Mathematical optimization for alloimmunization prevention

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Introduction

- Why do we want to issue extensively typed RBC units?
  - **Reduces** (eliminates) transfusion-induced **allo-antibodies**
  - Hemolytic disease of the fetus or newborn
  - Problems during subsequent blood transfusions
- Preventive matching strategies are only applied for specific groups of transfusion recipients
- The ambition is to provide **extensively matched RBC units to all transfusion recipients**
- This is **though to be impossible** in practice, however **its feasibility has never been determined**!

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Goal

Investigate to which extend **transfusion-induced alloimmunization** can be **prevented by matching** for different

- inventory sizes ($n = 60, 120, 250, 1000$)
- number of units requested ($k = 1, 2, 3, 5, 10$)

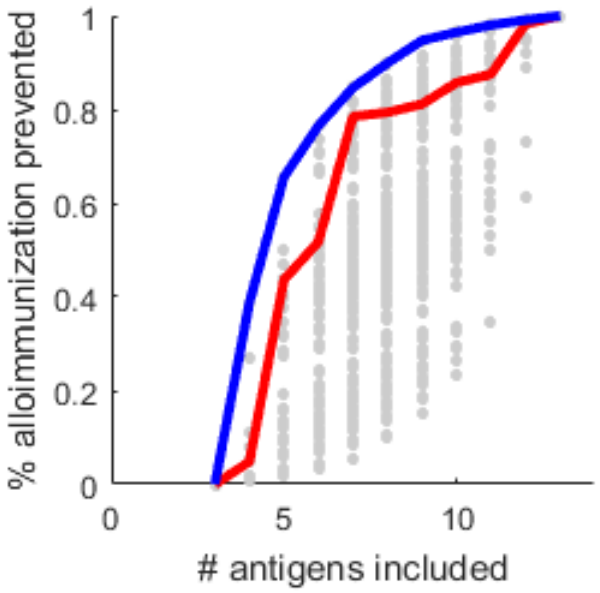
when both the **donor and transfusion recipient population are fully typed**

Two factors

1. Amount of antibodies formed against specific antigens
2. Likelihood that RBC units can be issued from a **finite inventory**

antibody	n (%)	antibody	n (%)
anti-E	177 (37%)	anti-S	8 (2%)
anti-K	122 (26%)	anti-Jk^{b}	7 (1%)
anti-Jk^{a}	50 (11%)	anti-Fy^{b}	5 (1%)
anti-c	37 (8%)	anti-e	4 (1%)
anti-Fy^{a}	24 (5%)	anti-s	0 (0%)
anti-C	22 (5%)		
anti-M	18 (4%)	All antibodies	474 (100%)

Evers et al. (2016) Lancet Haematology



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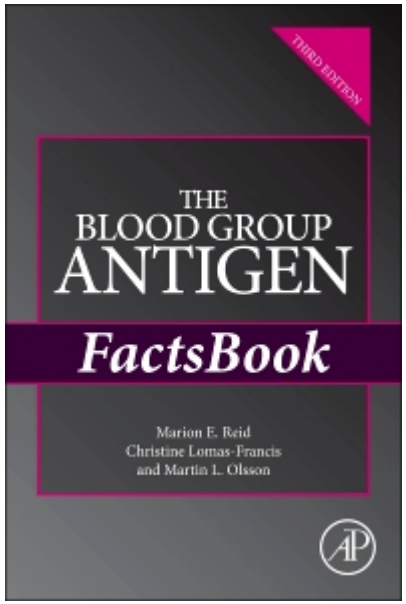
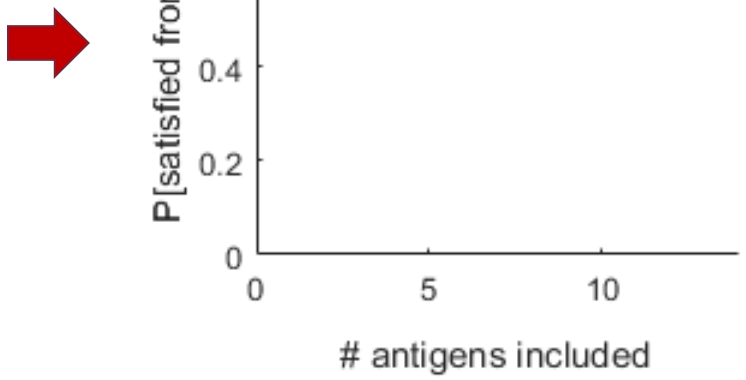


Reid et al. (2012) Academic Press



Two factors

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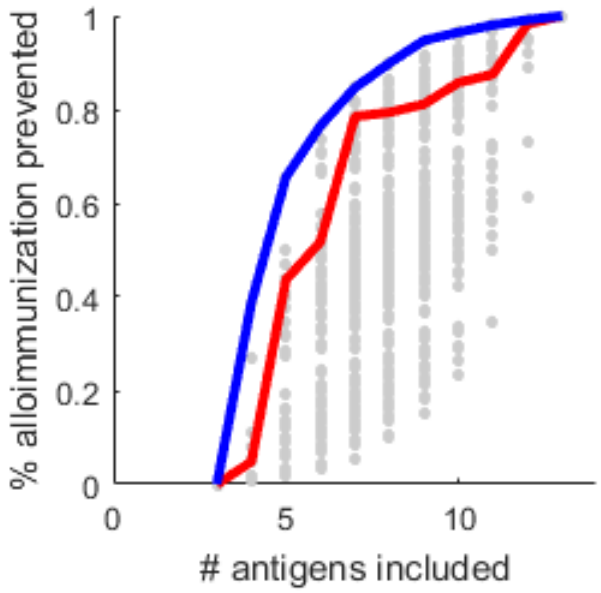

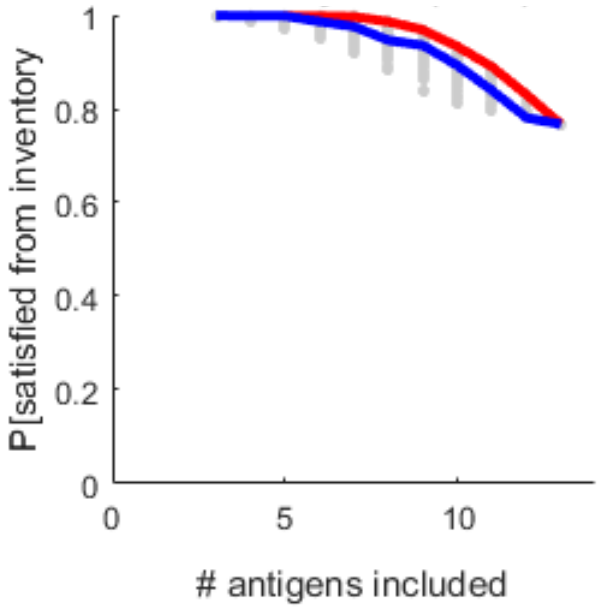

Practical optimization model

- Based on
    1. Amount of antibodies formed
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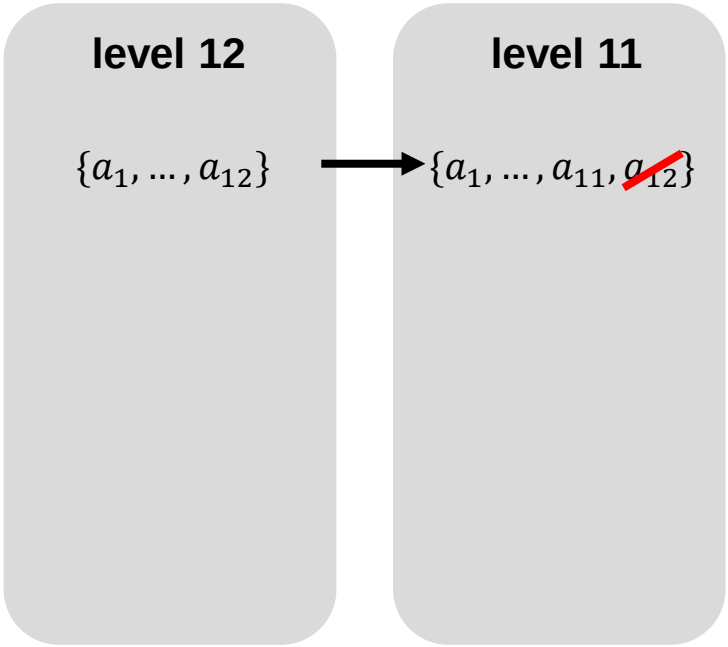

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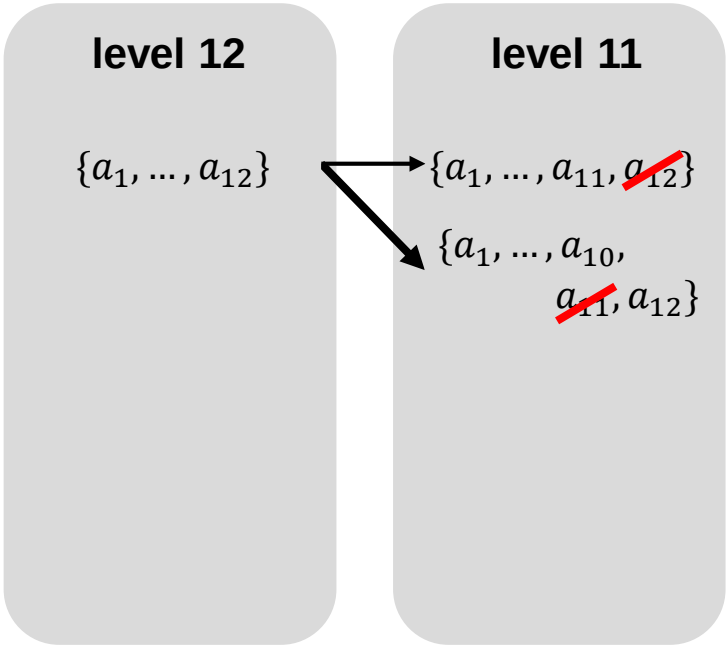

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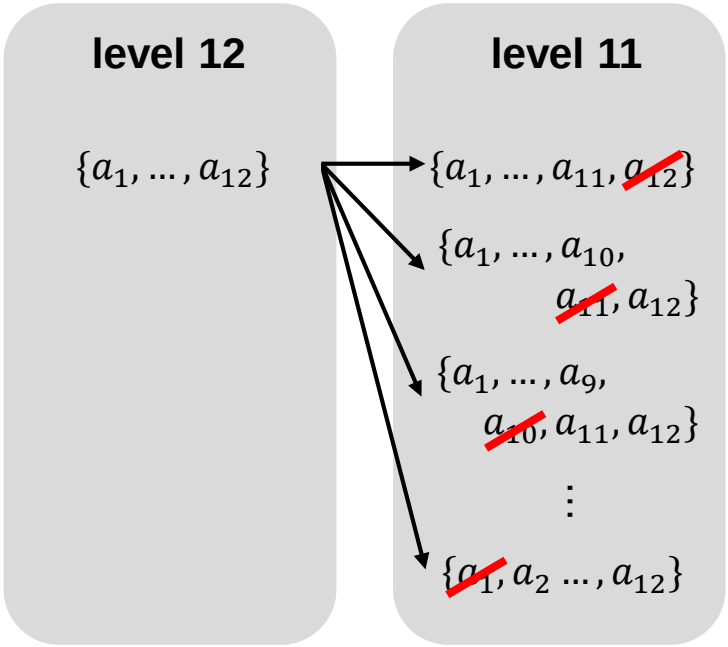

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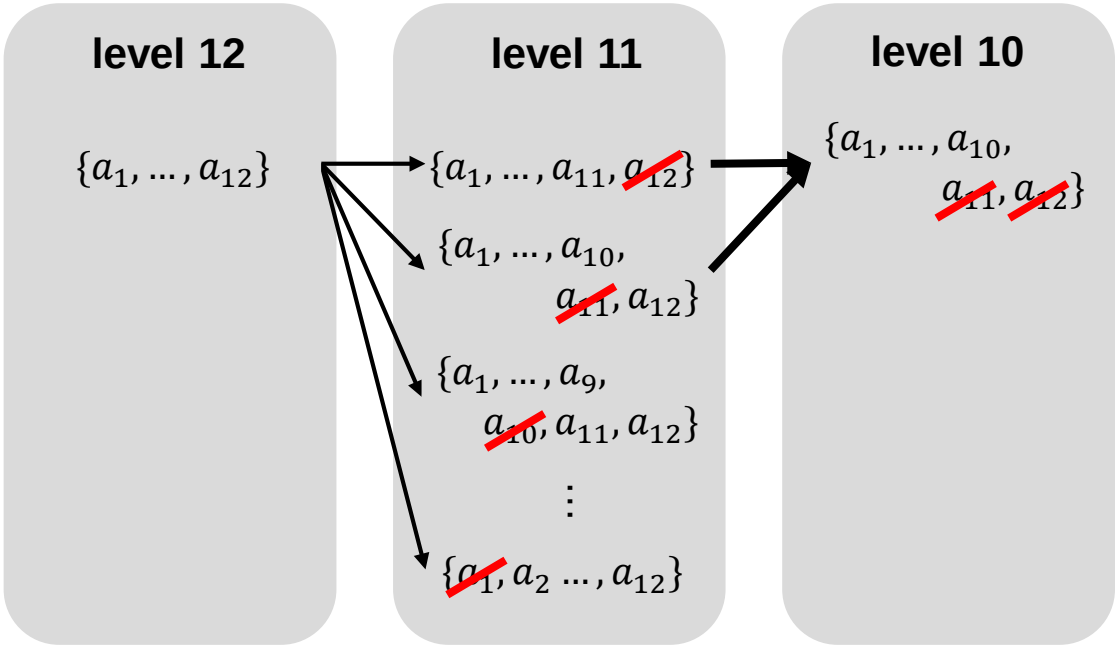

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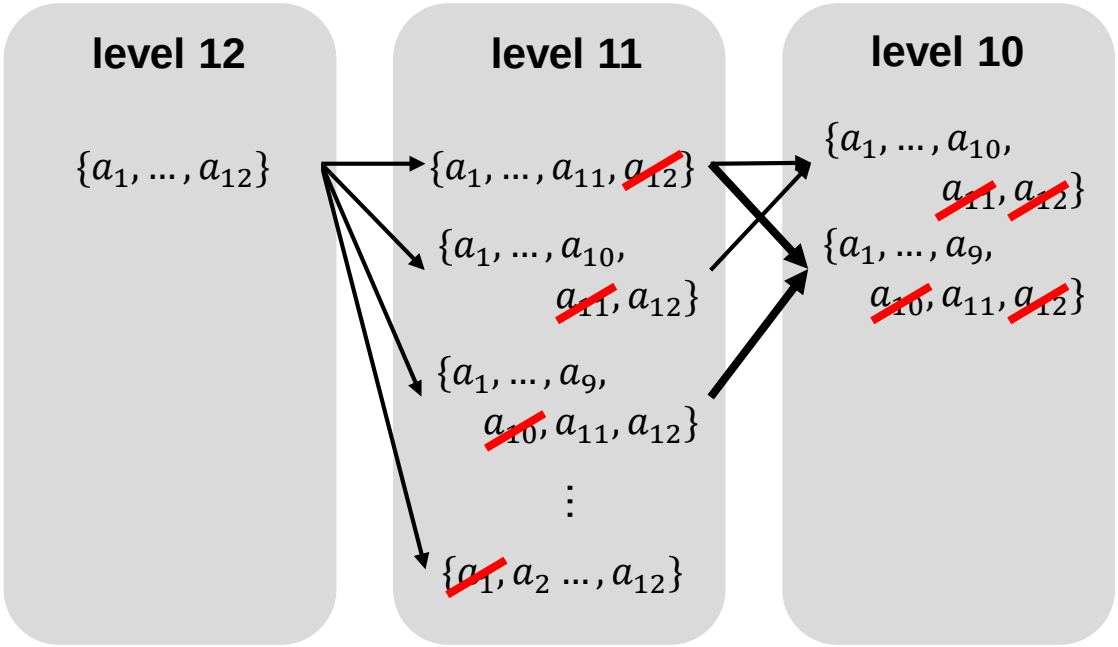

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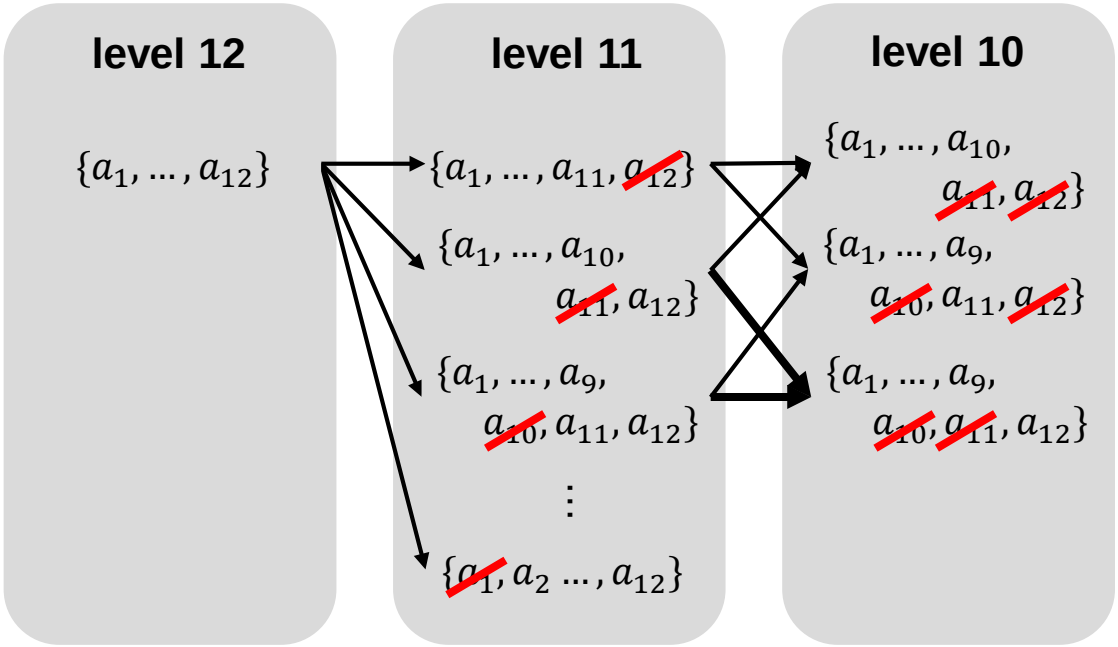

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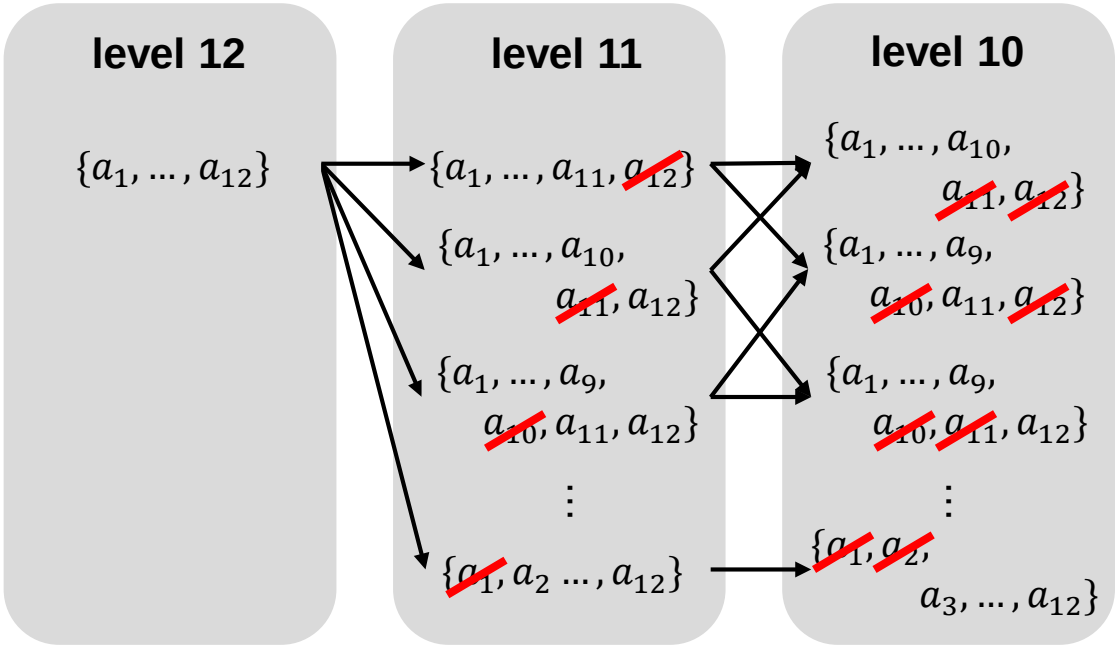

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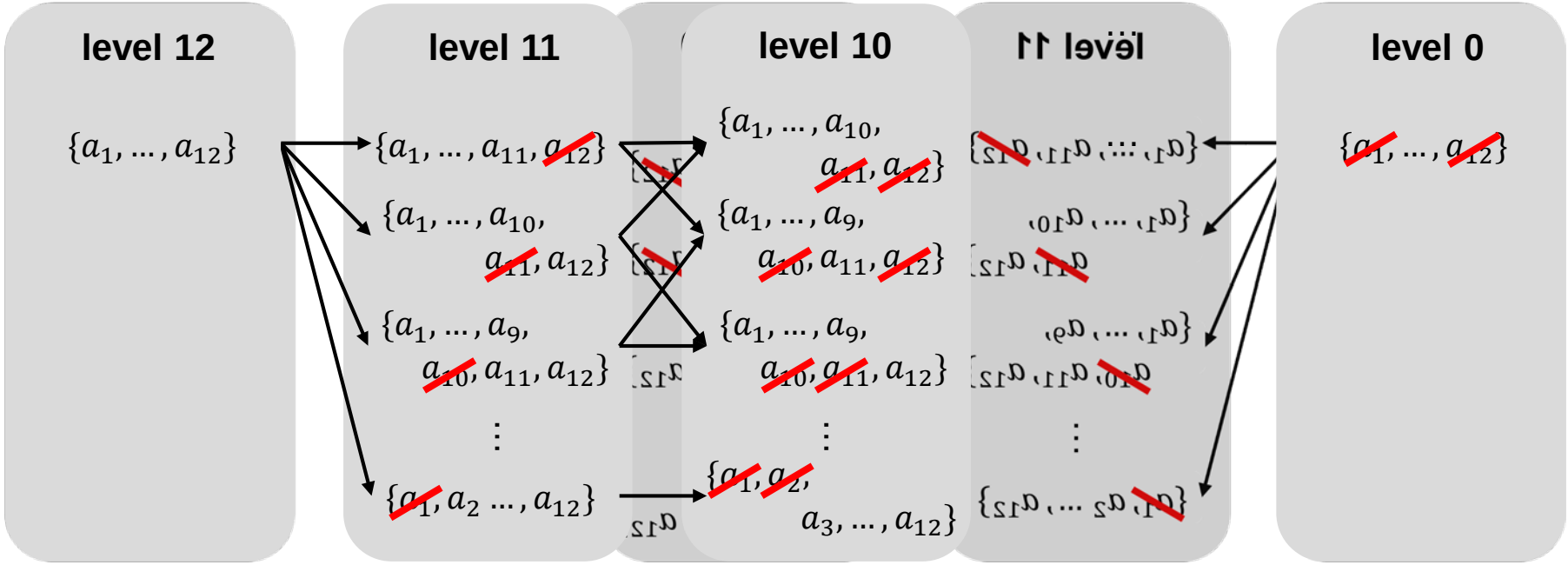

Mathematical optimization model

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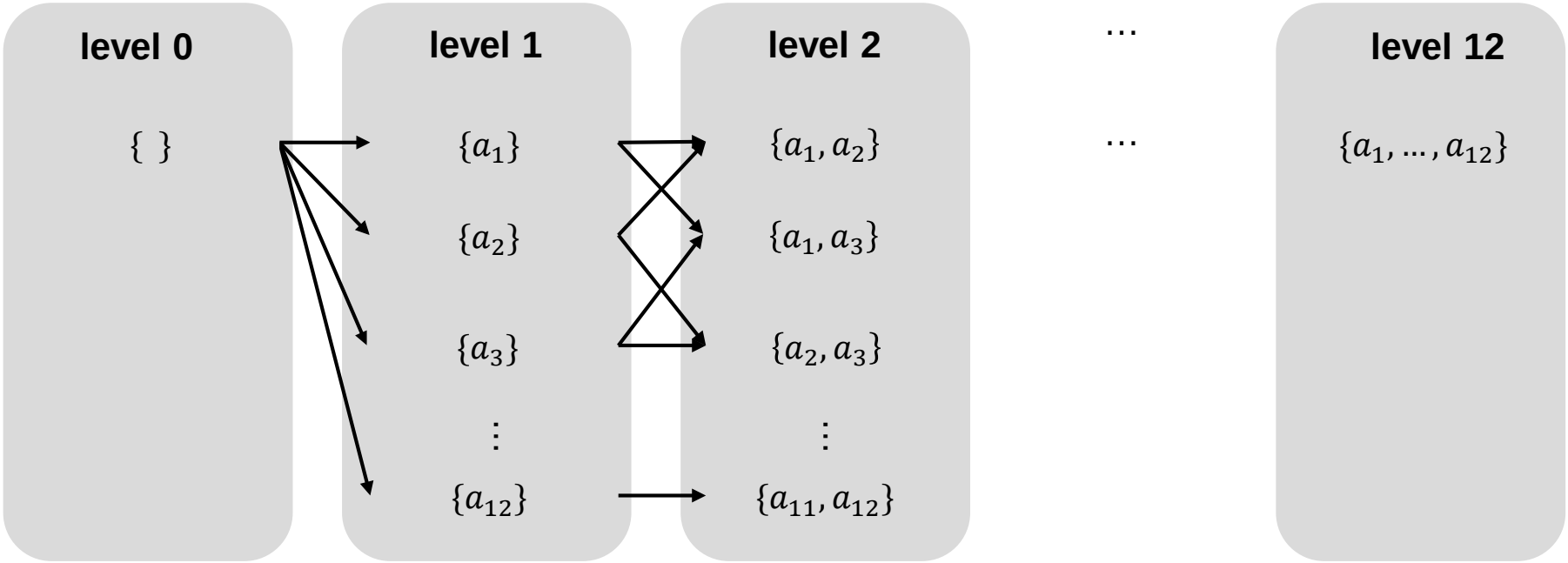

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Mathematical optimization model

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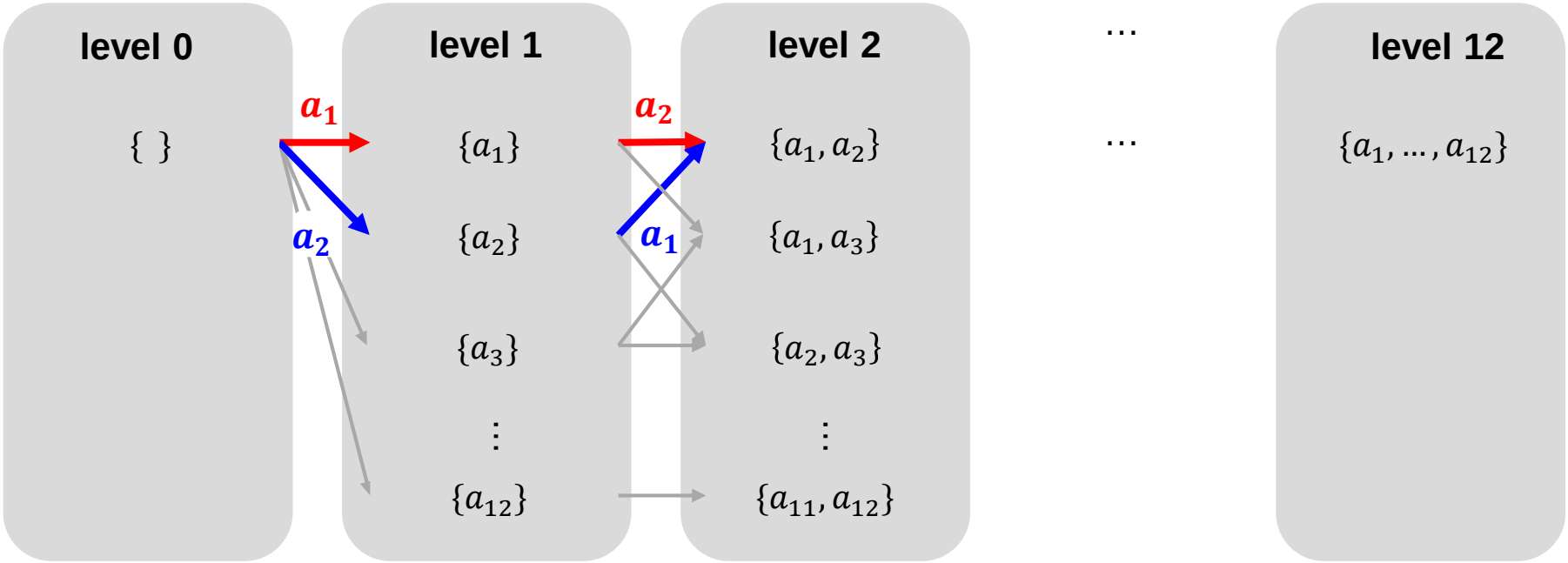

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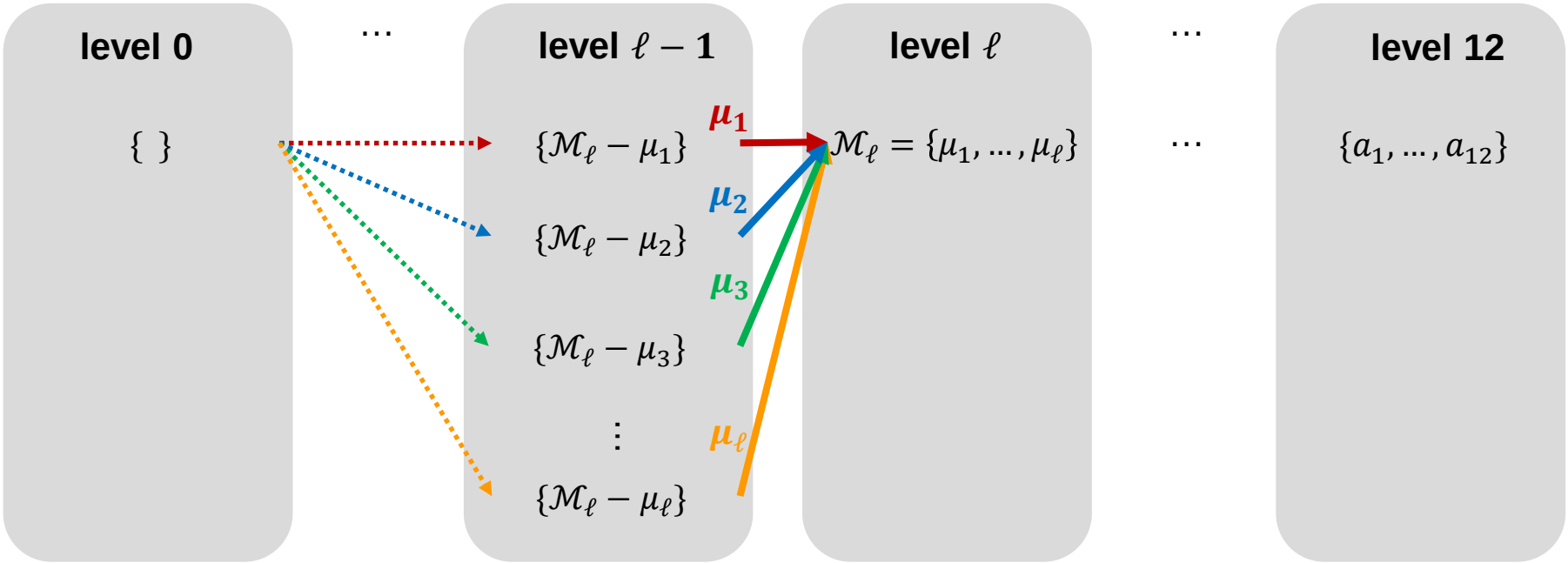

$$\underbrace{V(\mathcal{M}_\ell)}_{\ell \text{ antigens}} = \max_{i=1,\dots,\ell} \left\{ \underbrace{V(\mathcal{M}_\ell - \mu_i)}_{\ell-1 \text{ antigens}} + \underbrace{r_{\mathcal{M}_\ell}(\mu_i)}_{1 \text{ antigens}} \right\}$$

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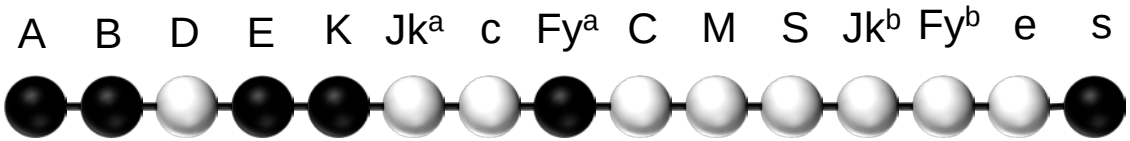
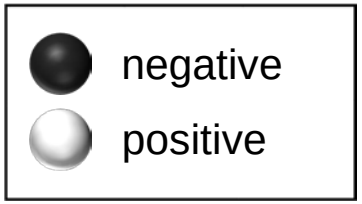
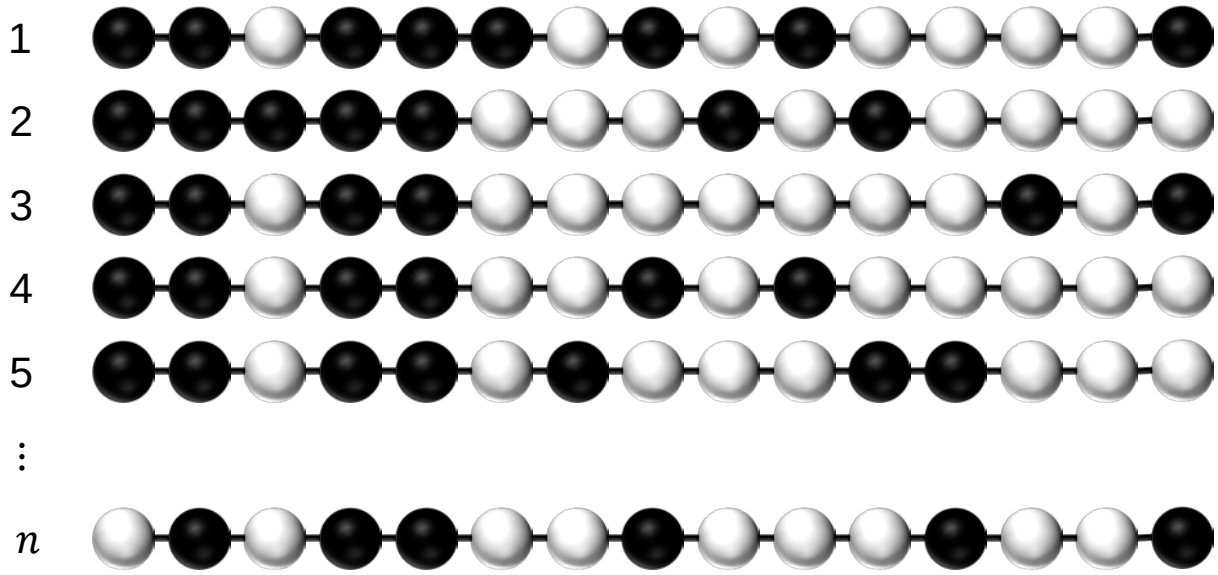
Issuing policy

Requested: O, E-neg, K-neg, Fy^{a}-neg, s-neg





Inventory:



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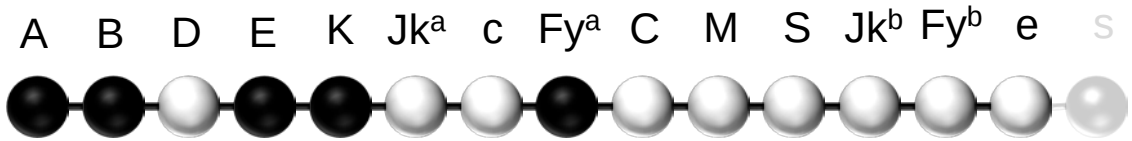

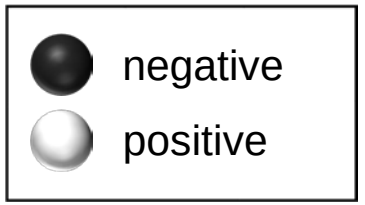

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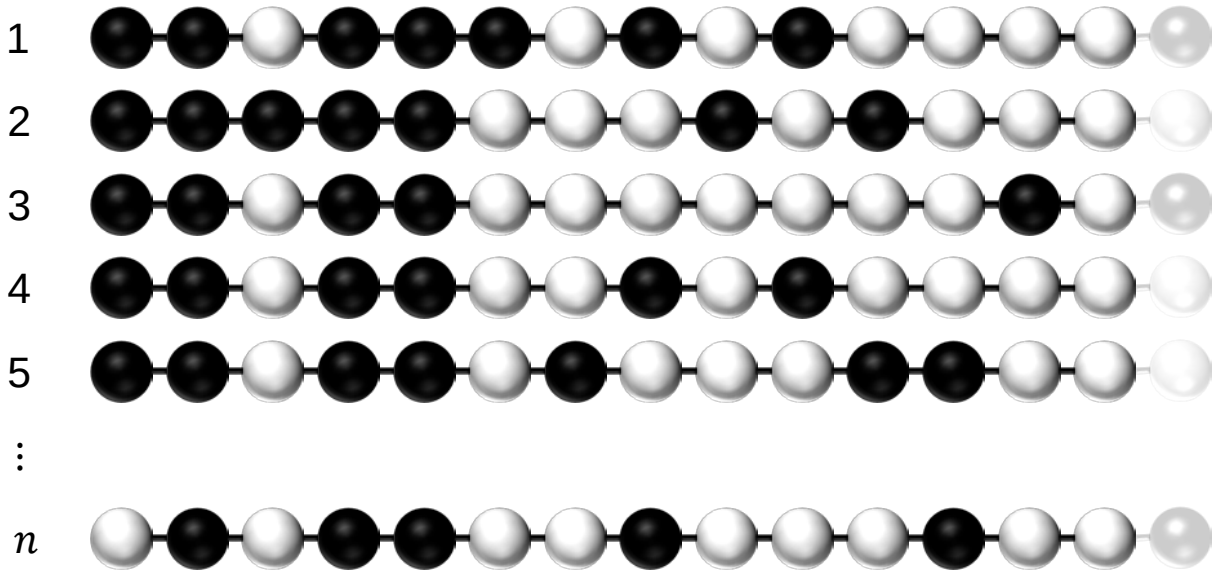

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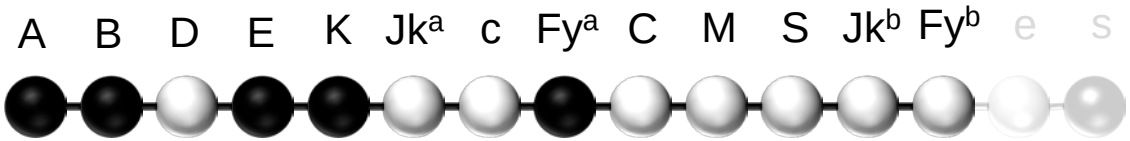

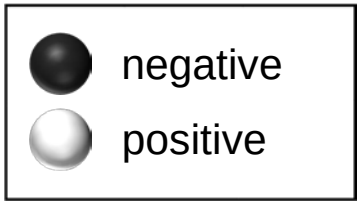

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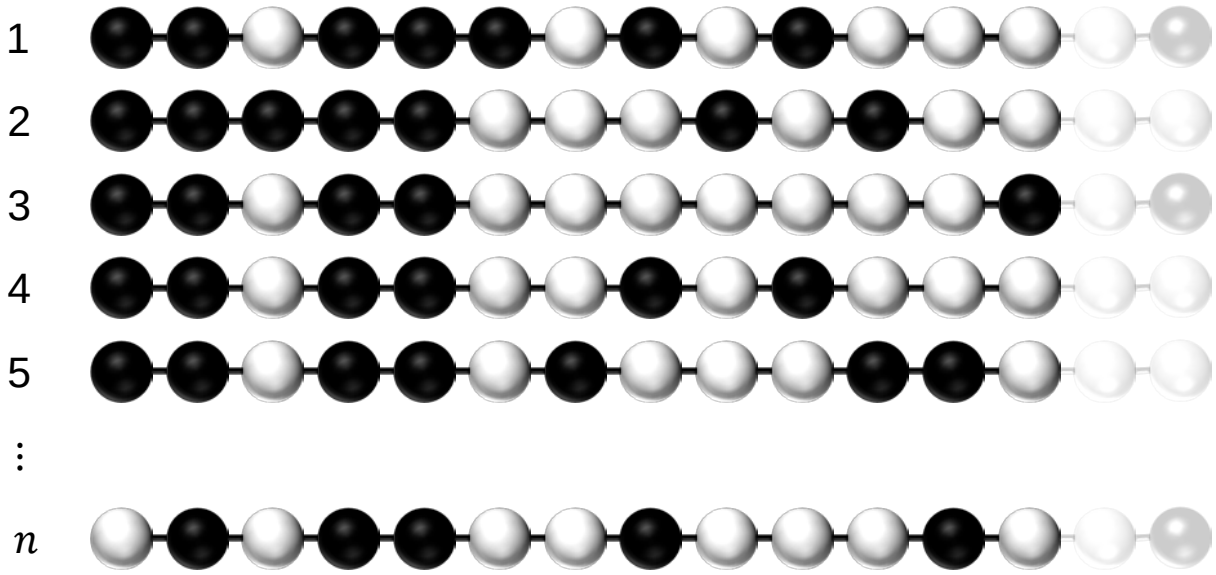

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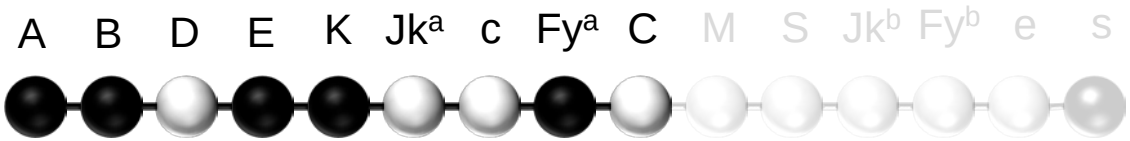

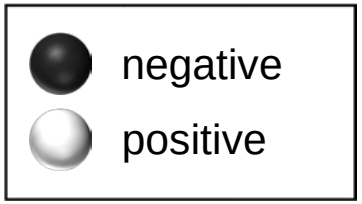

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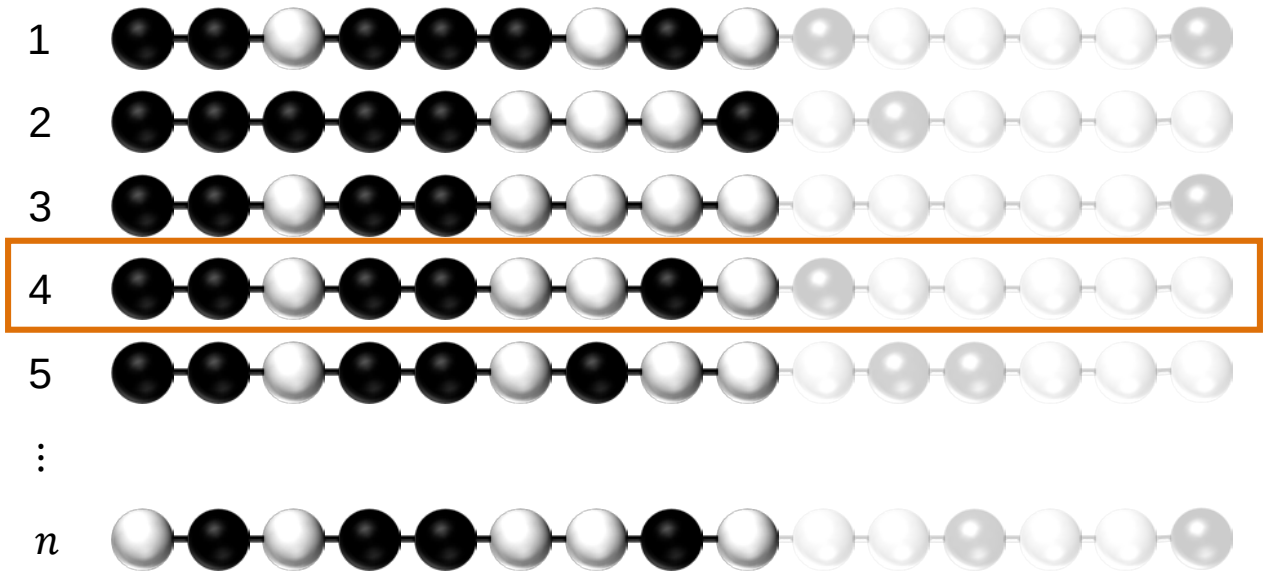

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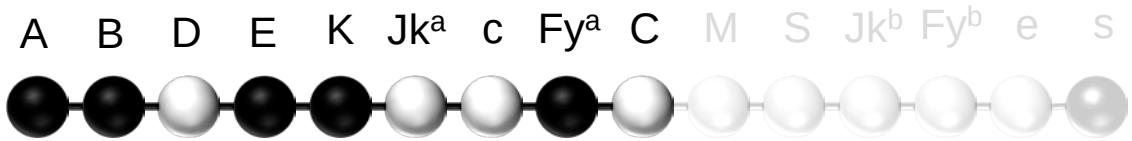
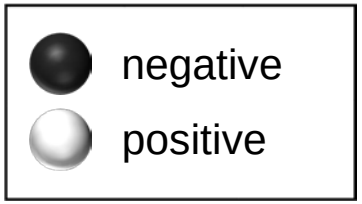
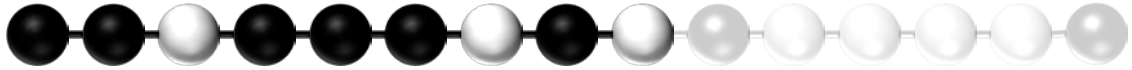


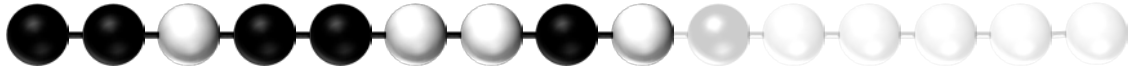


Inventory:

1



4



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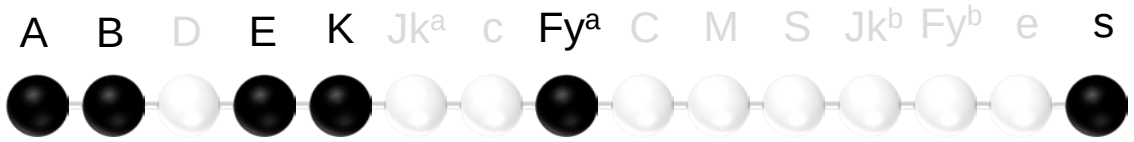

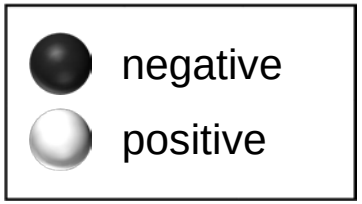

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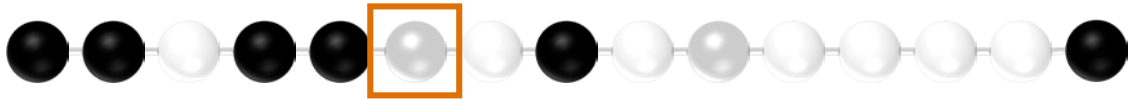
1



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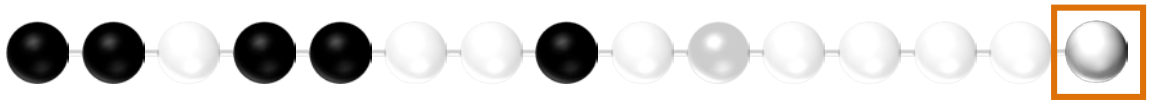
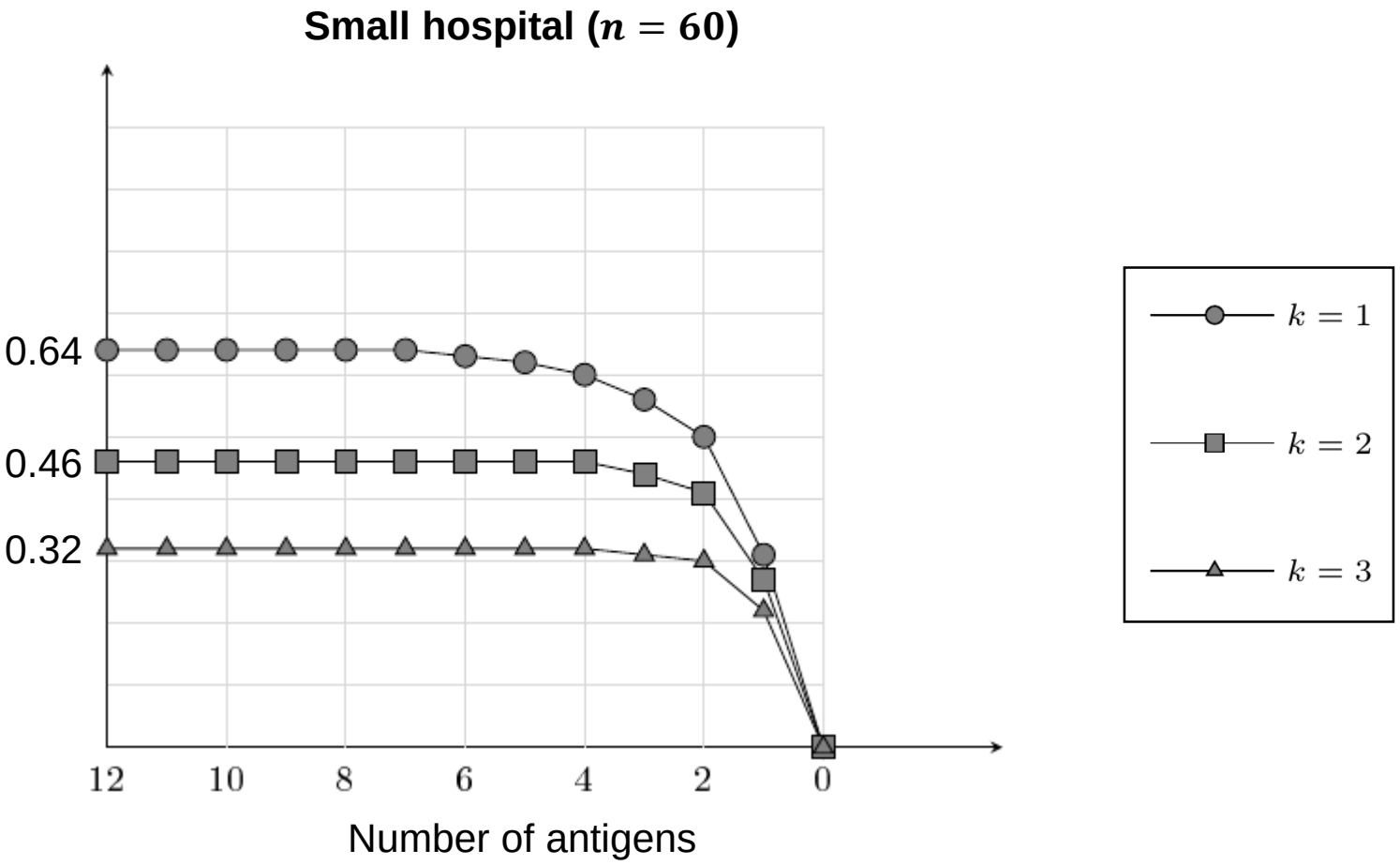
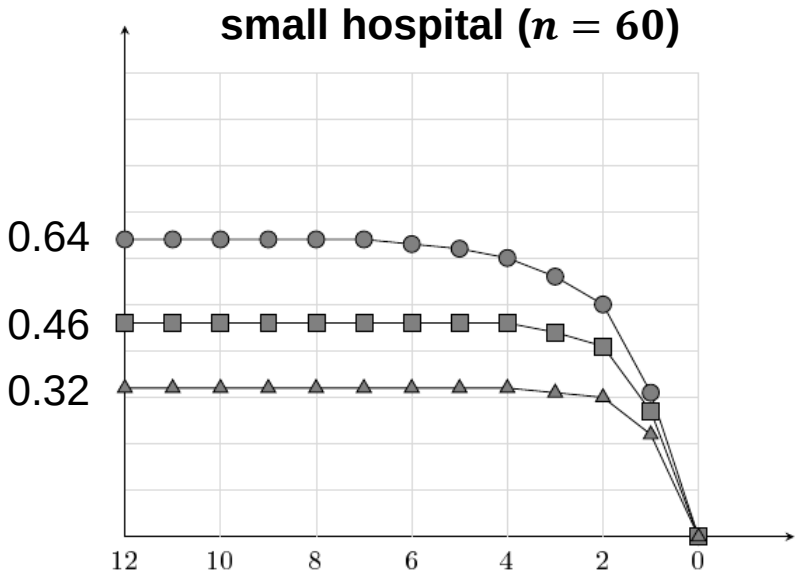
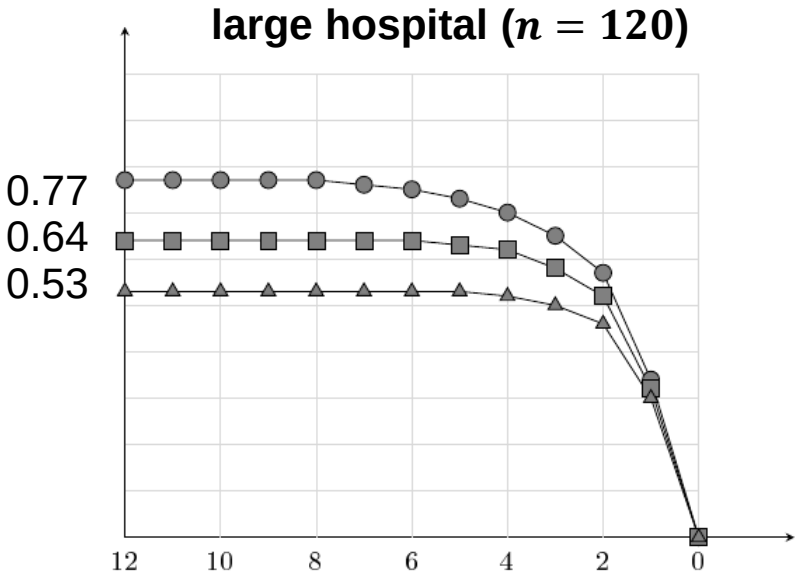
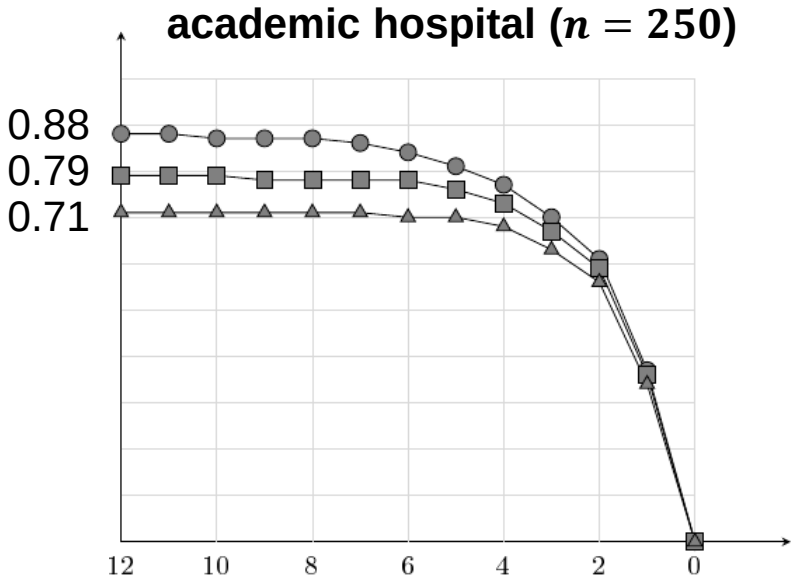


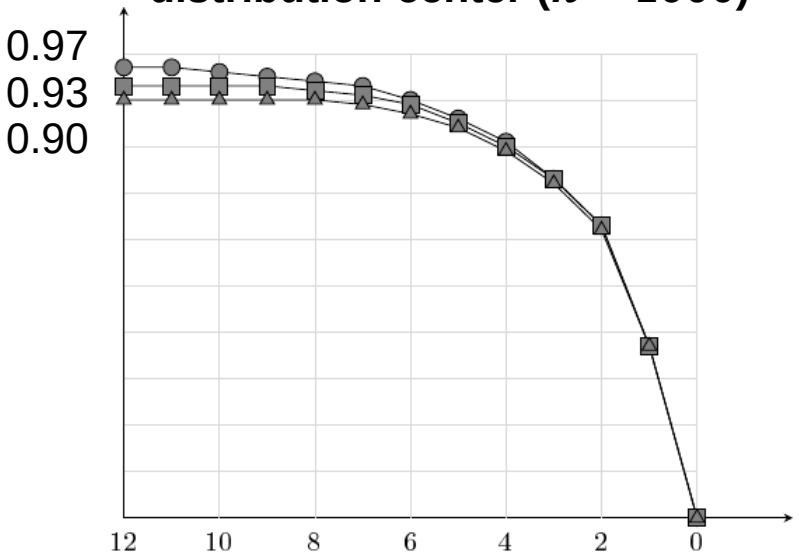
Proportion of alloimmunization prevented




small hospital ($n = 60$)
0.64
0.46
0.32
12
10
8
6
4
2
0


large hospital ($n = 120$)
0.77
0.64
0.53
12
10
8
6
4
2
0


academic hospital ($n = 250$)
0.88
0.79
0.71
12
10
8
6
4
2
0


distribution center ($n = 1000$)
0.97
0.93
0.90
12
10
8
6
4
2
0

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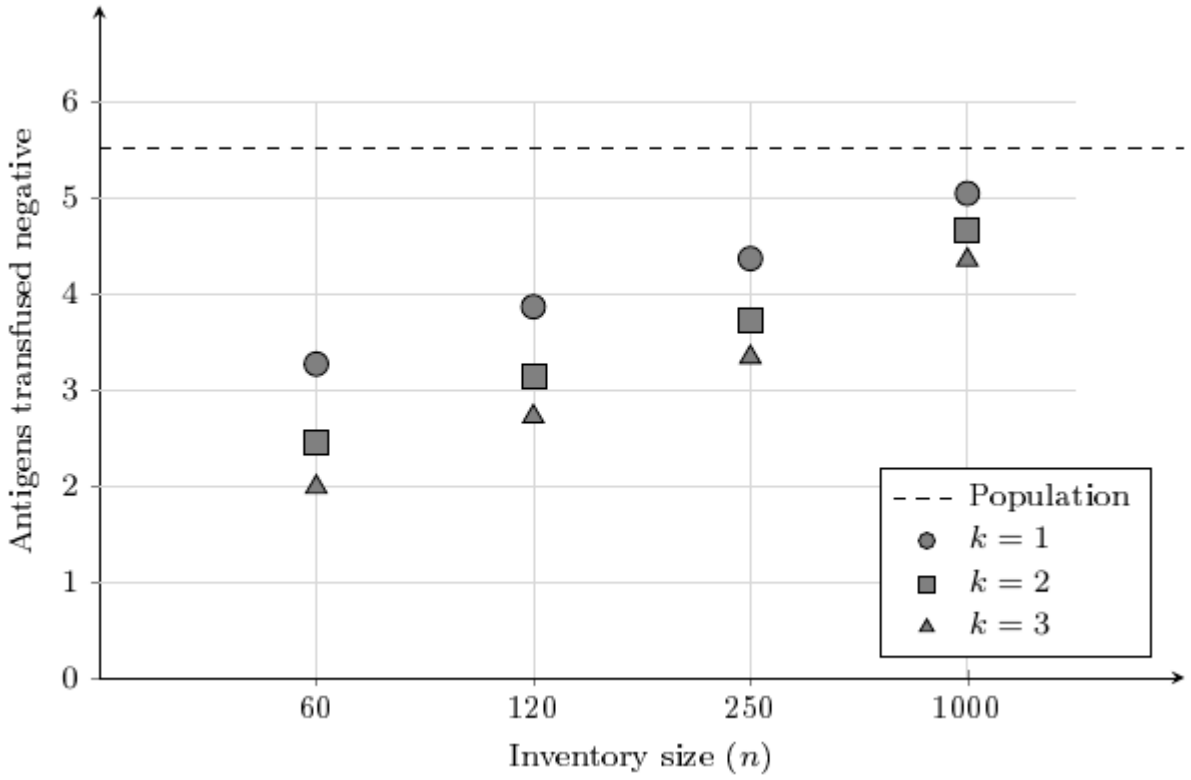
Average number of antigens negative

- Individual is on average **negative for 5.51 / 16 antigens**



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Conclusions

- If all donors and transfusion recipients are fully typed, **extensive preventive matching** for all transfusion recipients **is feasible**

- Alloimmunization prevented:

		number of units requested (k)		
		1	**2**	**3**
Inventory size (n)	**60**	64%	46%	32%
	120	77%	64%	53%
	250	88%	79%	71%
	1000	97%	93%	90%

- Optimal order: (transfusion recipients **typed for a limited number of antigens**)

*	1	2	3	4	5	6	7	8	9	10	11	12
ABD	E	K	Jk^a	c	C	Fy^a	e	M	S	Jk^b	Fy^b	s

Summary

antibody	n (%)	antibody	n (%)
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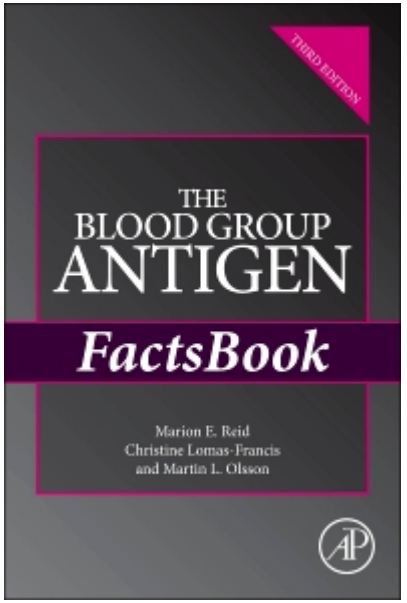

*	1	2	3	4	5	6	7	8	9	10	11	12	13
ABD	E	K	Jk^a	c	C	Fy^a	e	M	S	Jk^b	Fy^b	s	k

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Mathematical optimization for alloimmunization prevention

Thank you for your attention!

Questions?