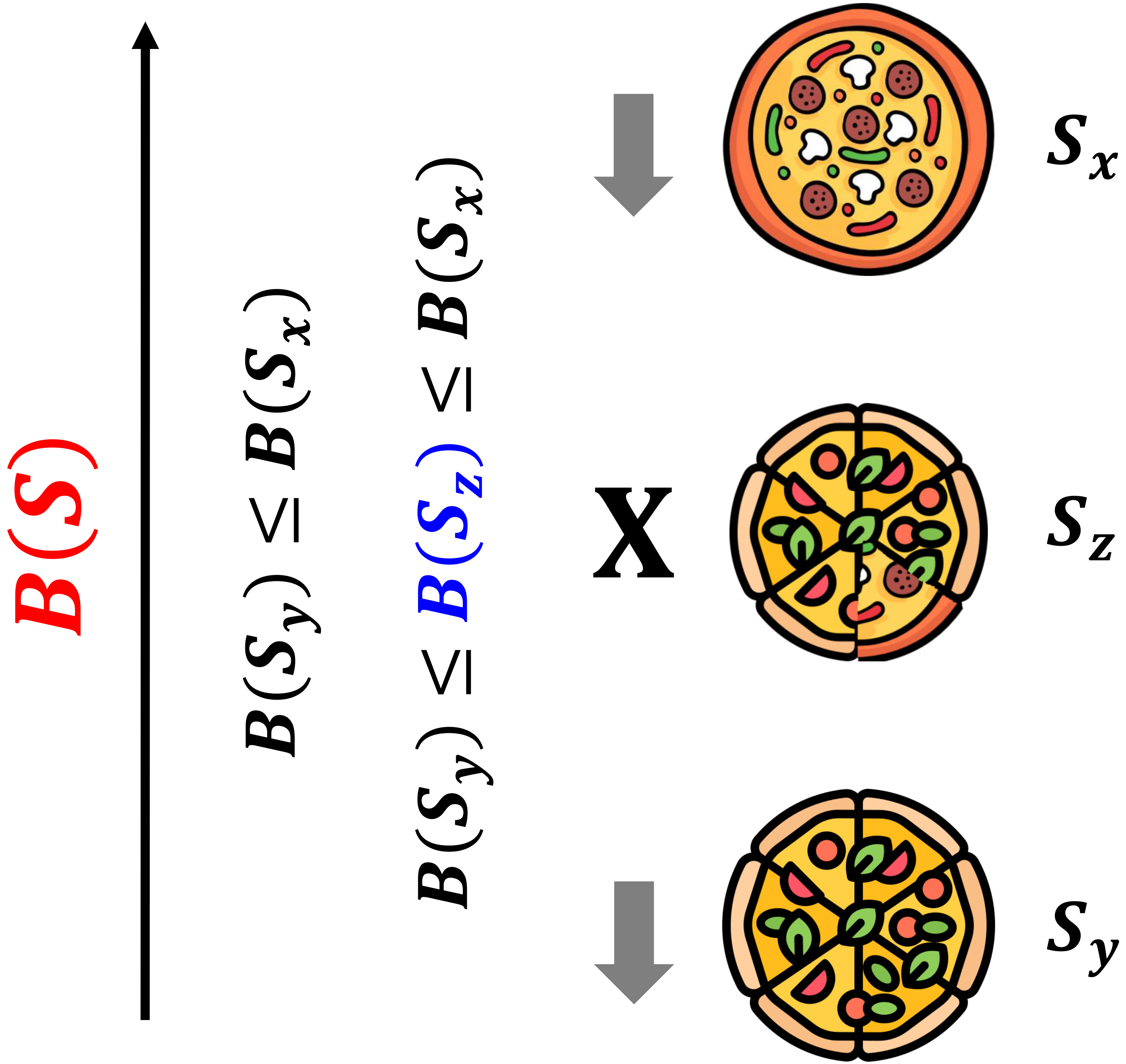


Huge
2
B(S)
Ω

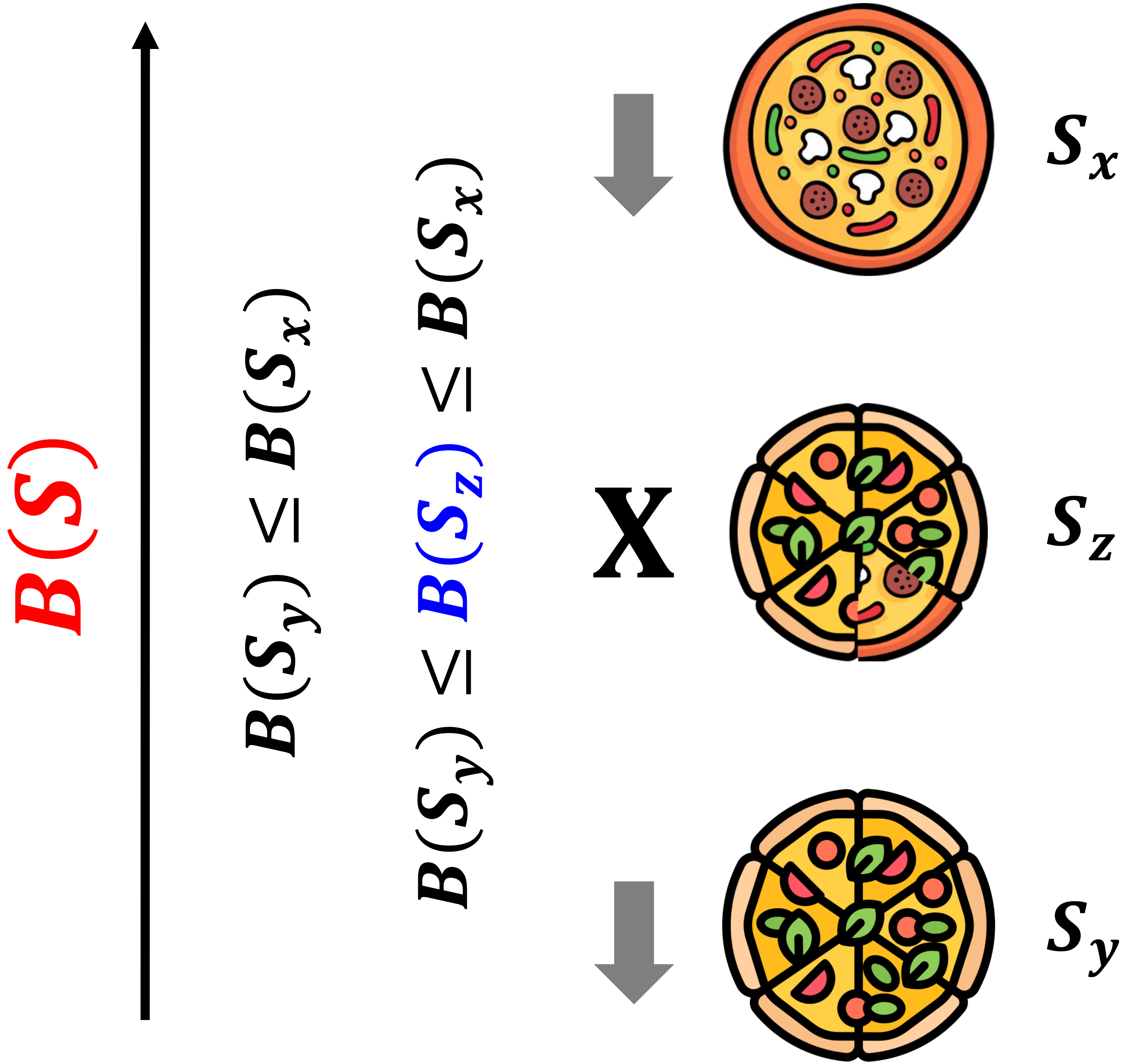

Huge
2
B(S)
Ω



2
Huge
B(S)
Ω



$B(S)$
$B(S_y) \leq B(S_x)$
$B(S_y) \leq B(S_z) \leq B(S_x)$
X
S_x
S_z
S_y



Upper bound

$$\frac{N-c}{v(\pi)}\left(\sigma(v(\pi)) - v(\pi)\right)$$

$B(S)$

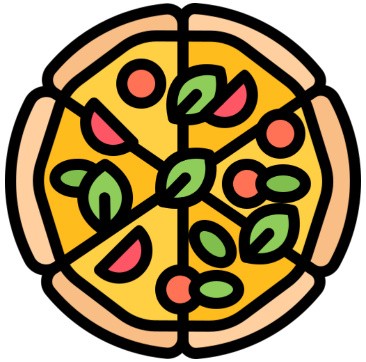
$B(S_y) \leq B(S_x)$

$B(S_y) \leq B(S_z) \leq B(S_x)$

S_x

X

S_z



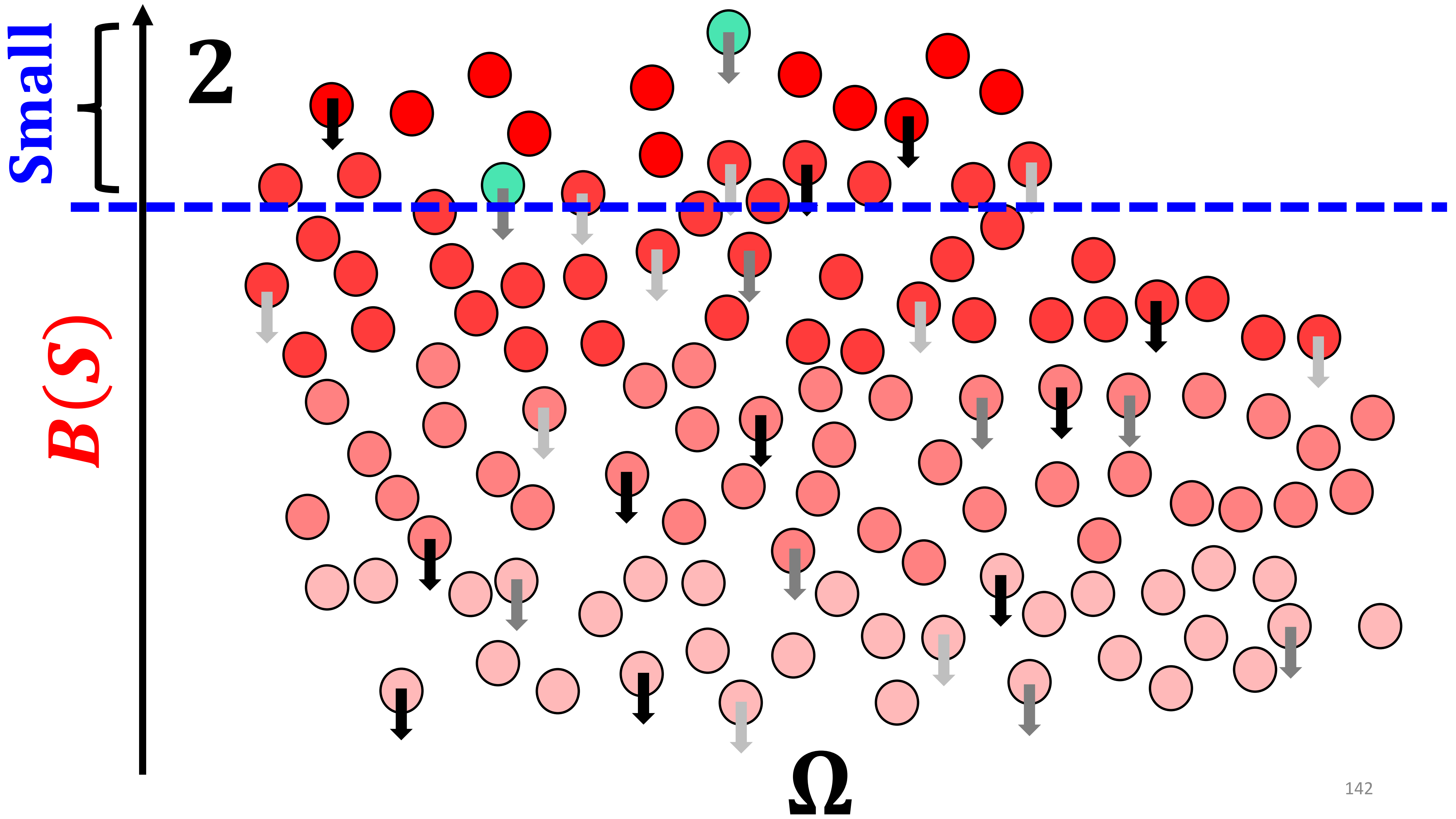
S_y

Upper bound

$$\boxed{\frac{N-c}{v(\pi)}\left(\sigma(v(\pi)) - v(\pi)\right)}$$

$$+$$

$$\boxed{N^2/16}$$



Small
2
B(S)
Ω

▶ **Lemma 28.** *For any two 2-fold rotational symmetric secondary structures, the maximum number of all distinct central internal loops is* $\sum_{s \in y} (\|A\|_s \|T\|_s + \|G\|_s \|C\|_s - \mathcal{I}_s) \leq N^2/16$, *where* $\pi = y^2$, *and* $\mathcal{I}_s$ *is an indicator function such that* $\mathcal{I}_s = \begin{cases} 1 & c > 2 \text{ and } s(1) = \overline{s(|s|)}. \\ 0 & \text{otherwise} \end{cases}$

Computational complexity of Minimum Free Energy algorithms

Level	Input Type	MFE
1	Single Strand (Maximum matching)	$O(N^3)$
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3	Multiple **unique** Strands, Bounded ($\leq$ c)	$O(N^3(c-1)!)$
4	Multiple Strands, Bounded ($\leq$ c)	?

N bases, c strands

Open problem for $\approx$ 20 years

Computational complexity of Minimum Free Energy algorithms

Level	Input Type	MFE
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2	Single Strand (Loop model)	$O(N^3)$
3	Multiple **unique** Strands, Bounded ($\leq$ c)	$O(N^3(c-1)!)$
4	Multiple Strands, Bounded ($\leq$ c)	$\mathbf{O}\left(\boldsymbol{N^4}(\mathbf{c}-\mathbf{1})!\right)$

N bases, c strands

Computational complexity of Minimum Free Energy algorithms

Level	Input Type	MFE
1	Single Strand (Maximum matching)	$O(N^3)$
2	Single Strand (Loop model)	$O(N^3)$
3	Multiple **unique** Strands, Bounded ($\leq$ c)	$O(N^3(c-1)!)$
4	Multiple Strands, Bounded ($\leq$ c)	$\mathbf{O(N^4(c-1)!)}$

N bases, c strands

Thanks

Maynooth University
National University of Ireland Maynooth

Hamilton Institute

dna.hamilton.ie

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Thanks

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