Can we spend our way out of the AIDS epidemic?

Robert Smith?

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Using math to solve real problems

Biological problem

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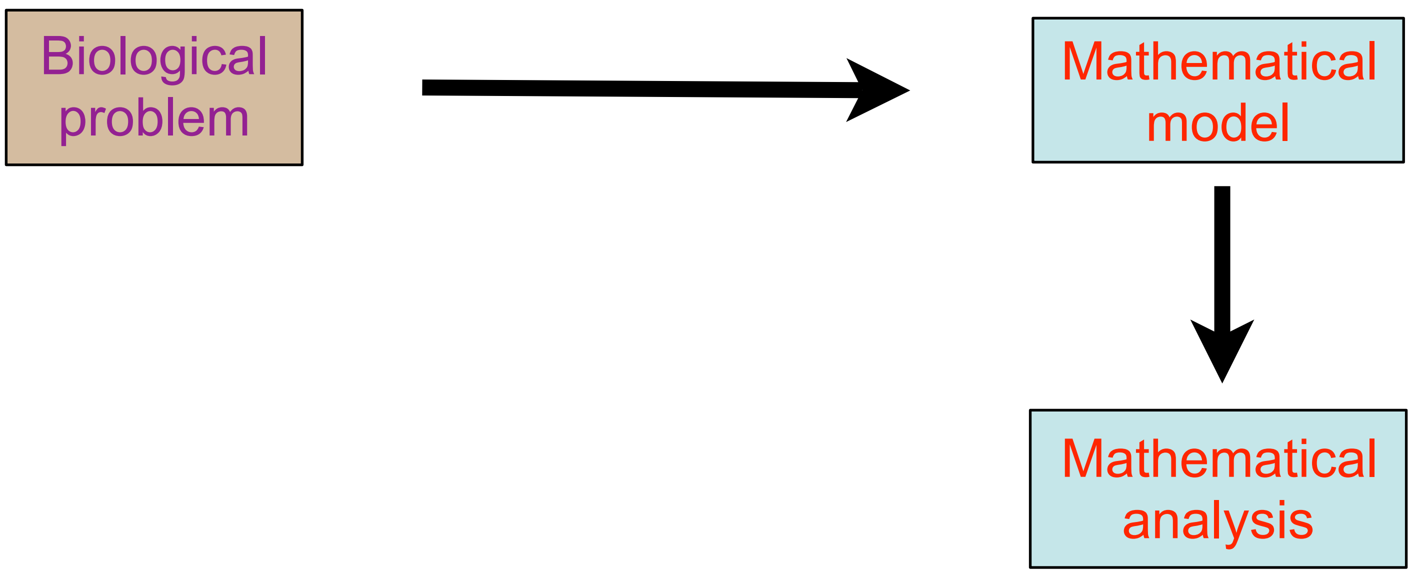

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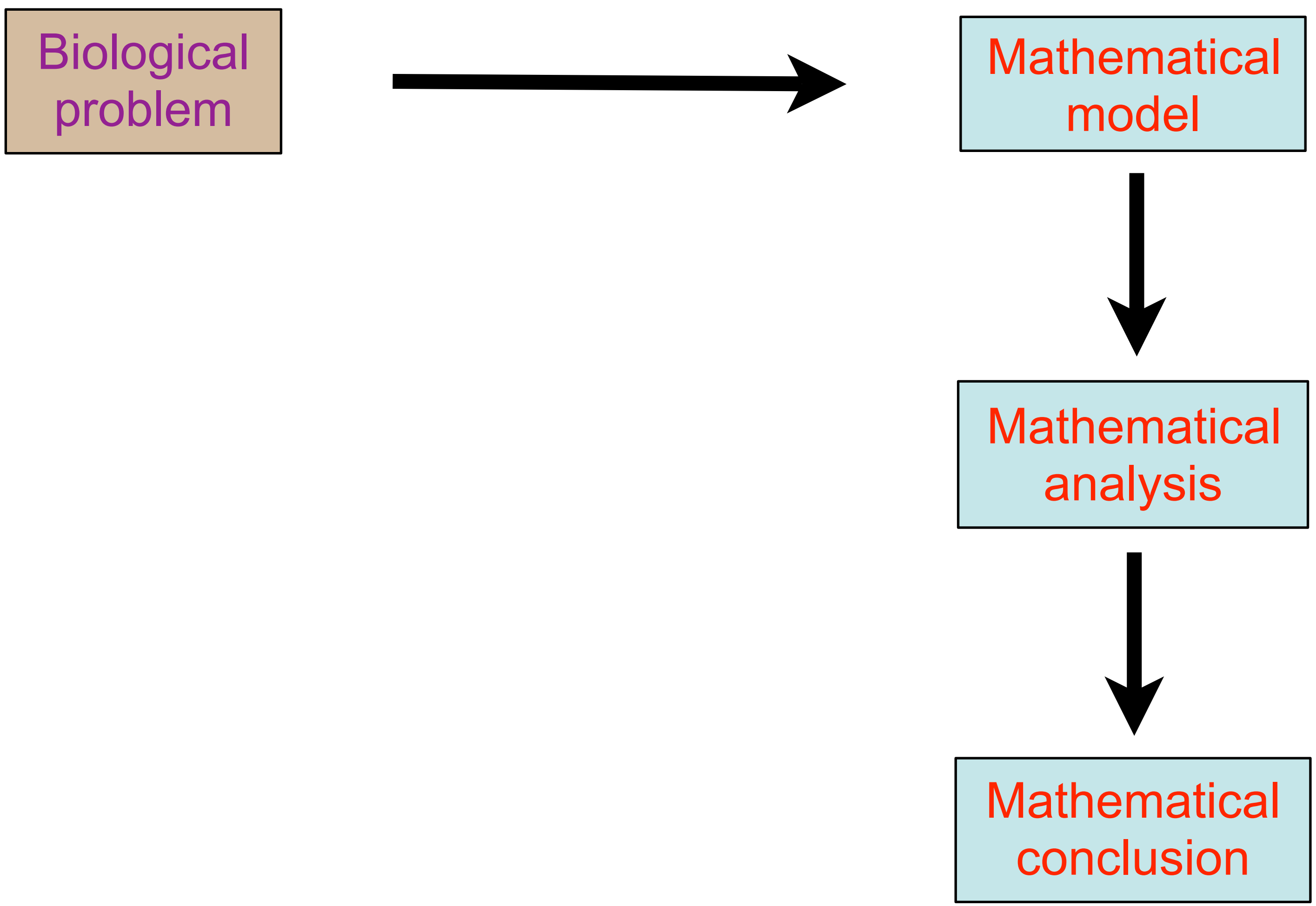

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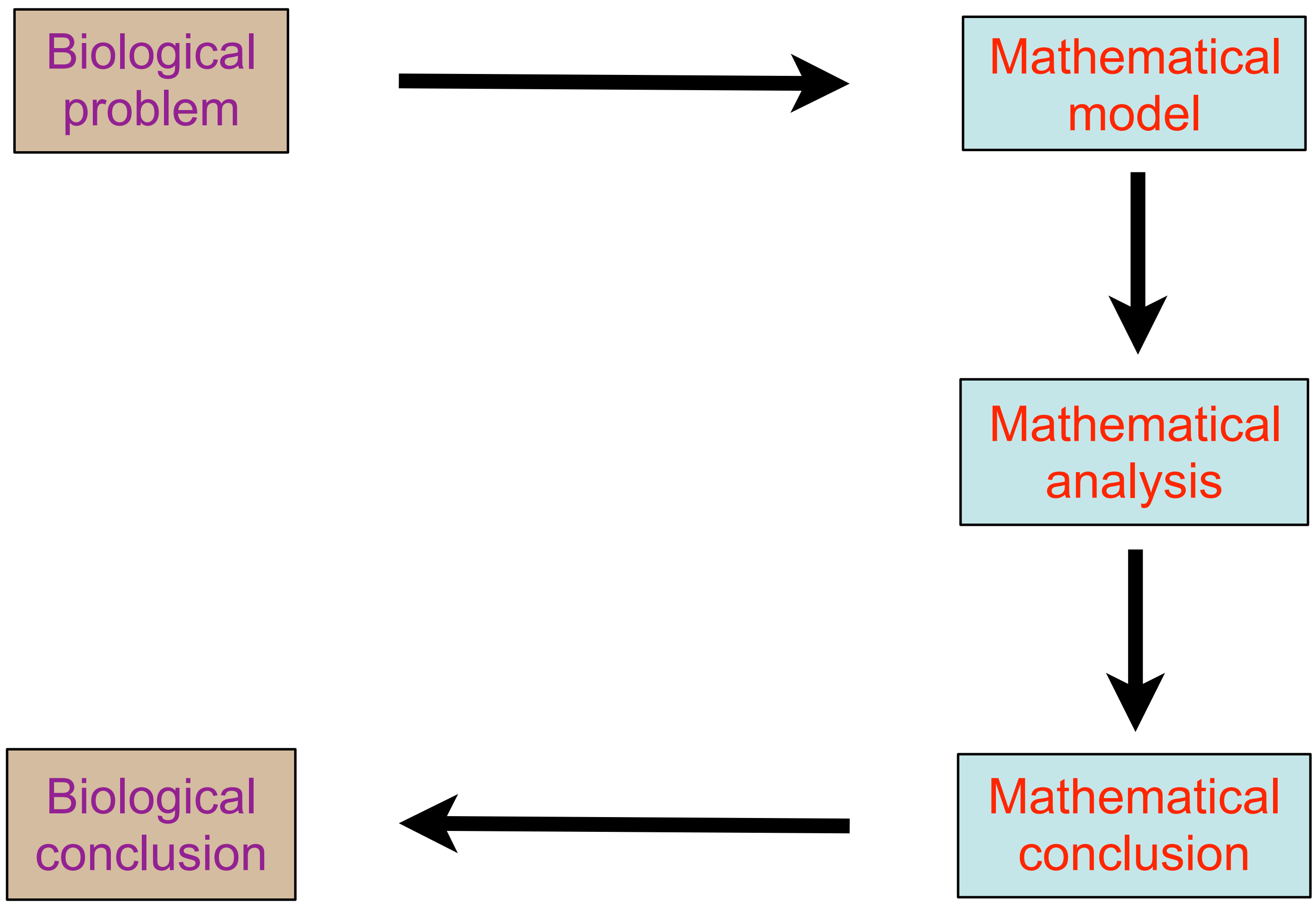

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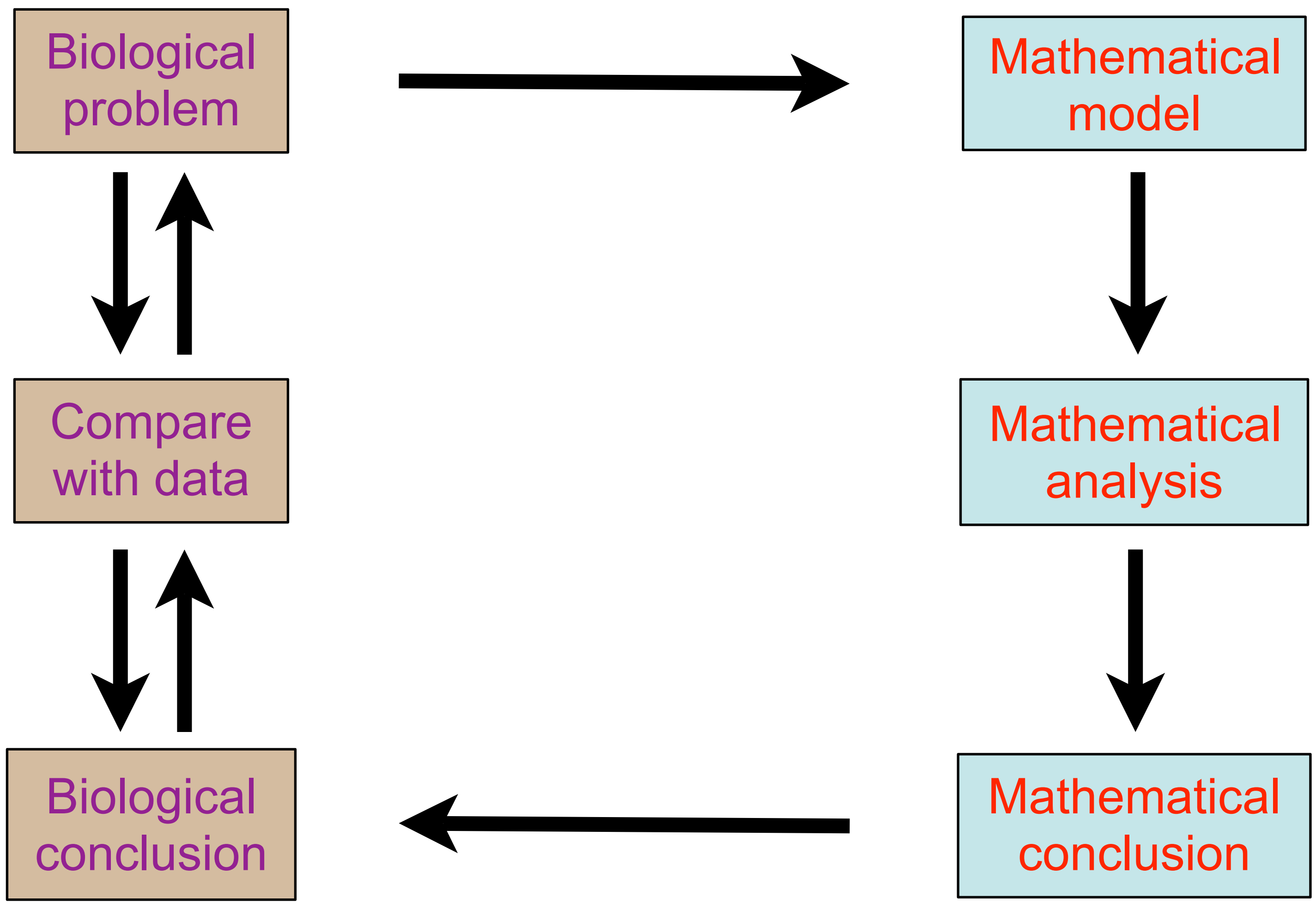

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"All models are wrong... but some are useful"
- George Box.

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- Defined as “the average number of secondary infections caused by a single infectious individual during their entire infectious lifetime.”

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"One of the foremost and most valuable ideas that mathematical thinking has brought to epidemic theory"

(Heesterbeek & Dietz, 1996).

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  - number of individuals infected within a single infected individual's entire infectious lifetime (epidemiology)
  - number of newly infected cells produced by a single infected cell
    (in-host dynamics).

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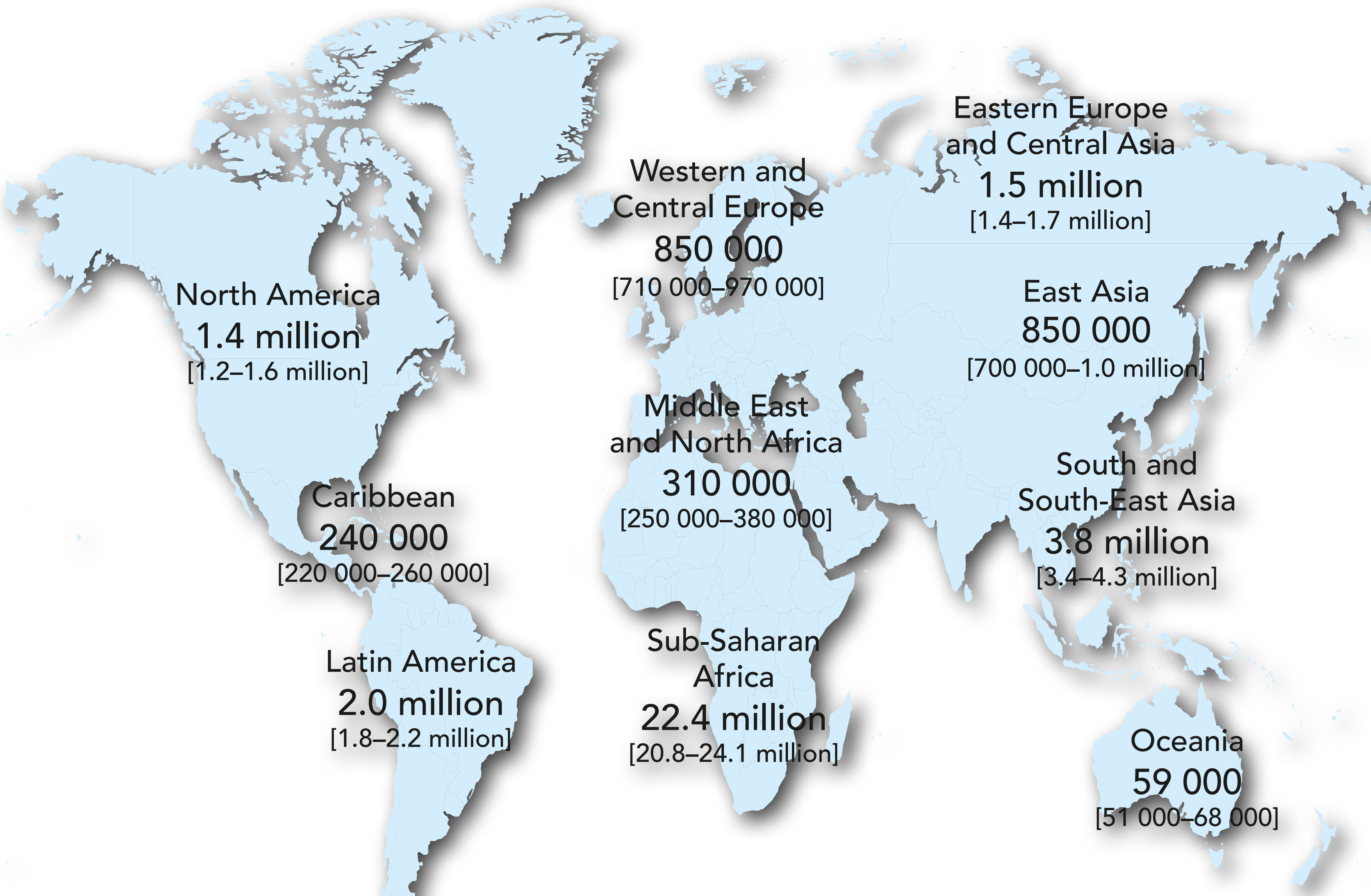
- This allows us to determine the effectiveness of control measures.

Adults and Children estimated to be living with HIV, 2008



Total: 33.4 million (31.1 -35.8 million)

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- Present plans are to hold the money in reserve and spent it slowly over 20 years
- What if we spend it all at once?

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- R_0 is a threshold parameter that determines whether a disease will remain endemic or be eradicated
- (The value calculated by mathematical models is an eradication threshold, not necessarily the average number of secondary infections).

Some issues

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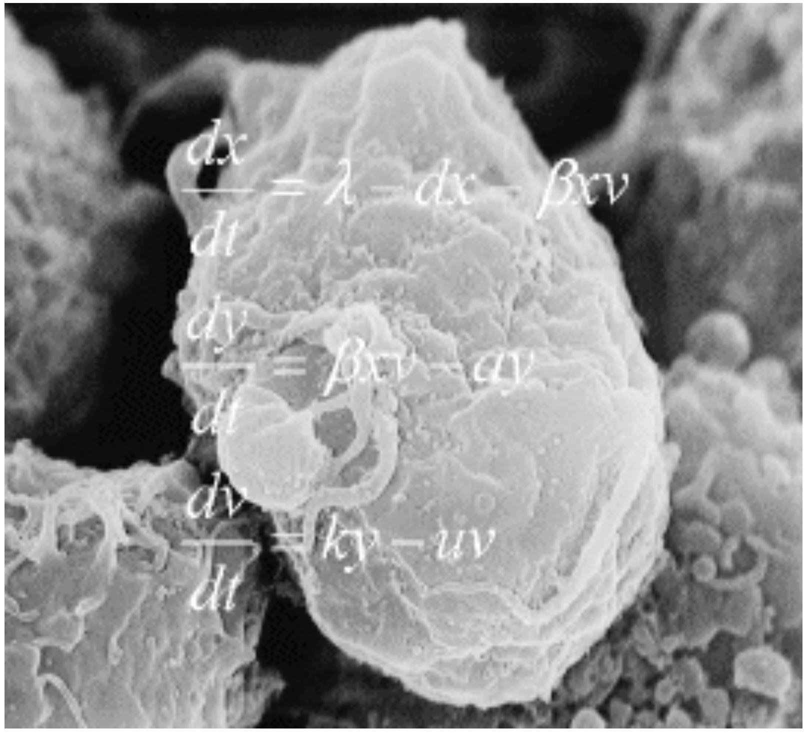

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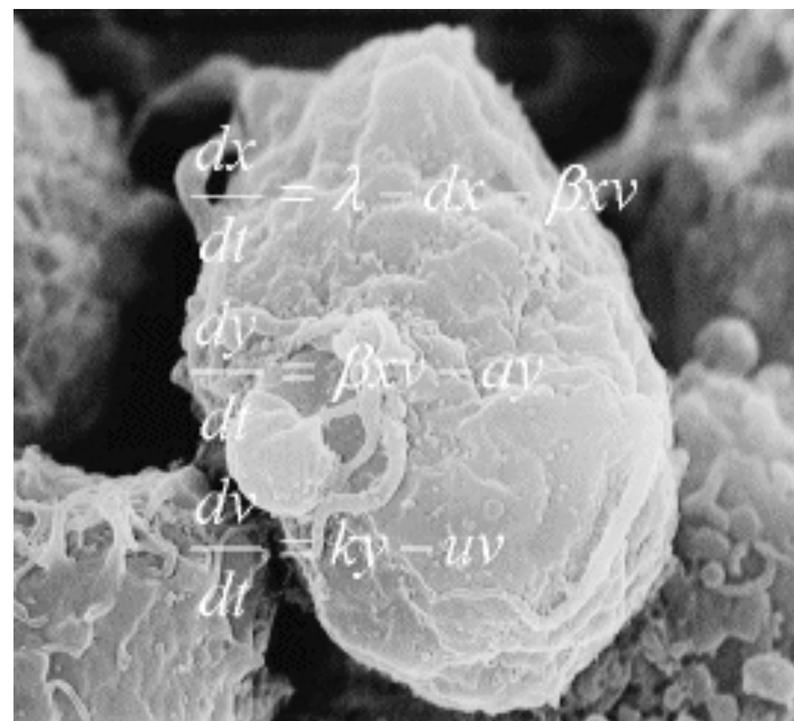

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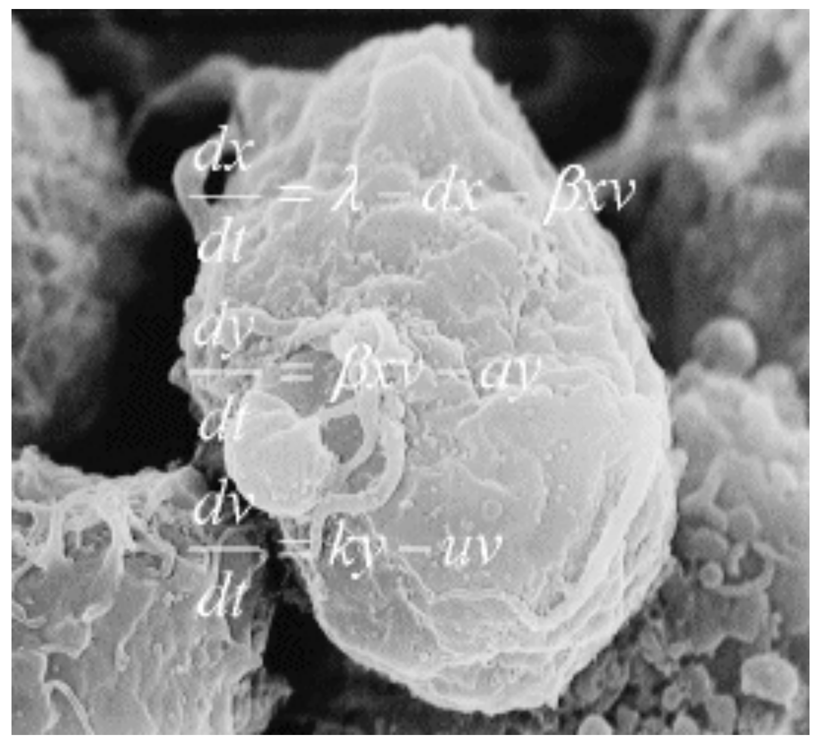

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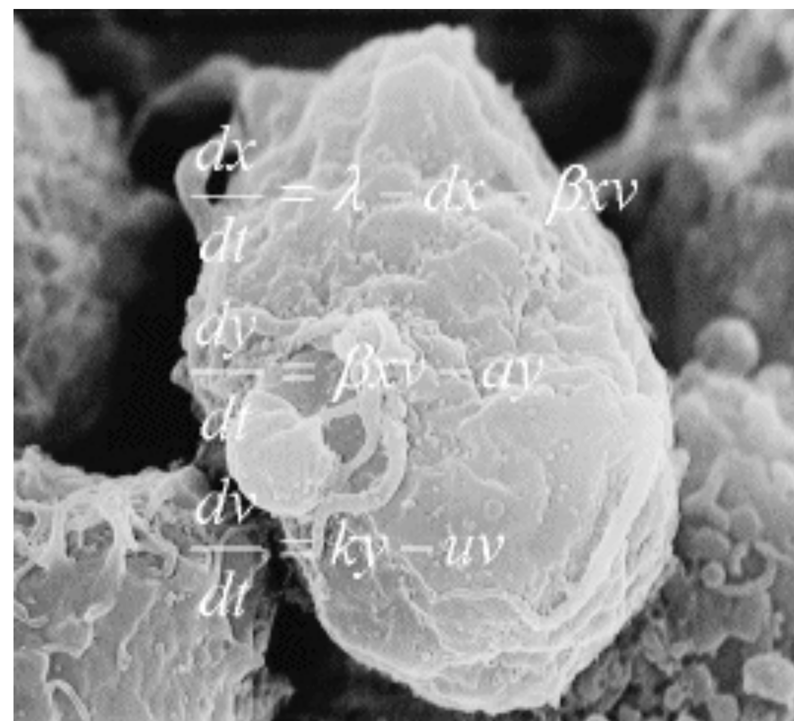

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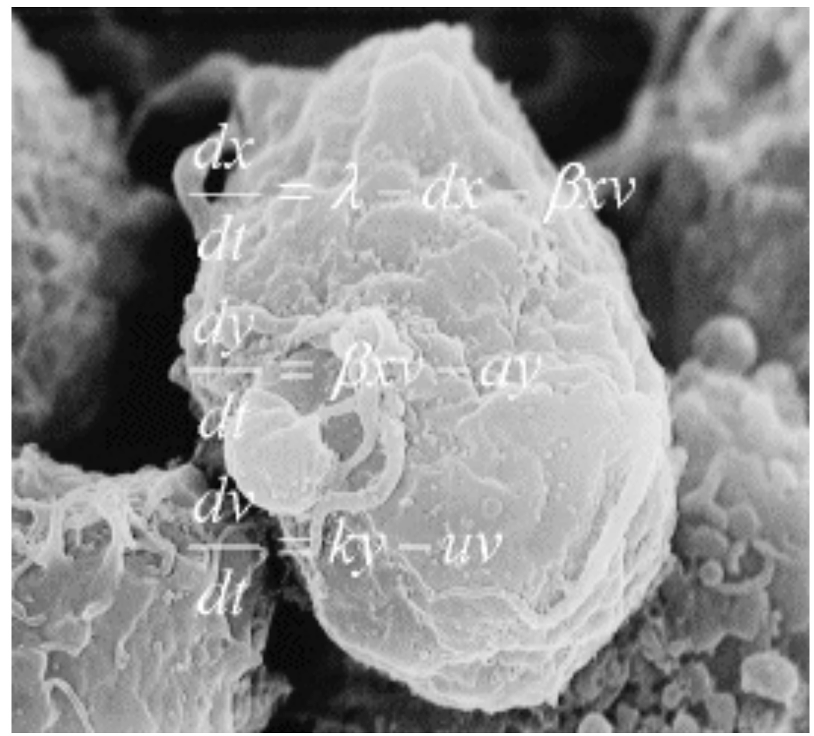

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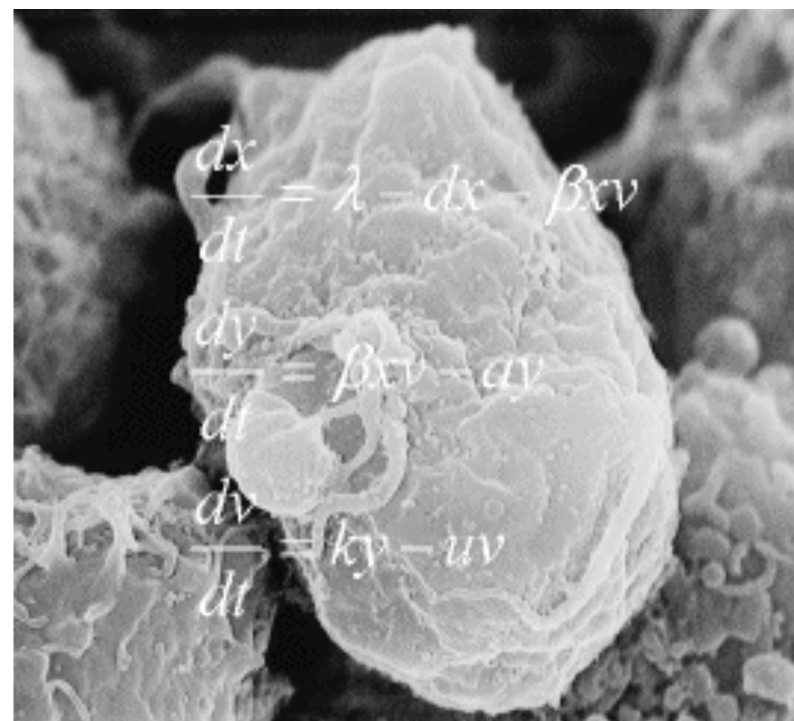
  - Surprisingly, no.



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- ...if it has the same eradication threshold as the more complicated model.

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$$T_0 = e^{s(\mathbf{K})}.$$

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- They depend, at a minimum, on the behaviour of susceptibles and their interaction with those infected
- Thus, this model does not capture the transient dynamics of infection and interaction.

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- If the disease-free equilibrium is stable, it's globally stable
- In this case, the disease will be eradicated.

SI model

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$$\frac{dS}{dt} = \Lambda - \beta S I - \mu S$$

$$\frac{dI}{dt} = \beta S I - \mu I - \gamma I$$

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$$\left(\frac{\Lambda}{\mu}, 0\right) \text{ and } \left(\frac{\mu+\gamma}{\beta}, \frac{\Lambda}{\mu} - \frac{\mu+\gamma}{\beta}\right).$$

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- This is π_i in our linear model.

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- It follows that there will be eradication in the linear model if and only if there is eradication in the SI model.

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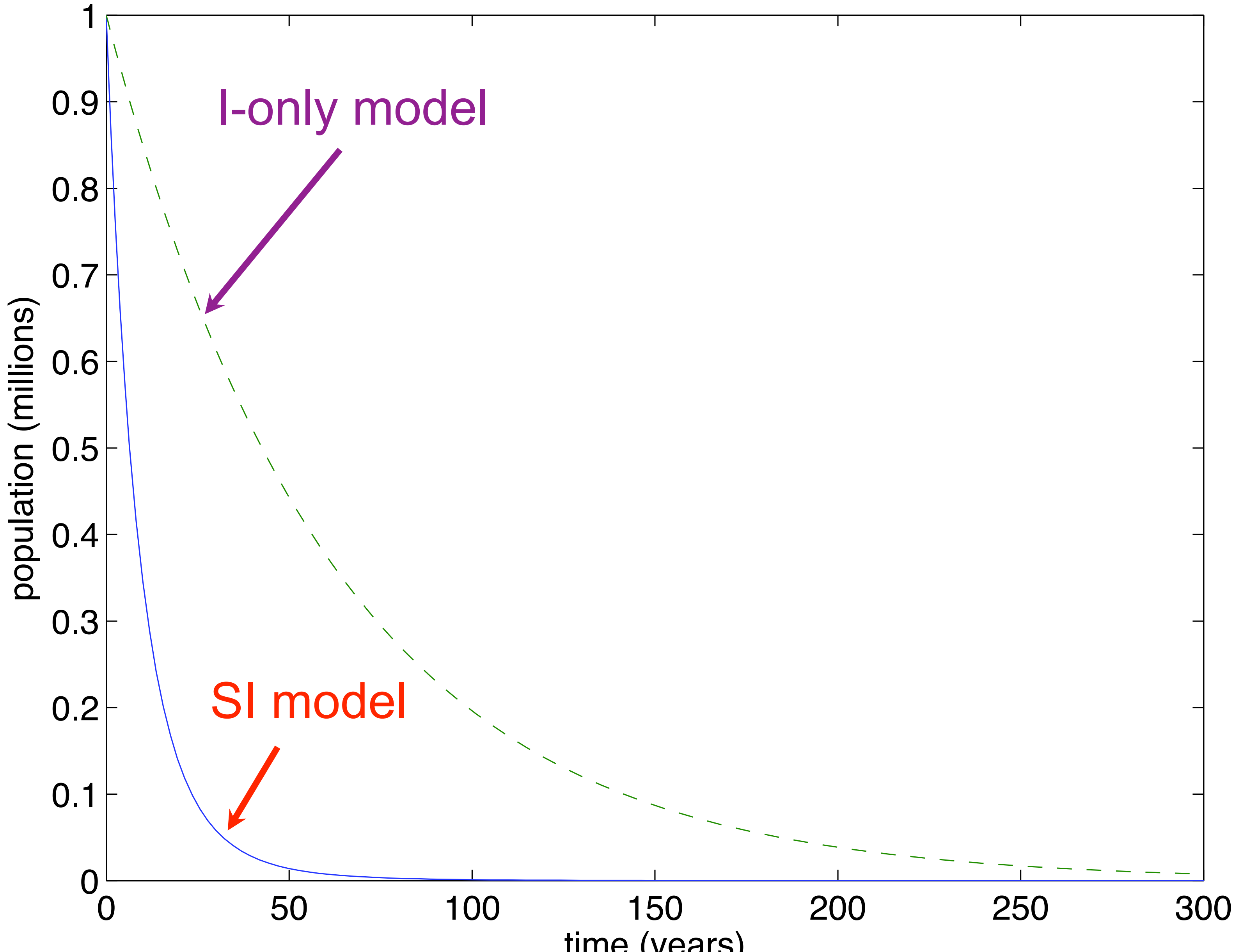
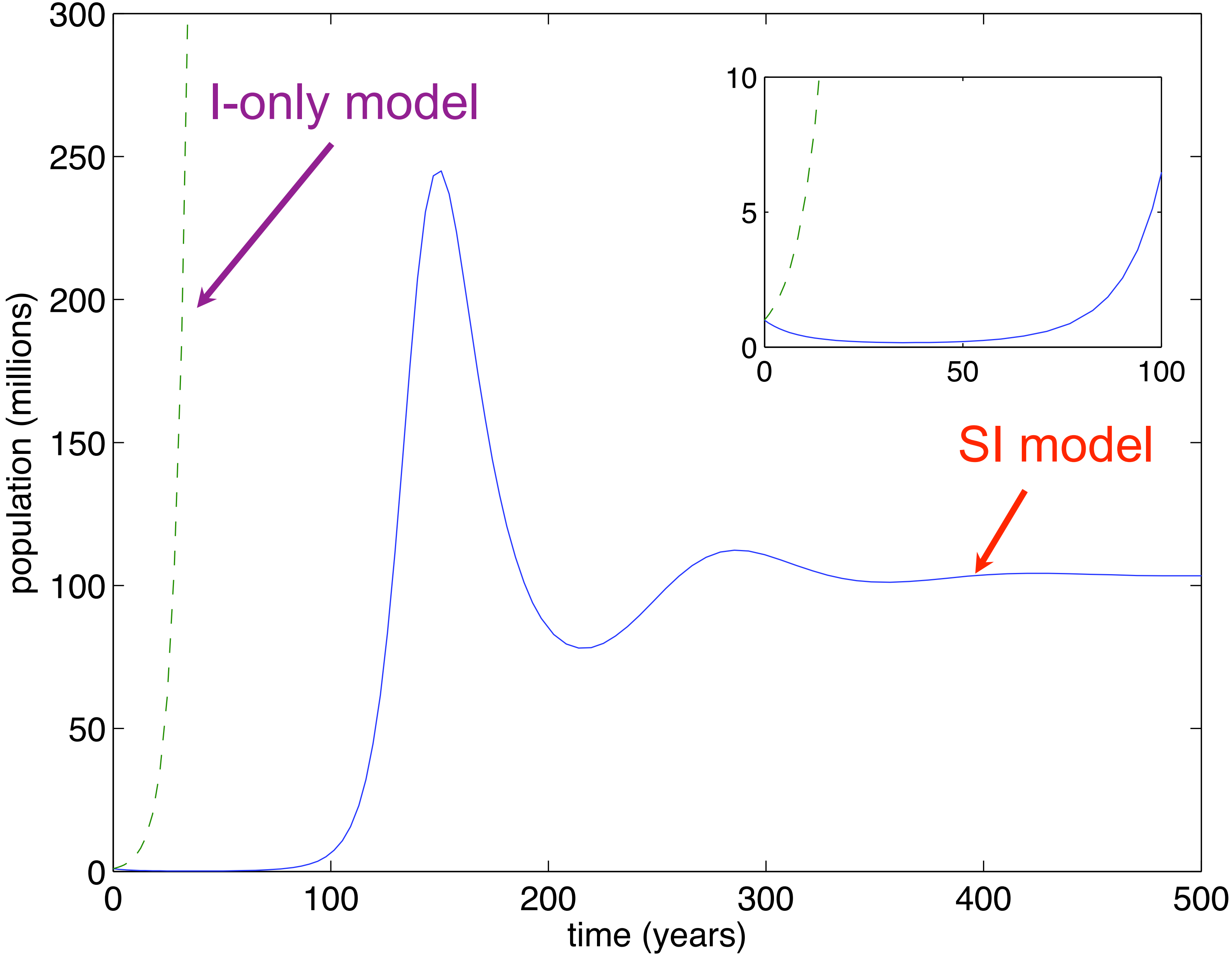
Eradication (R_0=0.8575)



Persistence (R_0=2.45)



A patch model with p regions

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- We can bound

$$S_i(t) \leq L^*, \text{ for } i = 1, \ldots, p$$

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$$\frac{dS_i}{dt} = \Lambda_i - \beta_i S_i I_i - \mu_i S_i + \sum_{j=1}^{p} n_{ij} S_j - \sum_{j=1}^{p} n_{ji} S_i$$

$$\frac{dI_i}{dt} = \beta_i S_i I_i - (\mu_I + \gamma_i) I_i + \sum_{j=1}^{p} m_{ij} I_j - \sum_{j=1}^{p} m_{ji} I_i$$

- We can bound

$$S_i(t) \leq L^*, \text{ for } i = 1, \ldots, p$$

where

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$$L^* = \frac{\Lambda_1 + \cdots + \Lambda_p}{\min\{\mu_1, \cdots, \mu_p\}}.$$

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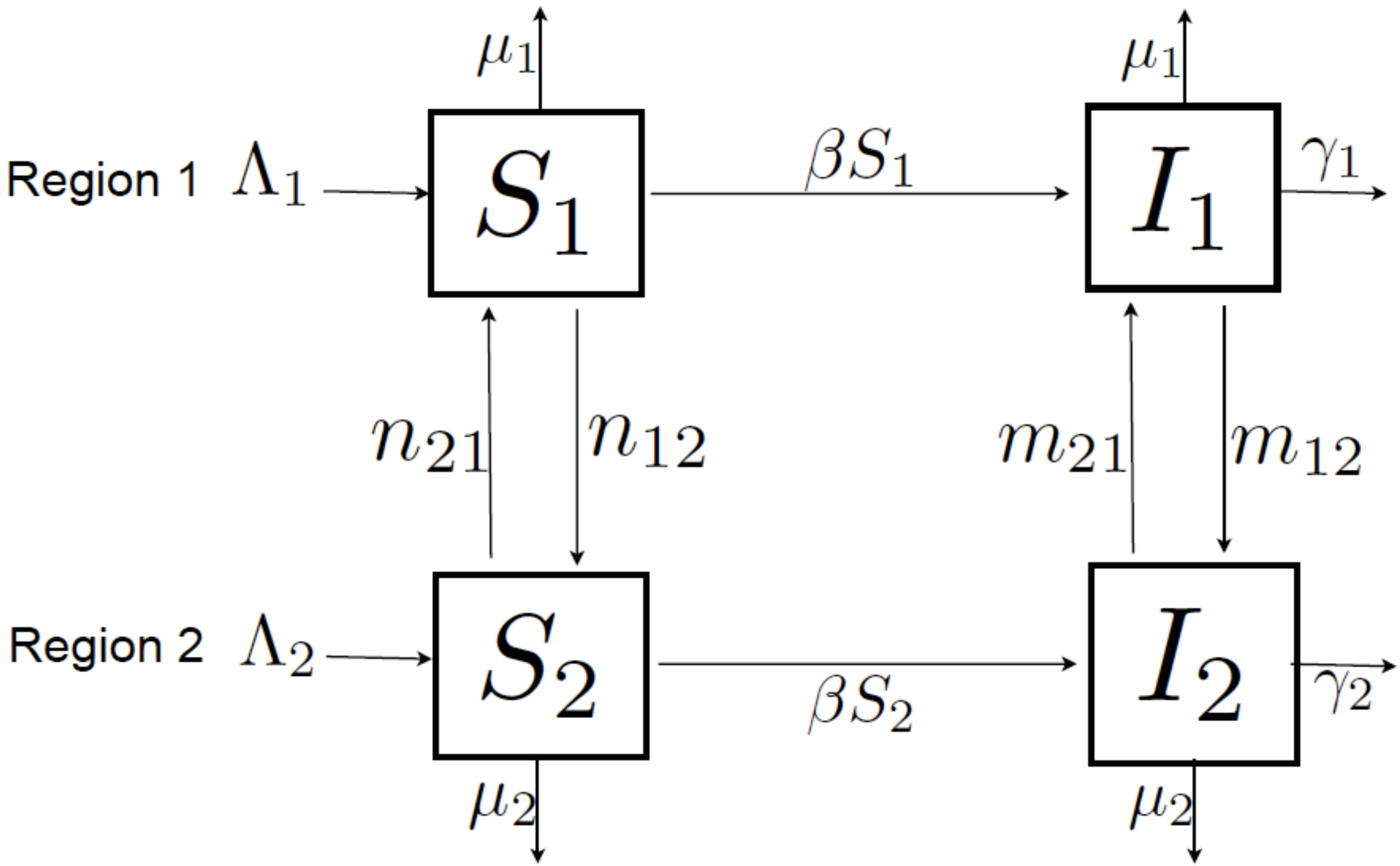
- For eradication purposes, the linear model should determine whether our control methods will be sufficient.

A two-region example: the flow chart



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Case 1: Two isolated regions

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- This is the same as the previous SI model.

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$$\frac{dS_1}{dt} = \Lambda_1 - \beta S_1 I_1 - \mu_1 S_1 + n_{12} S_2 - n_{21} S_1$$
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When only susceptibles travel...

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- Thus, travel restrictions are likely useless.

HIV is a world issue

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- eg, if the disease is eradicated in Europe, we would not have eradication unless it was also eradicated from Africa...
- ...and there was insufficient travel of susceptibles between regions
- This explains why HIV must be considered as a world problem, not just a problem for individual countries, or continents, to tackle independently.

A continent-level example

We divide the world into six regions:

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We divide the world into six regions:

1. Africa

A continent-level example

We divide the world into six regions:

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2. Asia

A continent-level example

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A continent-level example

We divide the world into six regions:

1. Africa
2. Asia
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4. North America

A continent-level example

We divide the world into six regions:

1. Africa
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5. Oceania

A continent-level example

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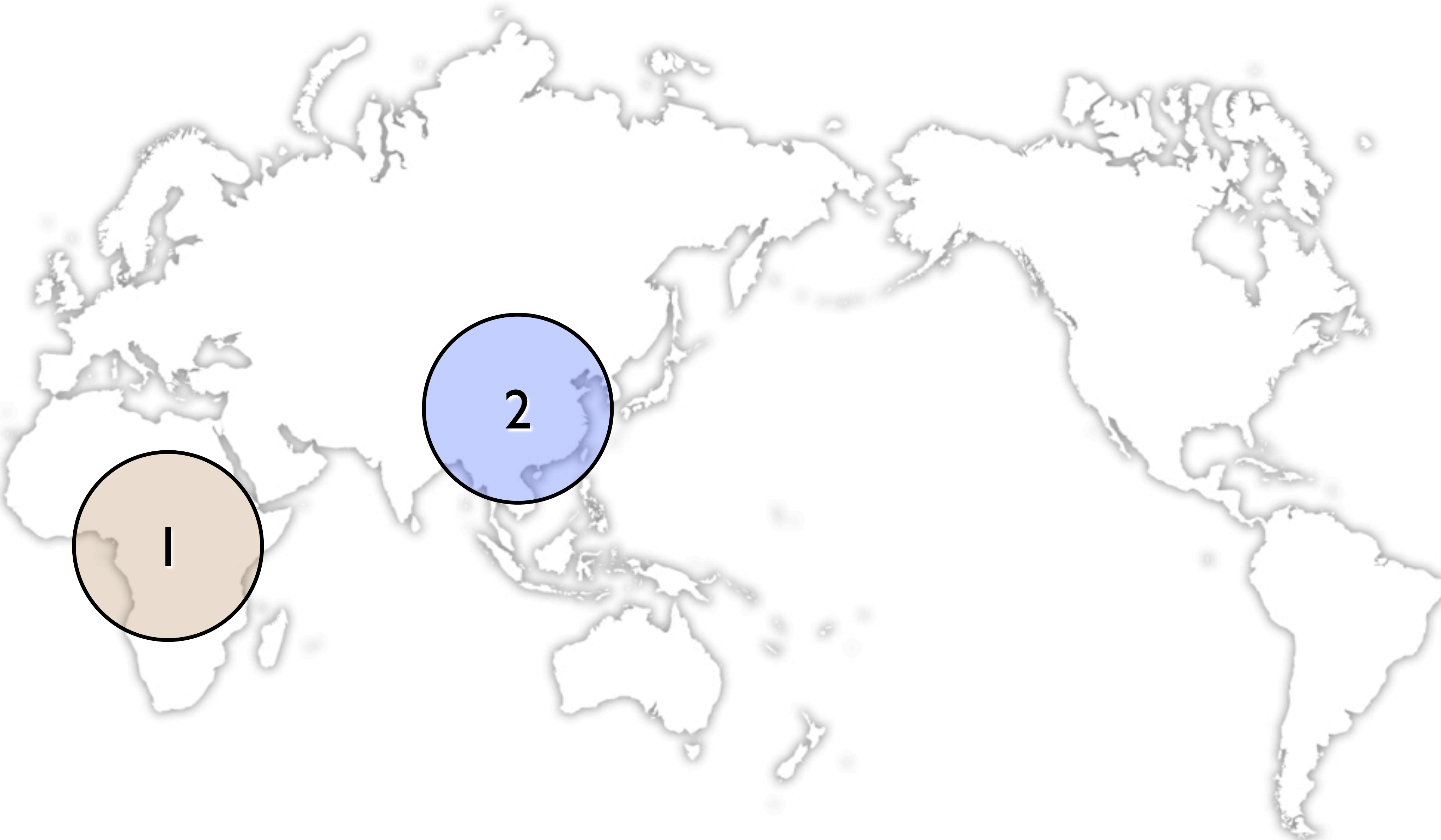
1. Africa
2. Asia
3. Europe
4. North America
5. Oceania
6. South America.


I



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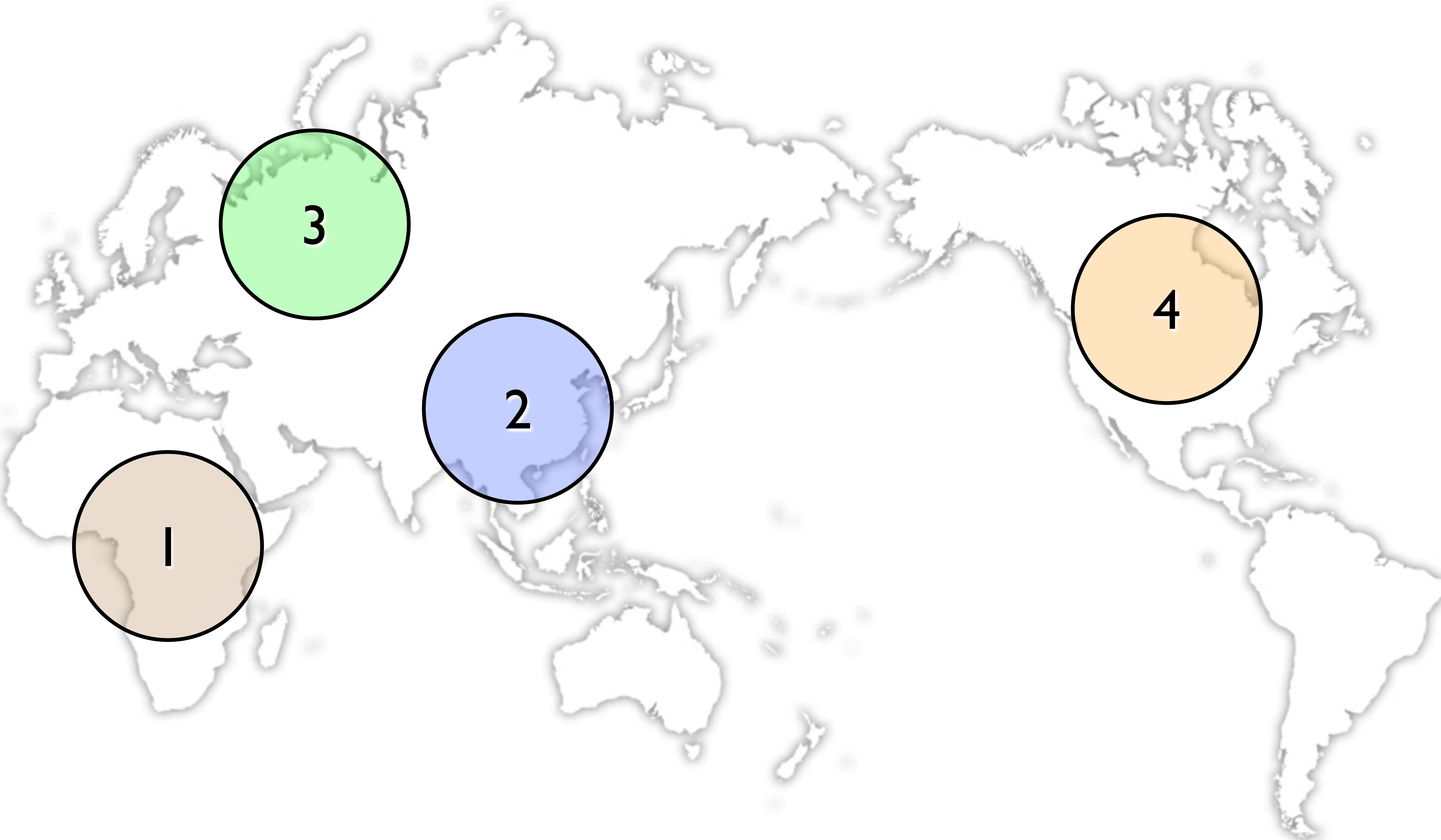
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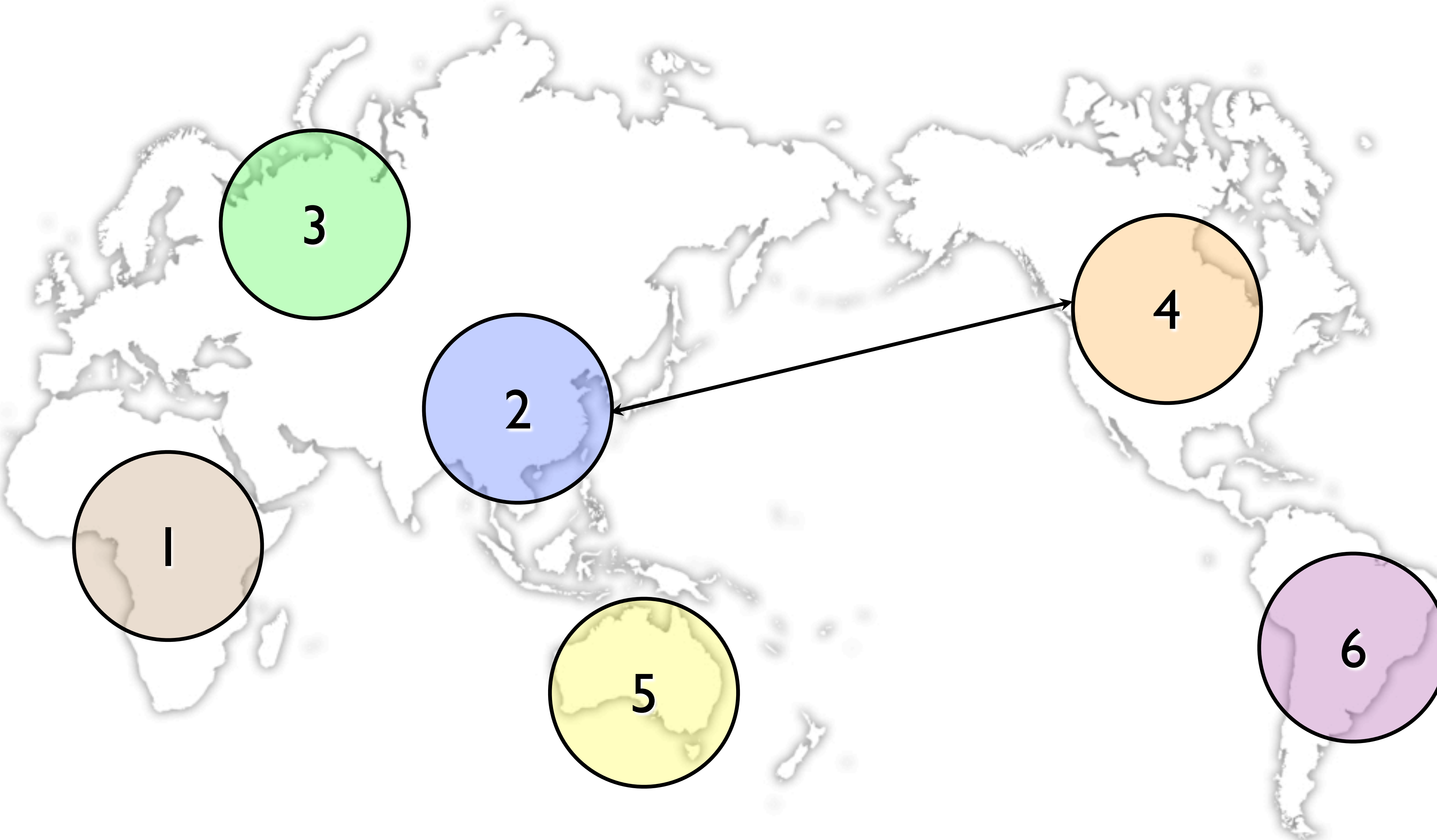

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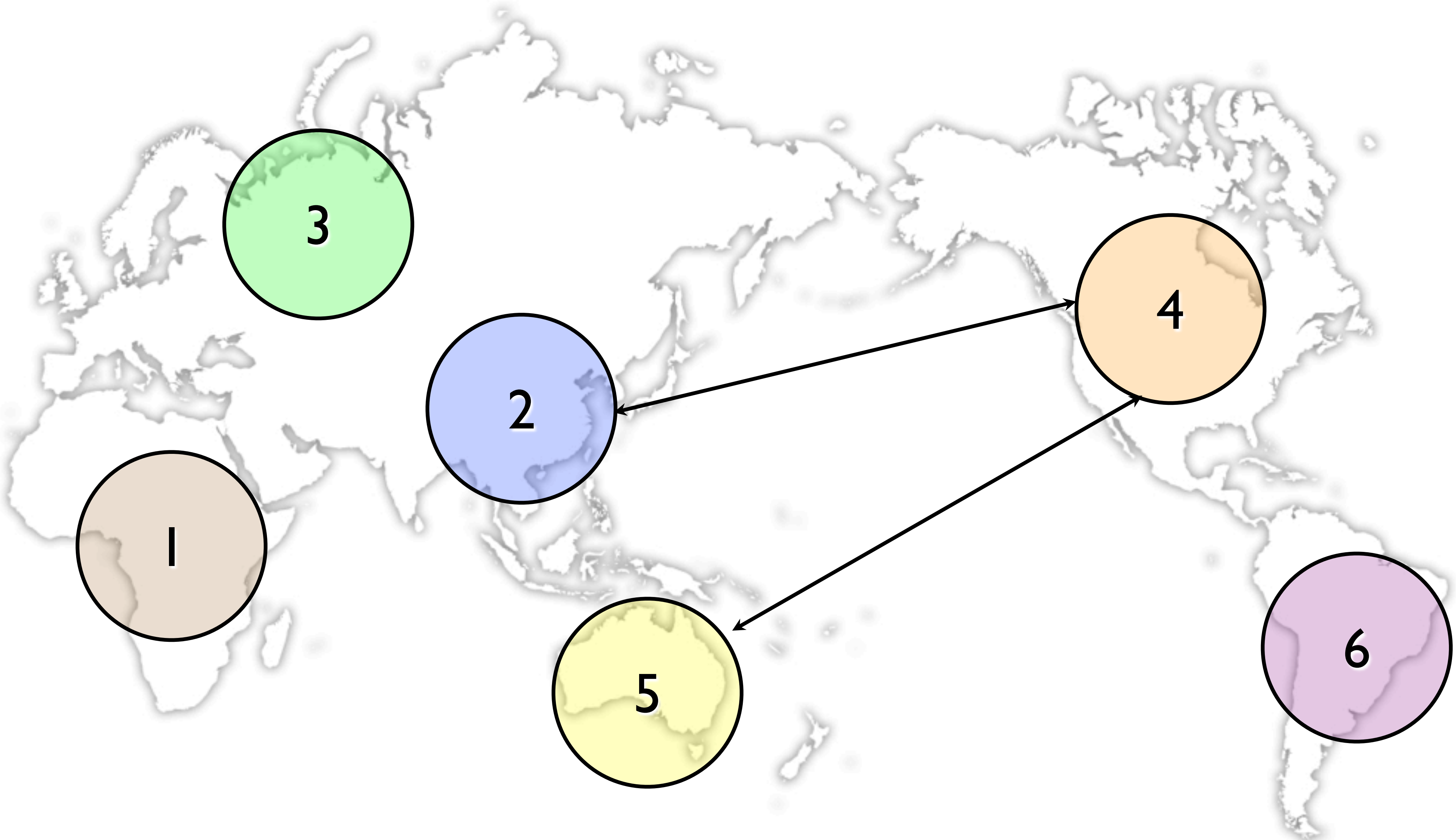
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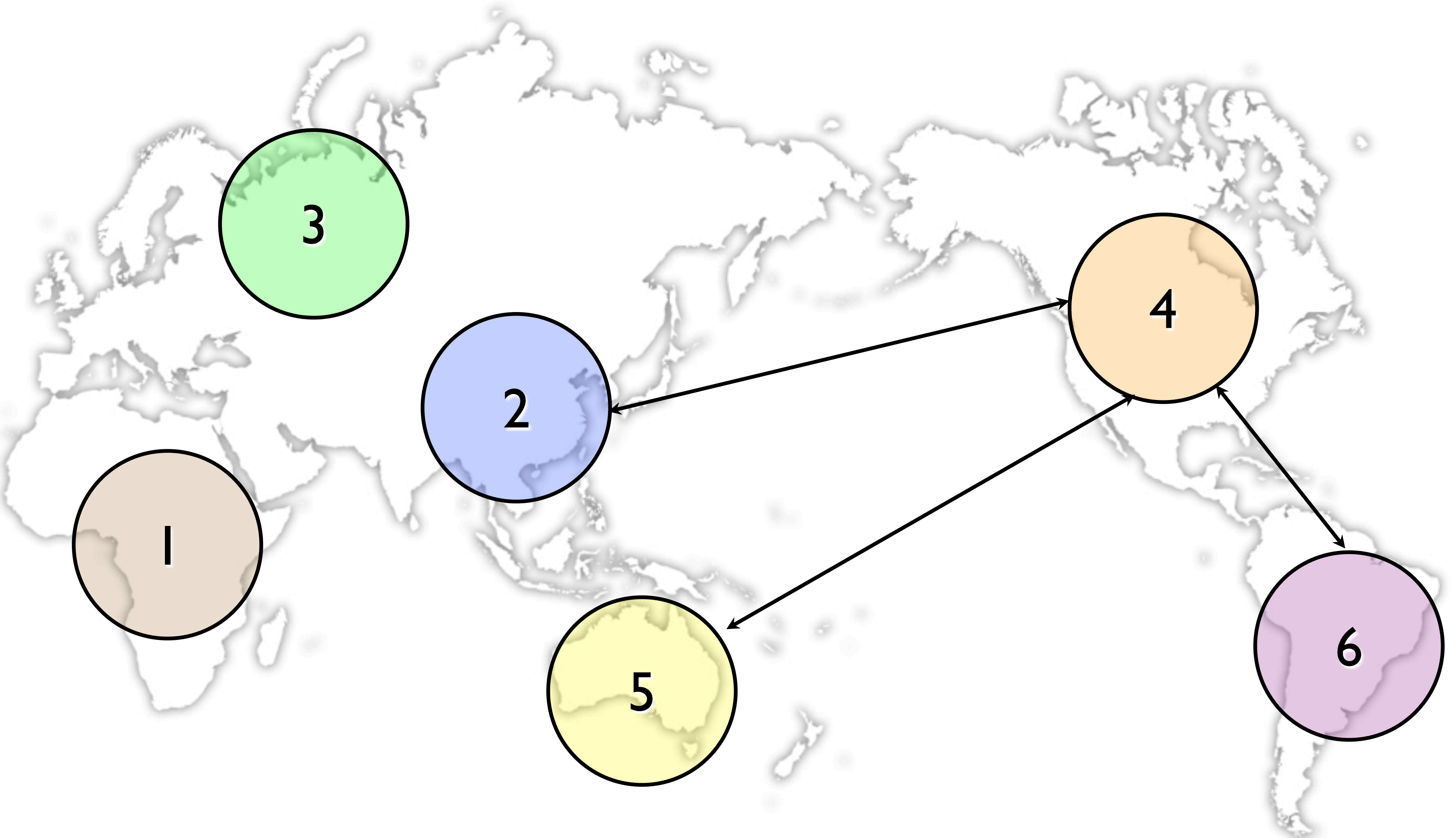

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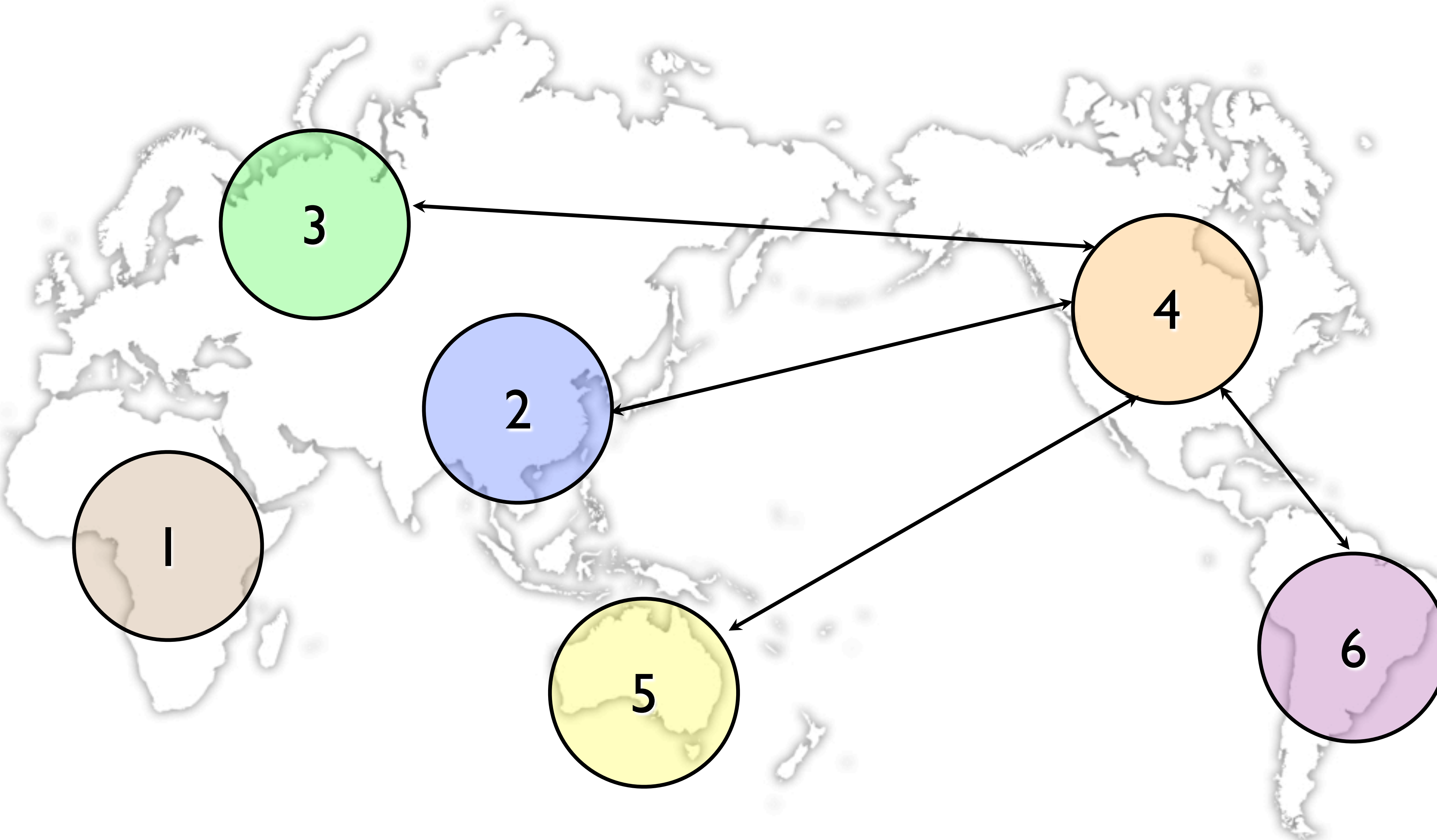

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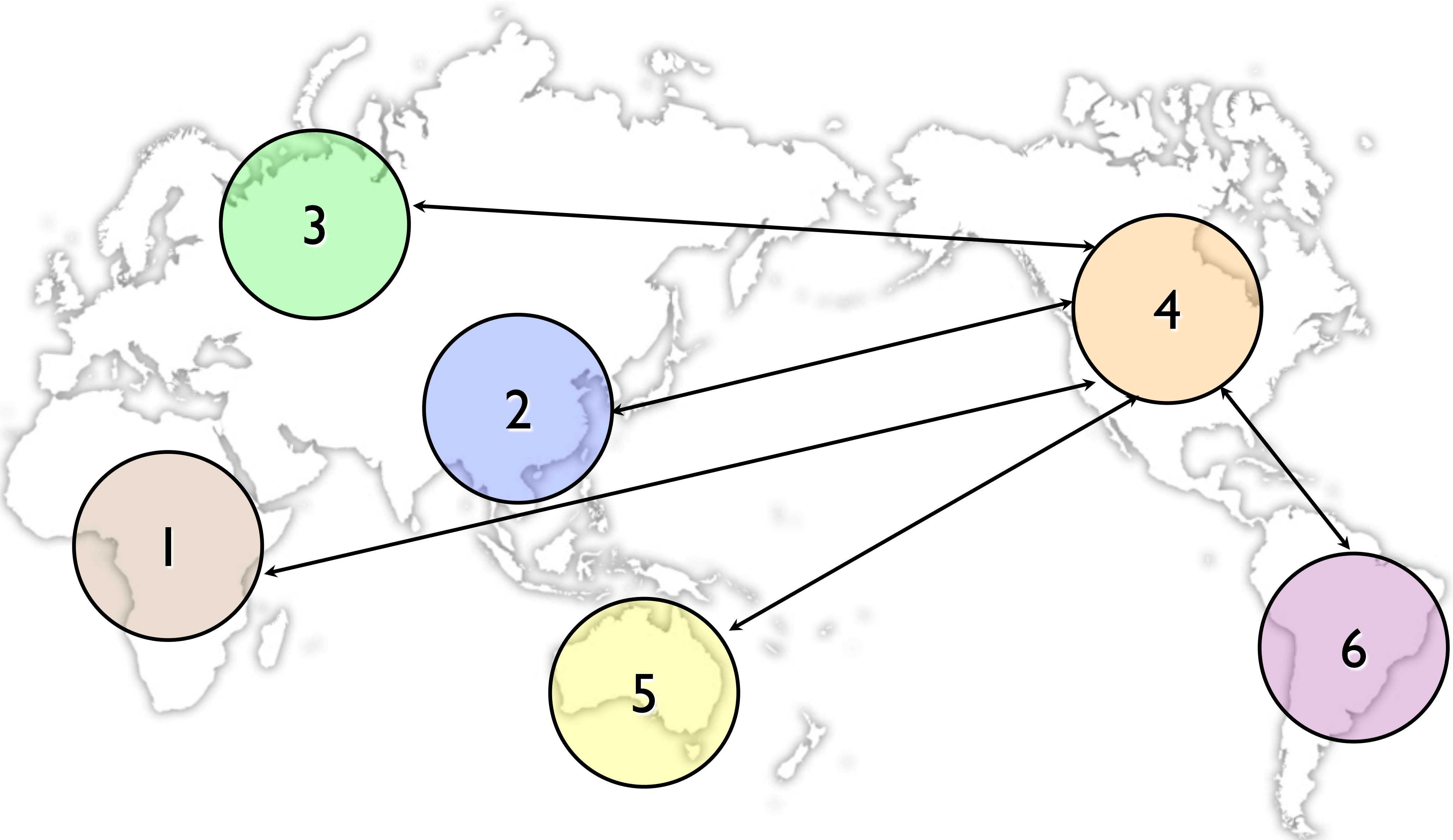
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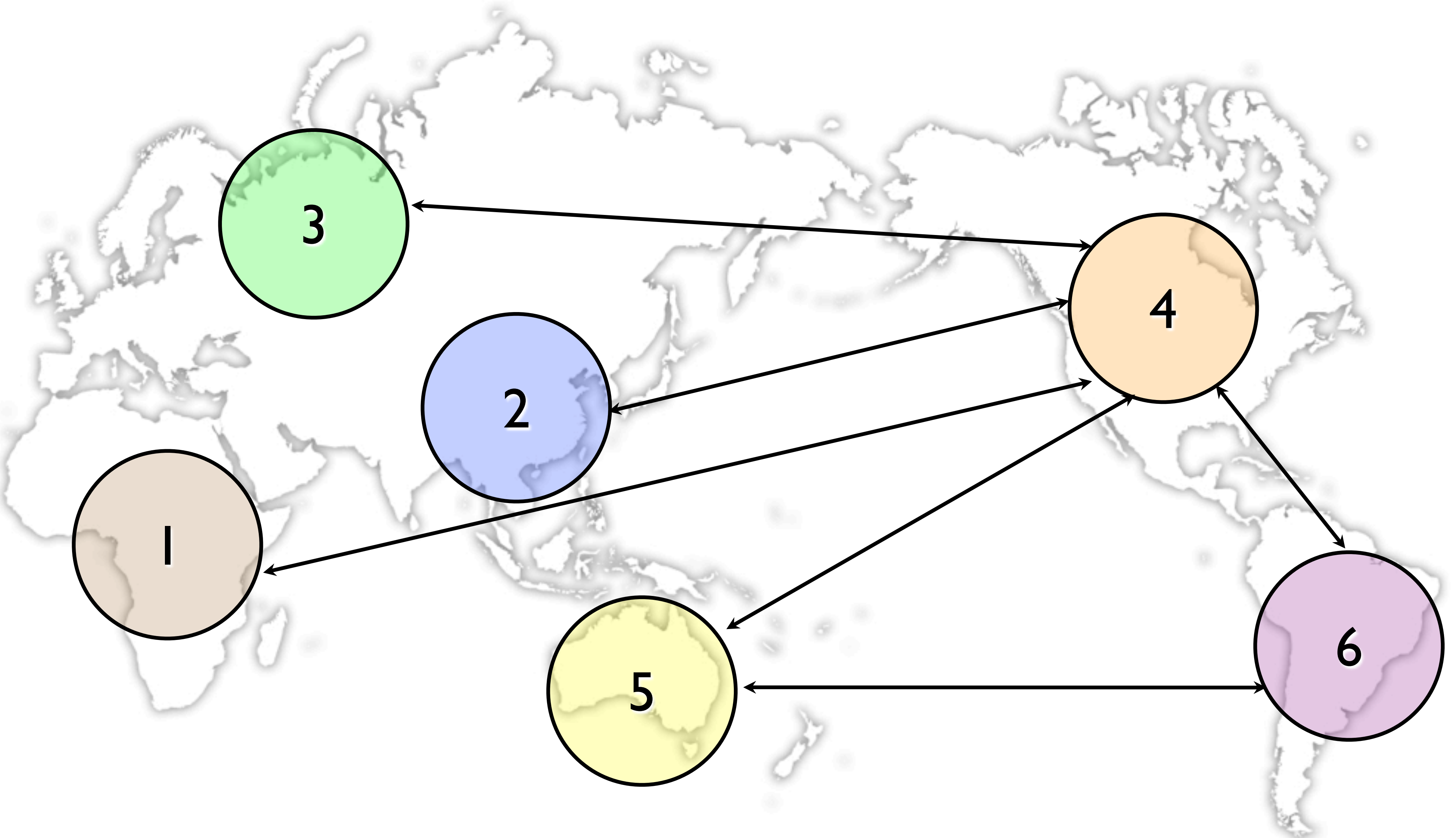
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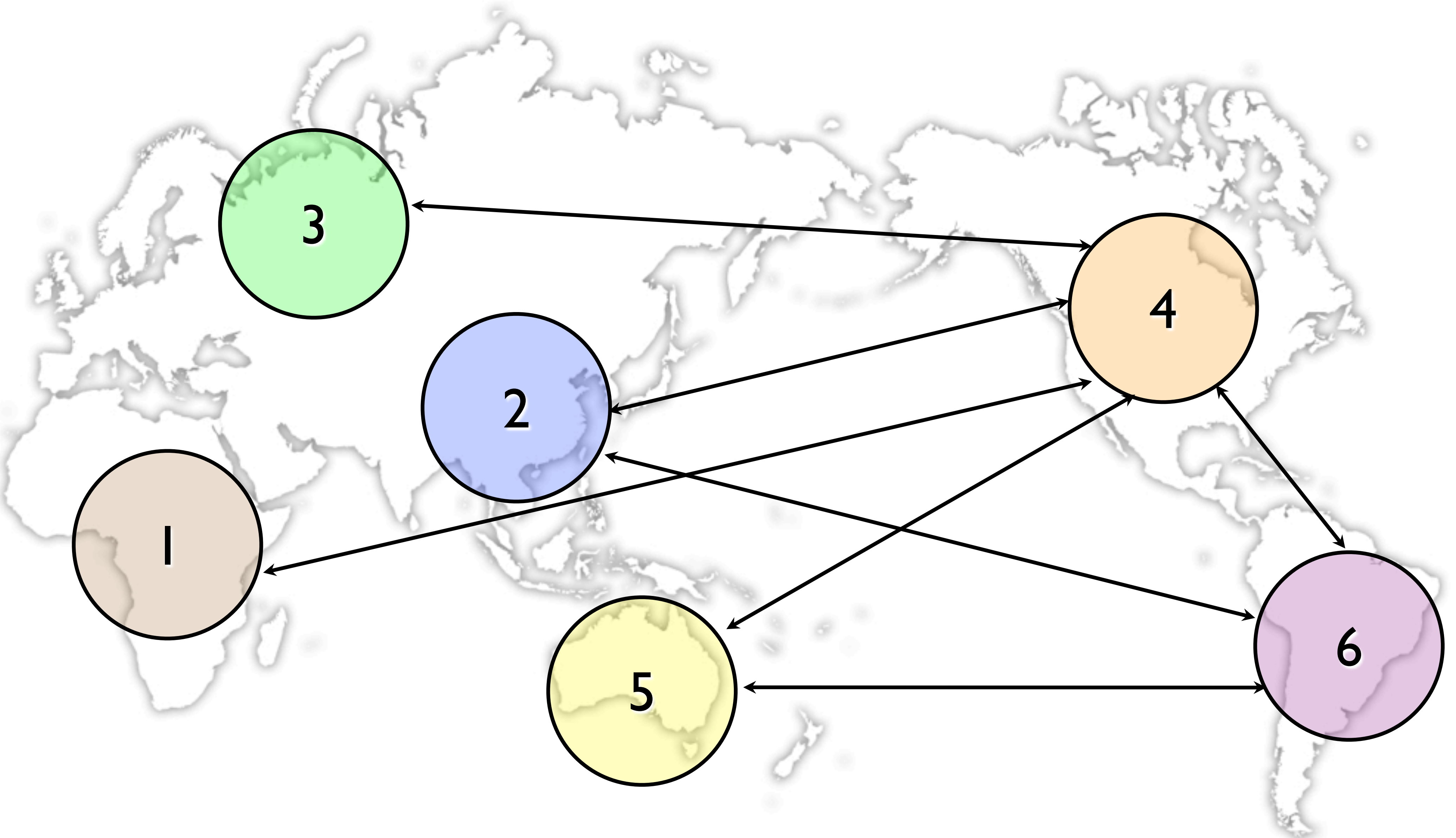
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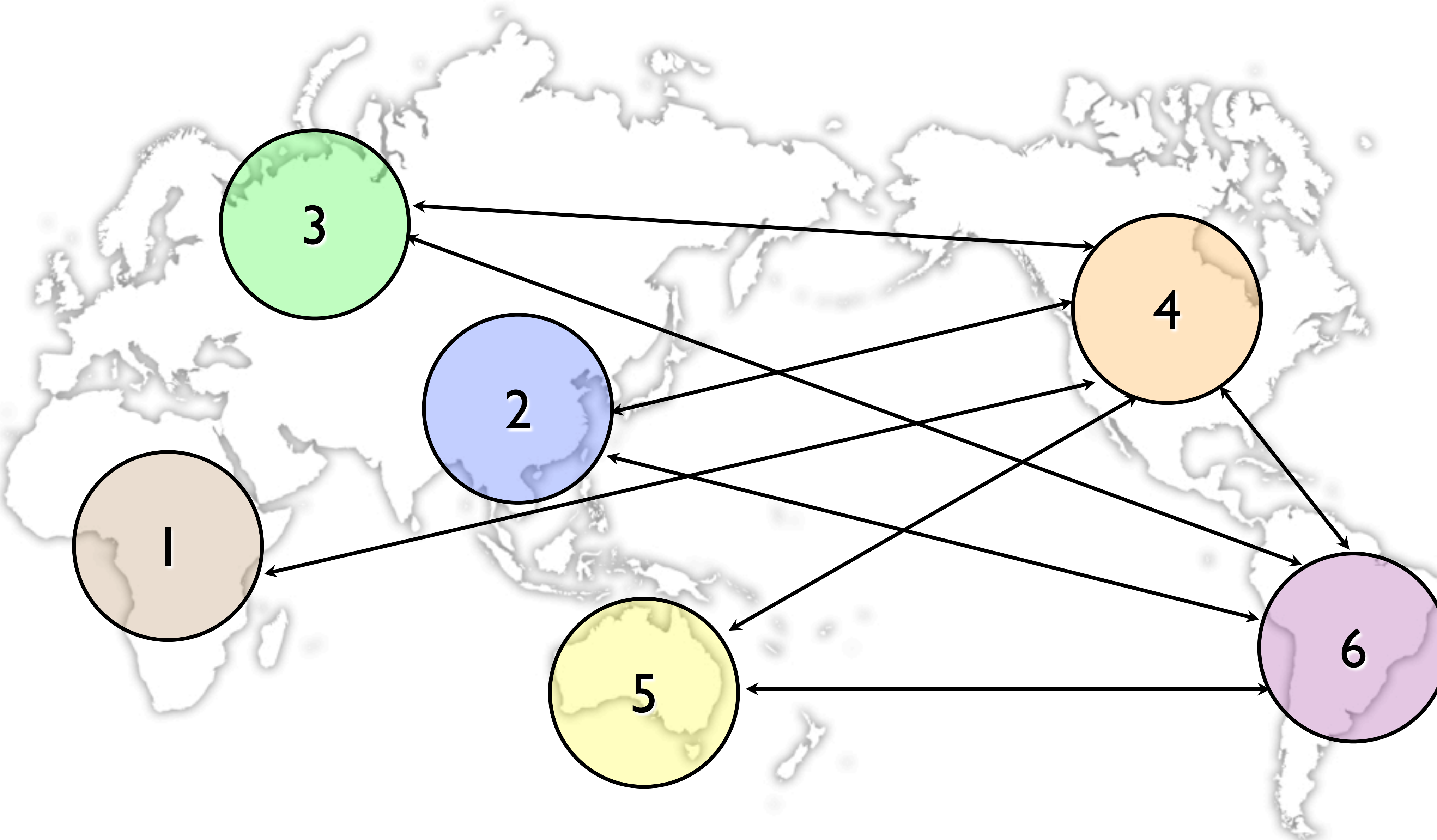
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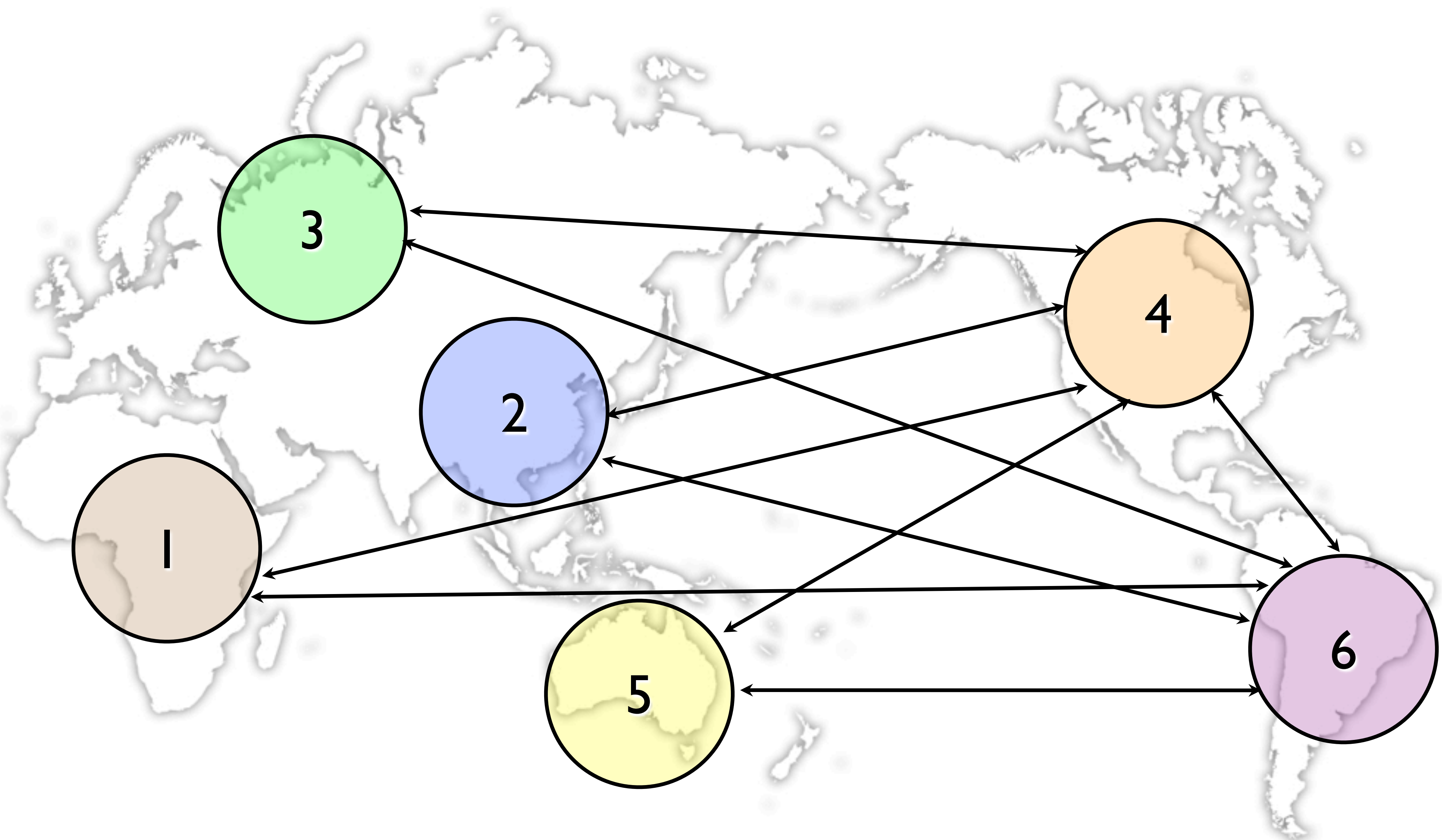

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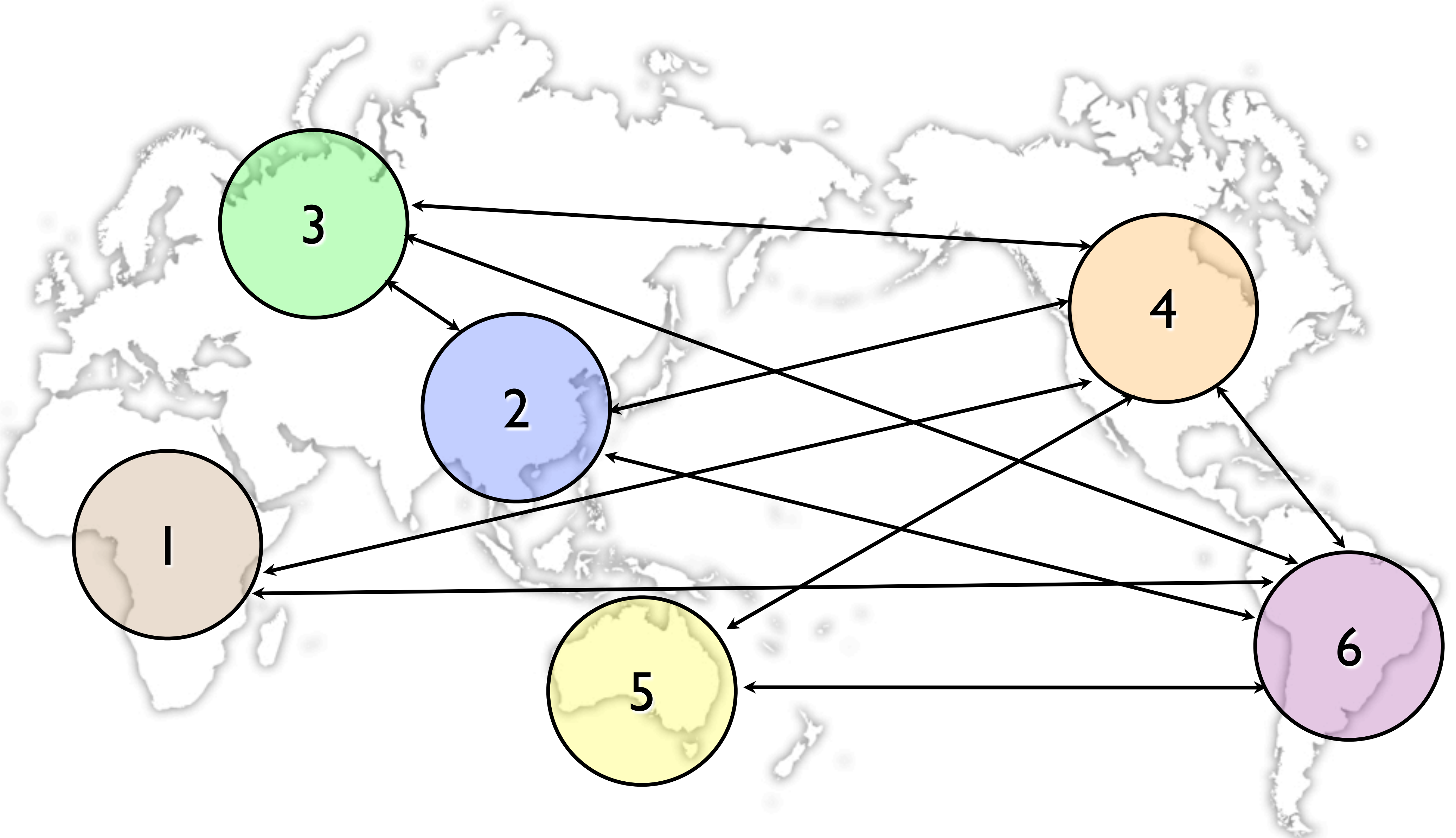
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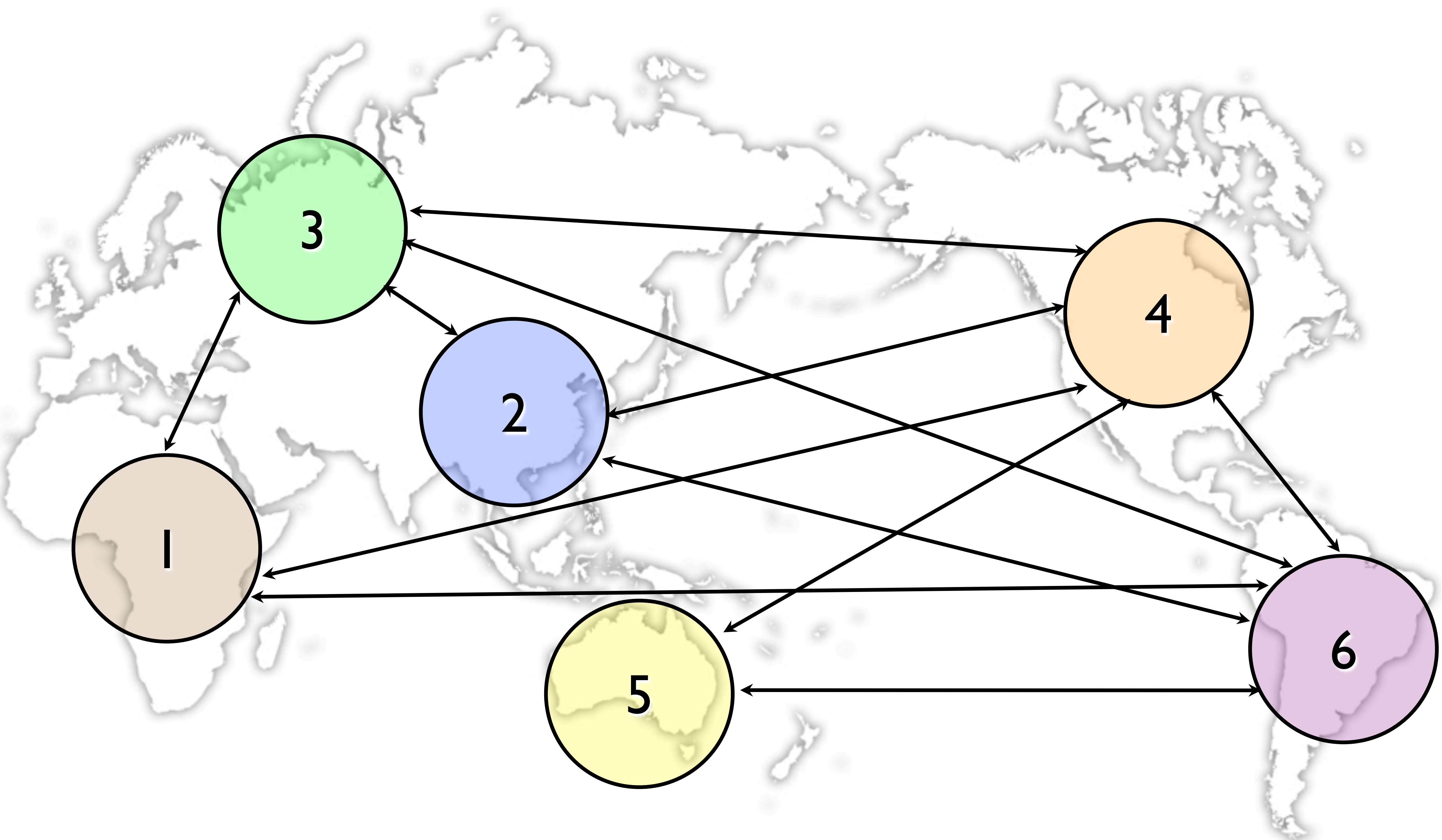
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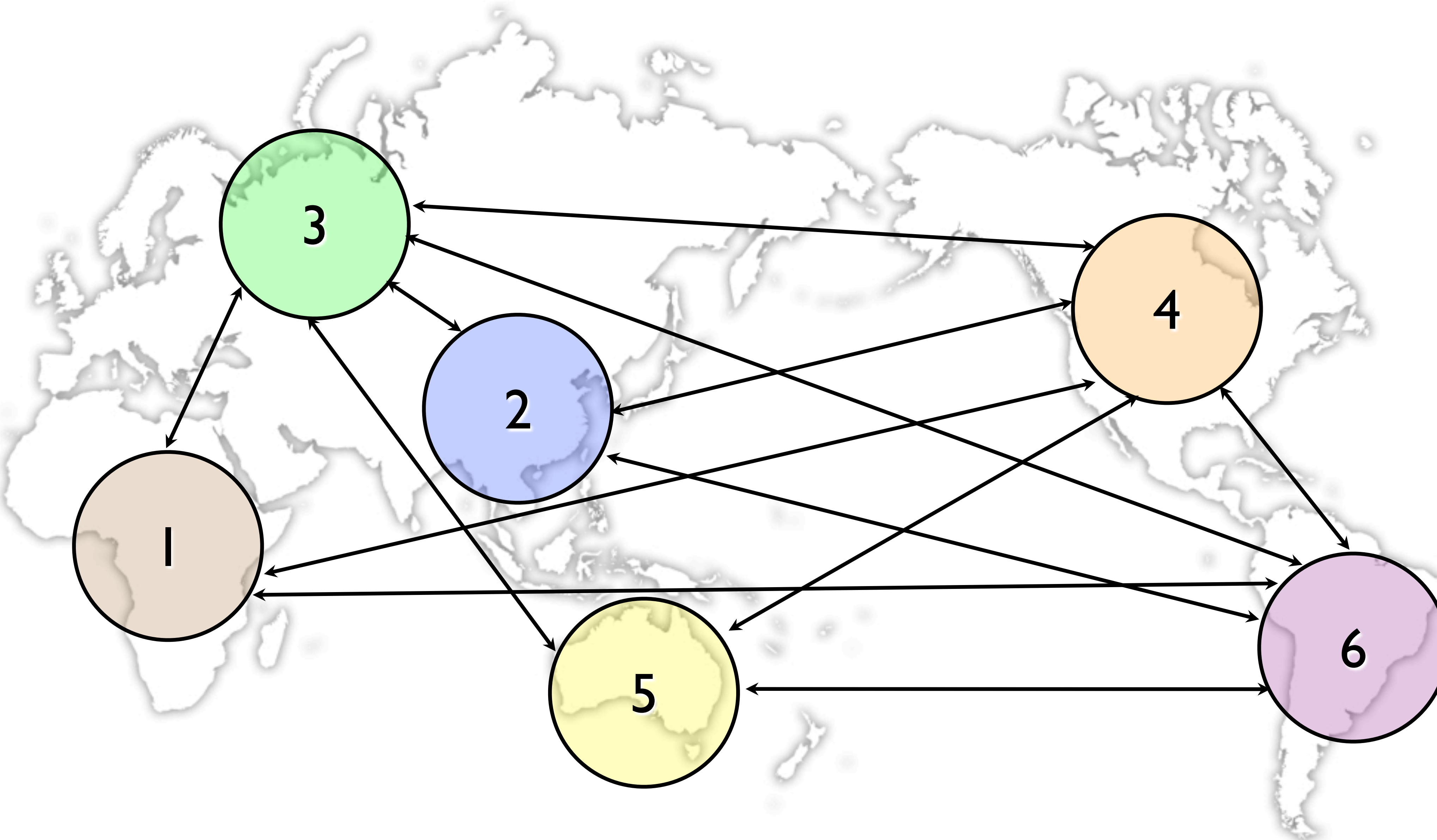

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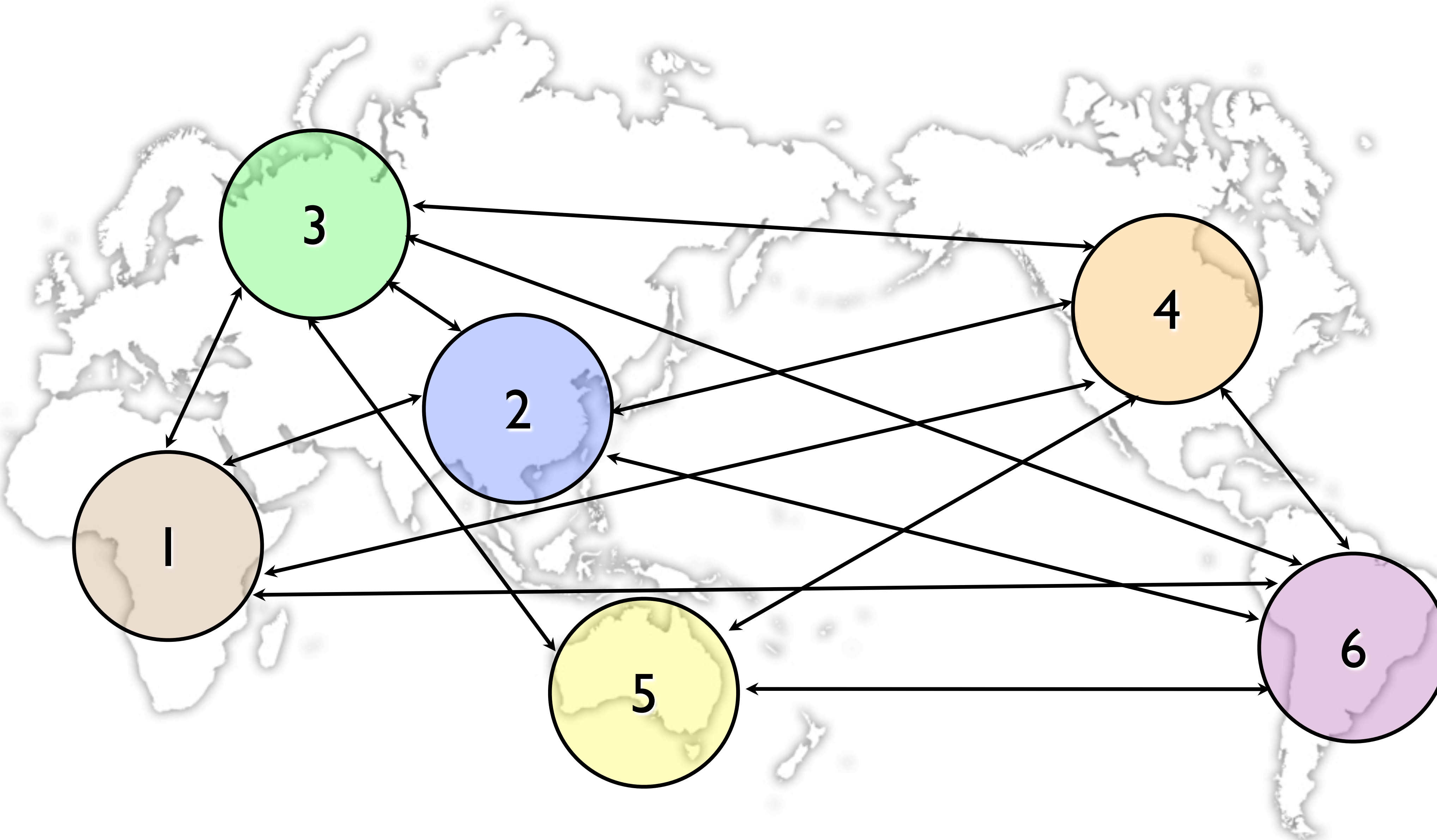
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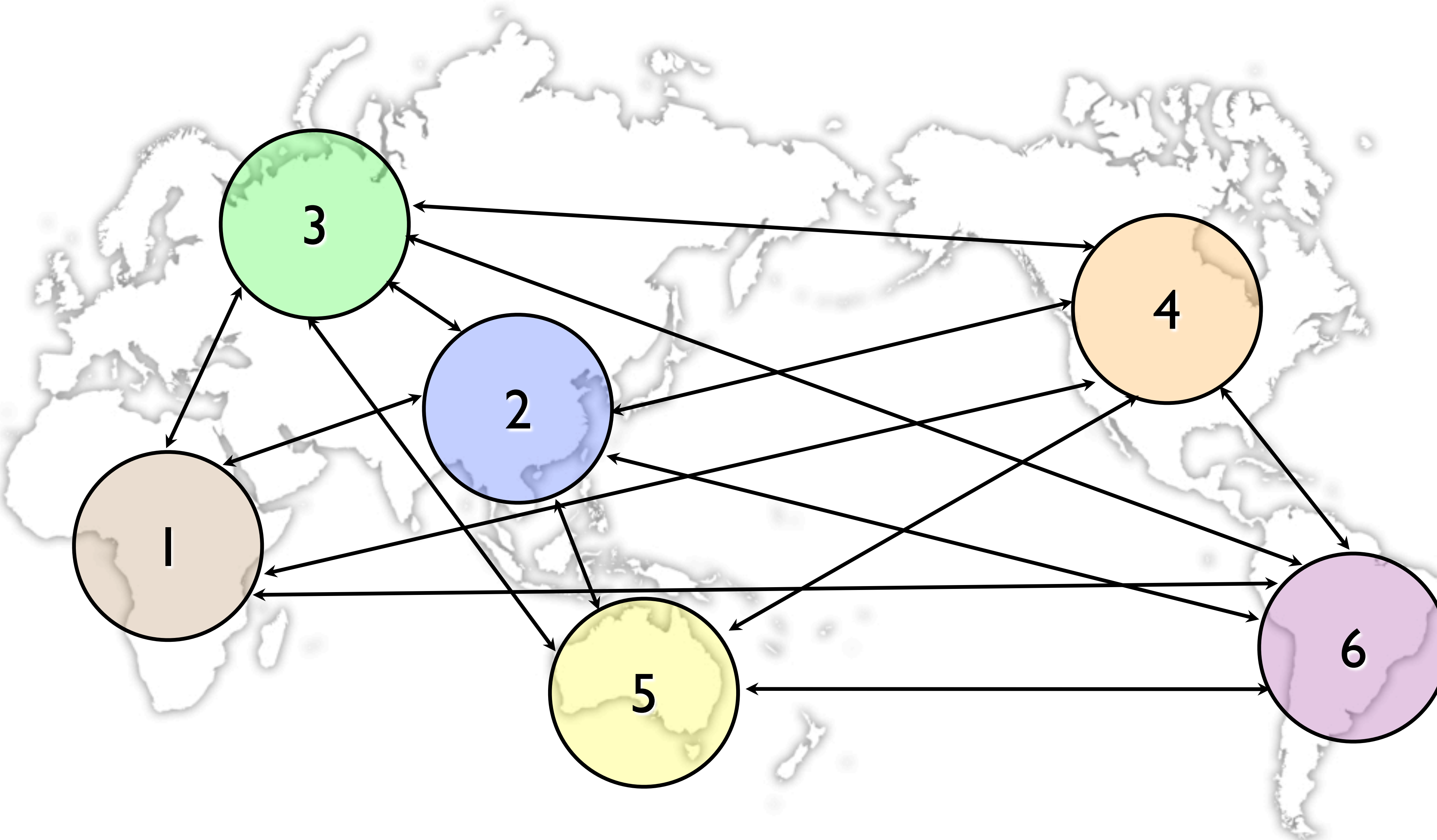
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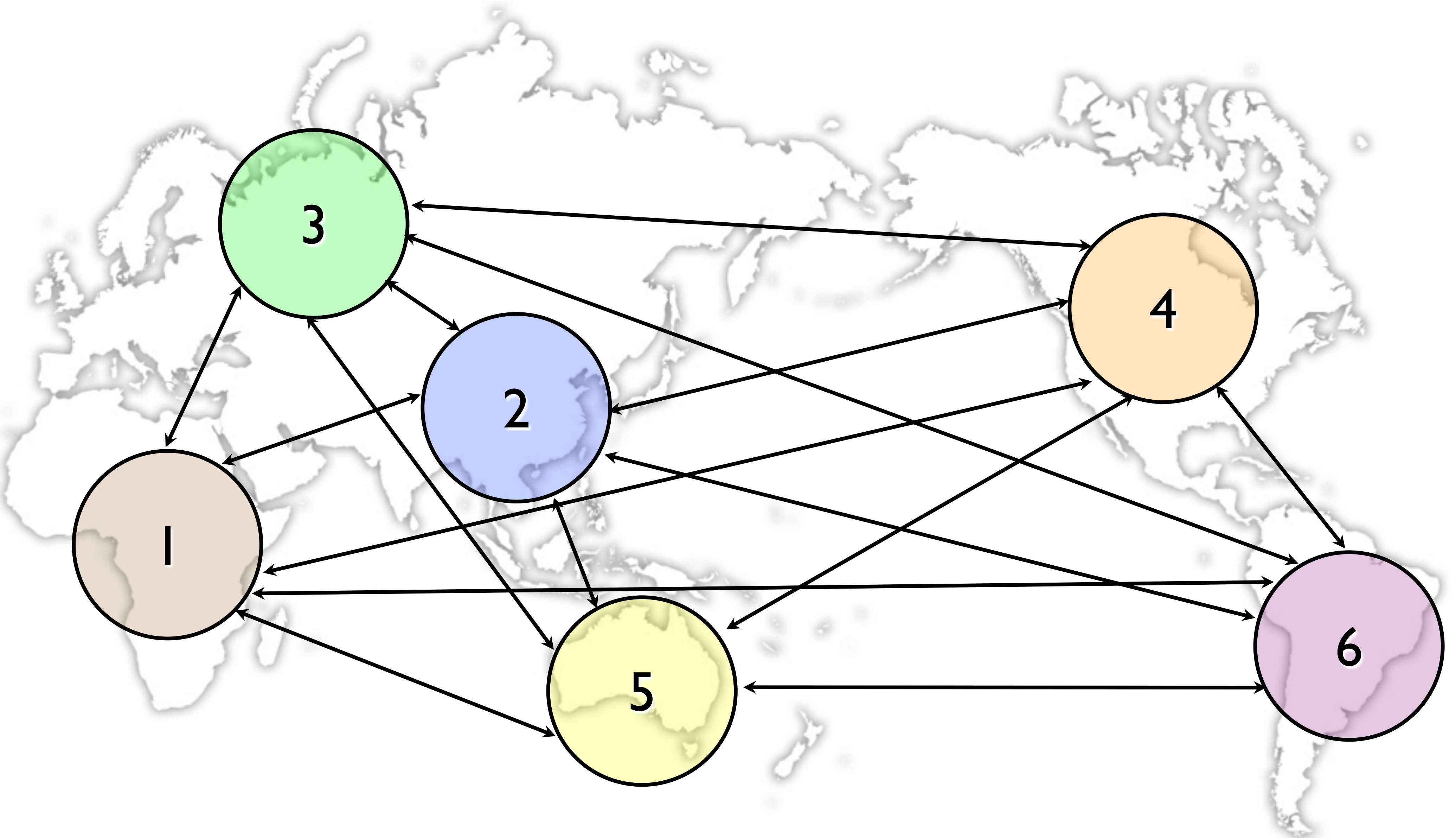

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The continent-level model

$$\frac{dI_1}{dt} = \pi_1 I_1 - d_1 I_1 + m_{12} I_2 + m_{13} I_3 + m_{14} I_4 + m_{15} I_5 + m_{16} I_6$$
$$- m_{21} I_1 - m_{31} I_1 - m_{41} I_1 - m_{51} I_1 - m_{61} I_1$$
$$\frac{dI_2}{dt} = \pi_2 I_2 - d_2 I_2 + m_{21} I_1 + m_{23} I_3 + m_{24} I_4 + m_{25} I_5 + m_{26} I_6$$
$$- m_{12} I_2 - m_{32} I_2 - m_{42} I_2 - m_{52} I_2 - m_{62} I_2$$
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$$- m_{14} I_4 - m_{24} I_4 - m_{34} I_4 - m_{54} I_4 - m_{64} I_4$$
$$\frac{dI_5}{dt} = \pi_5 I_5 - d_5 I_5 + m_{41} I_1 + m_{42} I_2 + m_{43} I_3 + m_{45} I_5 + m_{46} I_6$$
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$$- m_{16} I_6 - m_{26} I_6 - m_{36} I_6 - m_{46} I_6 - m_{56} I_6 \, .$$

π_i=influx of infectives
d_i=death rate
m_{ik}=migration rate

Birth and death rates by continent

	Population	Births/Popn	Birth Rate	Deaths/Popn	Death Rate
AF	954879489	33203380	0.0348	12625314	0.0132
AS	4043347897	76536061	0.0189	27947177	0.0069
EU	729546003	7321919	0.0100	8437988	0.0116
NA	527814776	8712554	0.0165	3798366	0.0072
OC	33970173	545421	0.0161	244250	0.0072
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- Data from the CIA world factbook (2008).

Immigration data

Des/Ori	AF	AS	EU	NA	OC	SA
AF		15973	16987	4263	0	0
AS	286806		298431	13062	1621	32500
EU	5312095	3566013		1167954	252860	1337972
NA	1176374	9690228	8573379		353095	4466748
OC	221003	1380652	2470078	136804		76873
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- Data from the Global Migrant Origin Database (2007)
- Gives number of foreign born individuals by country of origin and destination.

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- All other factors remain constant.

Reducing the infection rate by 3/5

- β=0.0002 people^{-1}years^{-1}, $\Lambda=p_i c/\mu_i$, where p_i is the continent's birth rate, c is 20 uninfected sex partners per year and $1/\gamma$=10 years

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- However, this assumes no change in population growth

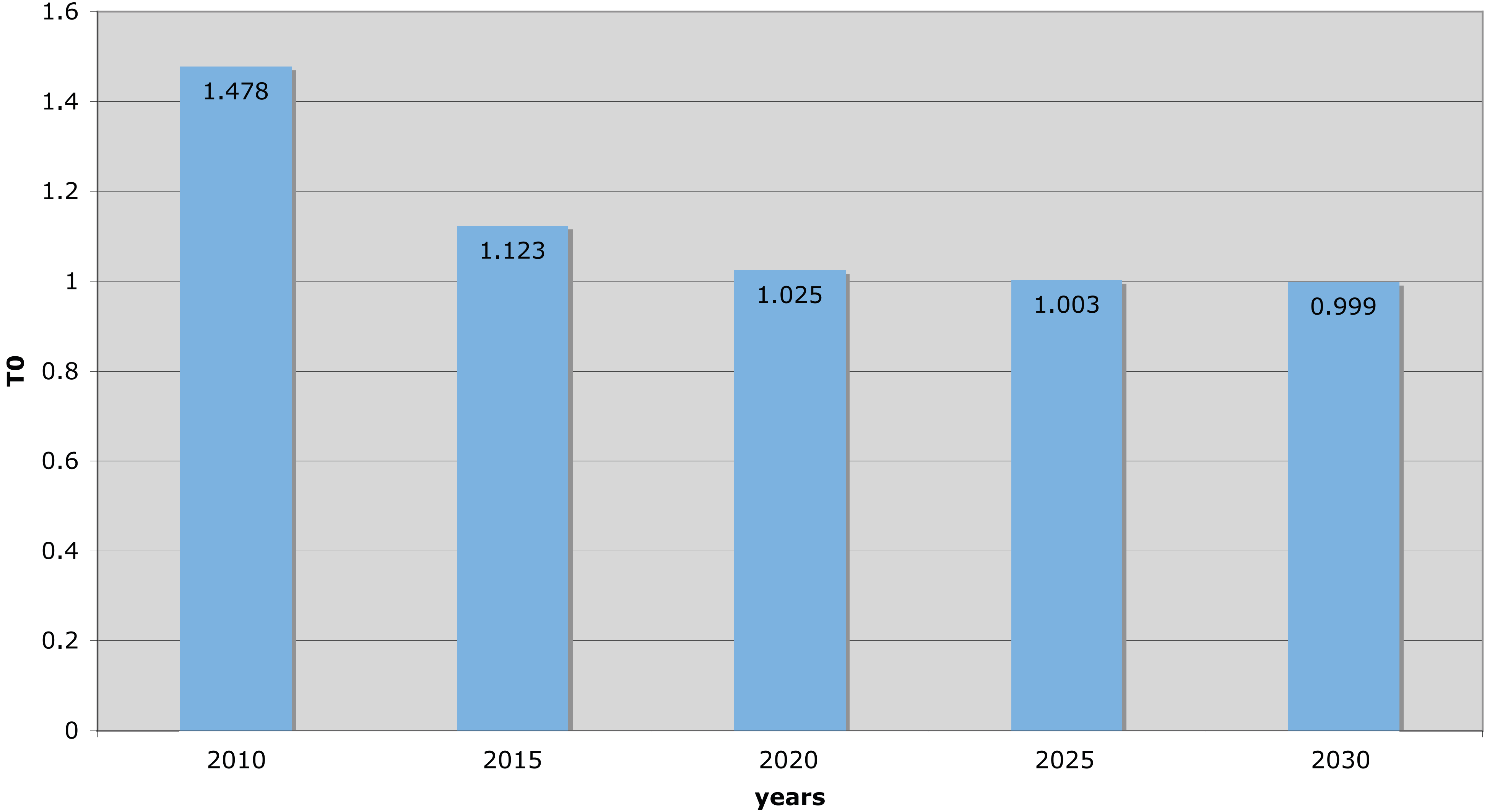
Reducing the infection rate by 3/5

- β=0.0002 people^{-1}years^{-1}, $\Lambda = p_i c/\mu_i$, where p_i is the continent's birth rate, c is 20 uninfected sex partners per year and $1/\gamma$=10 years
- If we reduce the infection rate by 3/5, then

$$T_0 = e^{-7.59\times 10^{-5}} < 1$$

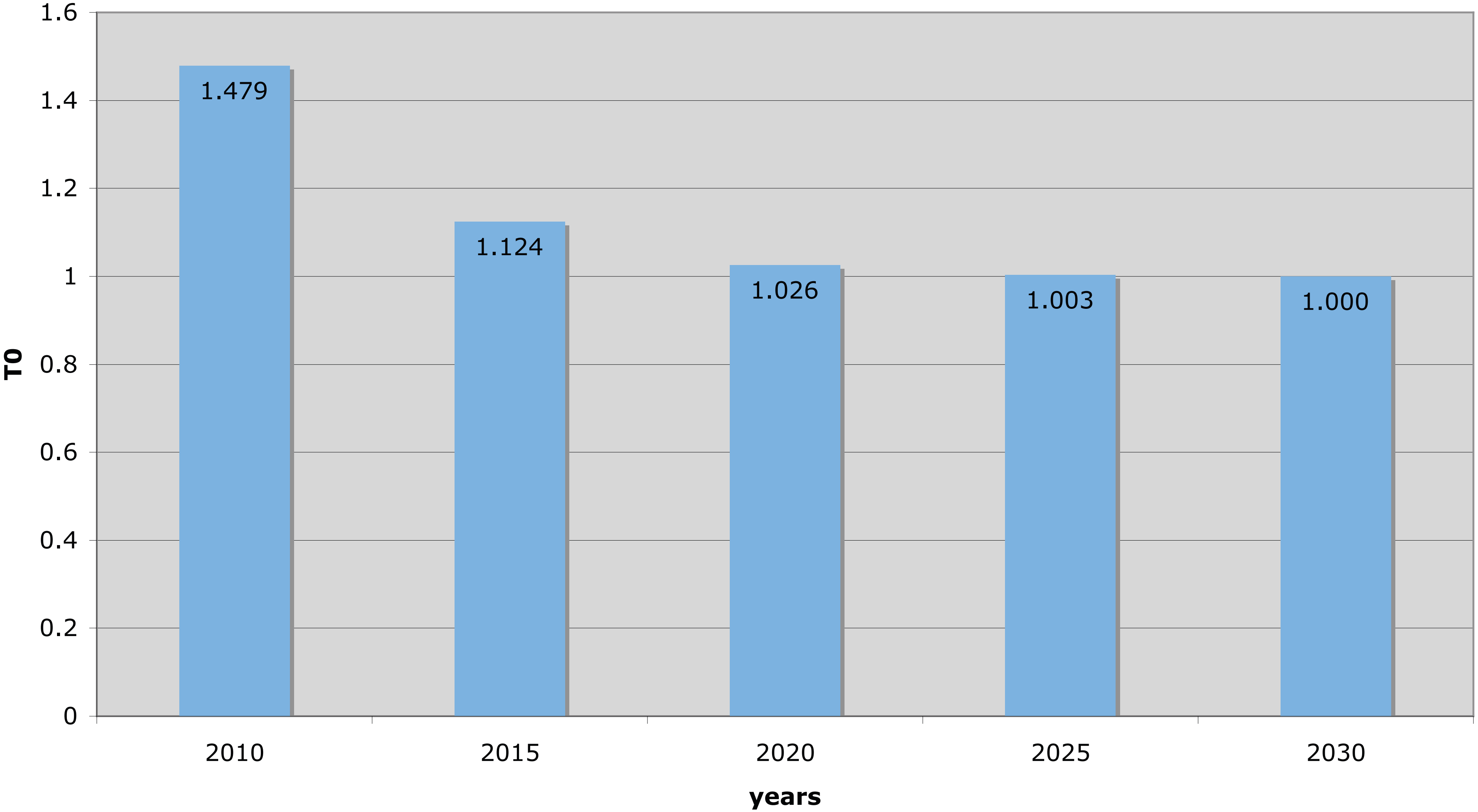
- This trips the eradication threshold
- However, this assumes no change in population growth
- Over a 20 year timeframe, we might need to take population growth into account.

Reduction in transmission



Assuming population demographics remain unchanged.

Reduction in transmission



Assuming 3% population growth per year results in the inability to eradicate the disease.

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  (so the infection rate will need to be lowered even further).

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- Can we trip the eradication threshold using available money?

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Male condom	$0.02 per condom.

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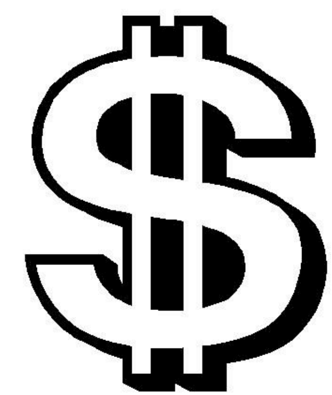

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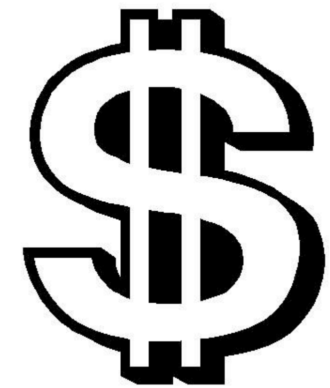

$$C(n,m,r) = 3 \times 10^9 \times \frac{1.03^r - 1}{0.03} \times 100 \times 0.02 \times n + 6 \times 10^6$$

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- Third term: one tenth of infected individuals require treatment, 3% population growth, average cost of $2500 per year.

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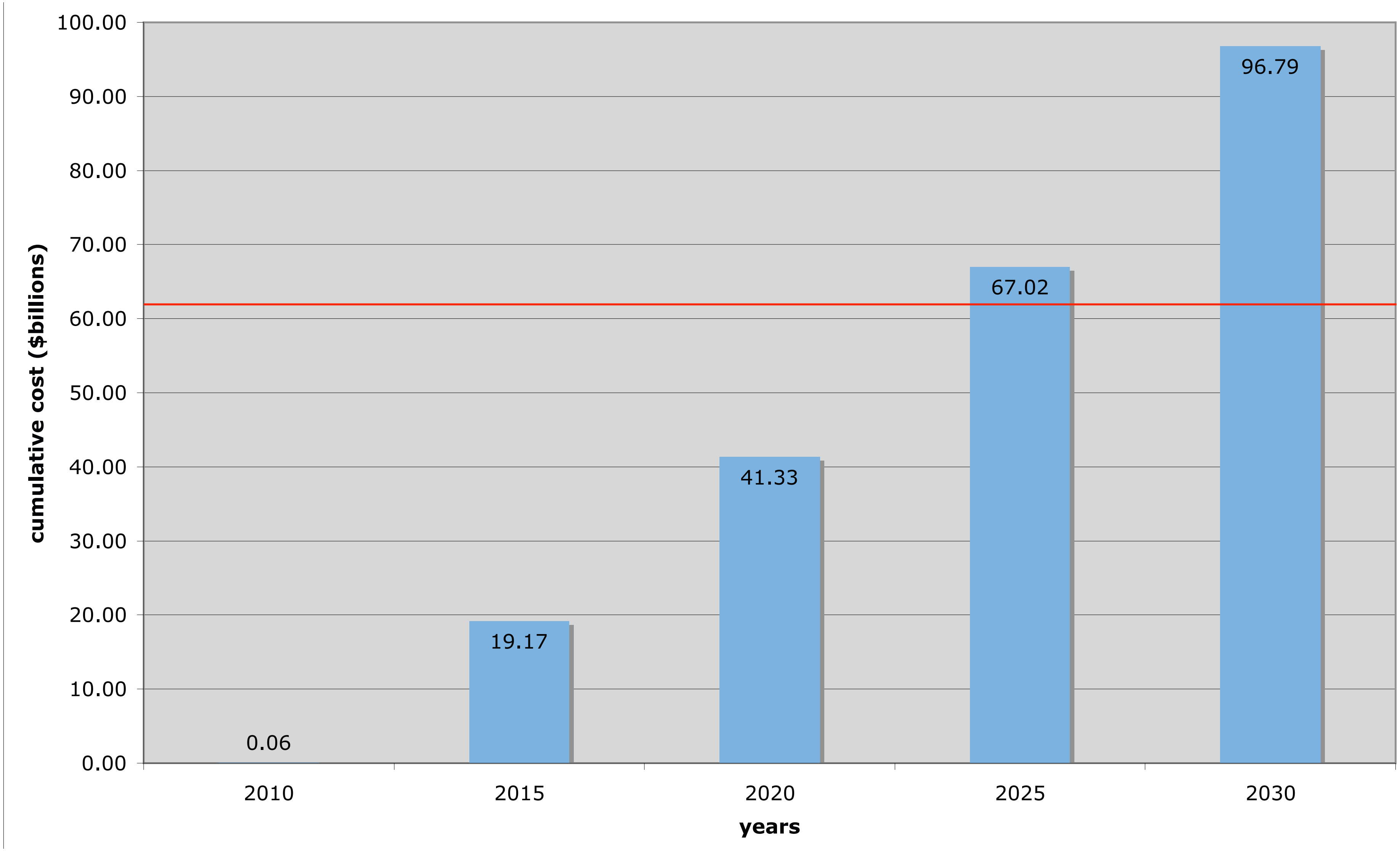
- Thus, interventions spread over 20 years are unaffordable.

Cumulative cost will blow up



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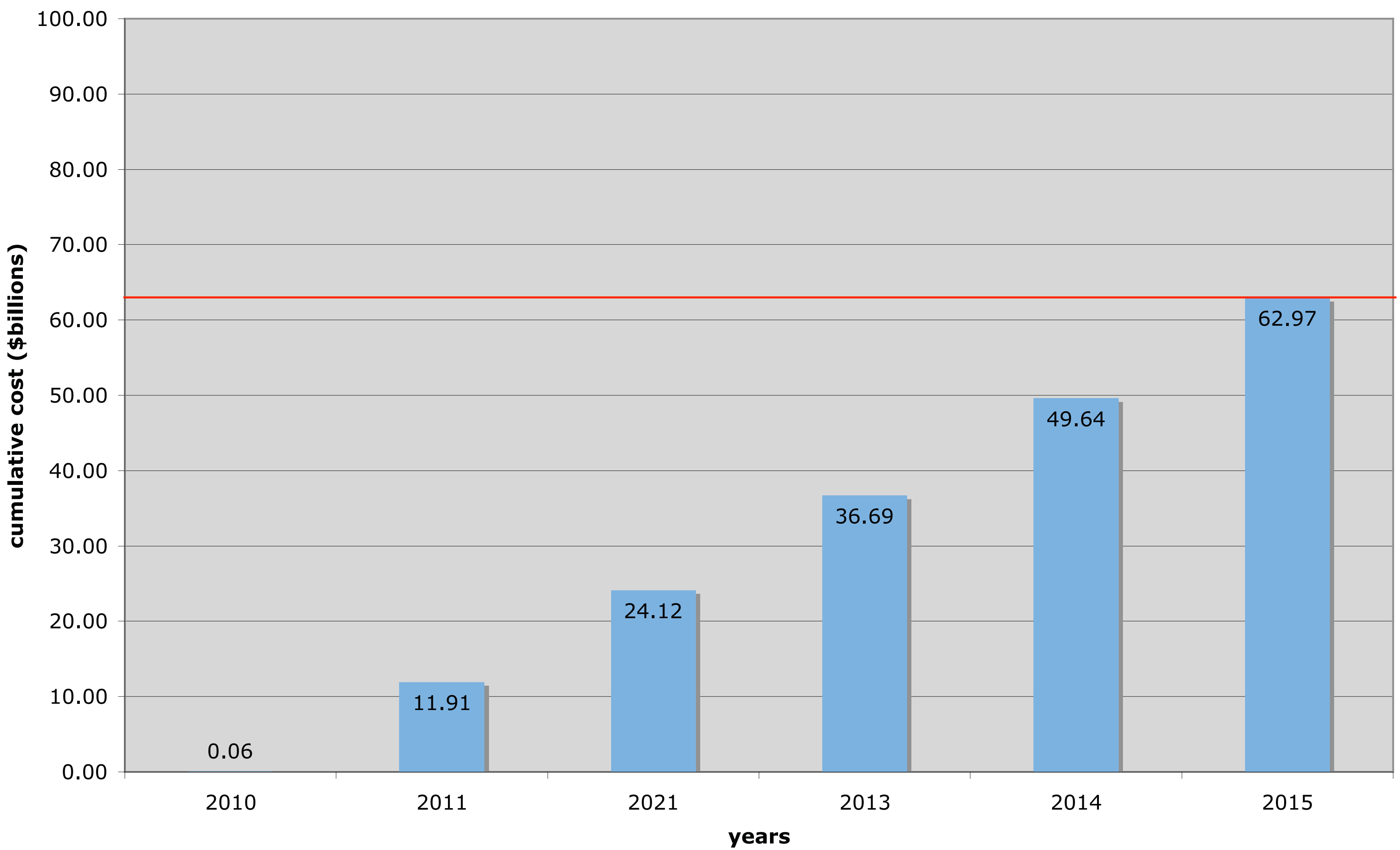

The cumulative cost of reducing the infection rate to 2/5 of its current rate over the next 5 years and treating everybody who requires it.

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- This (independently) matches our estimates.

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- The strategy we have used could be adopted by countries with different epidemic patterns.

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  ...and when to do it: right now.

Key References

- R.J. Smith? and R. Gordon, The OptAIDS Project: Towards global halting of HIV/AIDS
- R.J. Smith?, J. Li, R. Gordon and J.M. Heffernan, Can we spend our way out of the AIDS epidemic? A World Halting AIDS Model (BMC Public Health 2009, 9(Suppl 1):S15).

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