Why networks matter

DAIDD, White Oaks, Florida. December 2016

Brian Williams

South African Centre for Epidemiological Modelling and Analysis

The purpose of models is not to fit the data but to sharpen the question.

S. Karlin: 11th R.A. Fisher Memorial Lecture. 20 April 1983.

Bad news

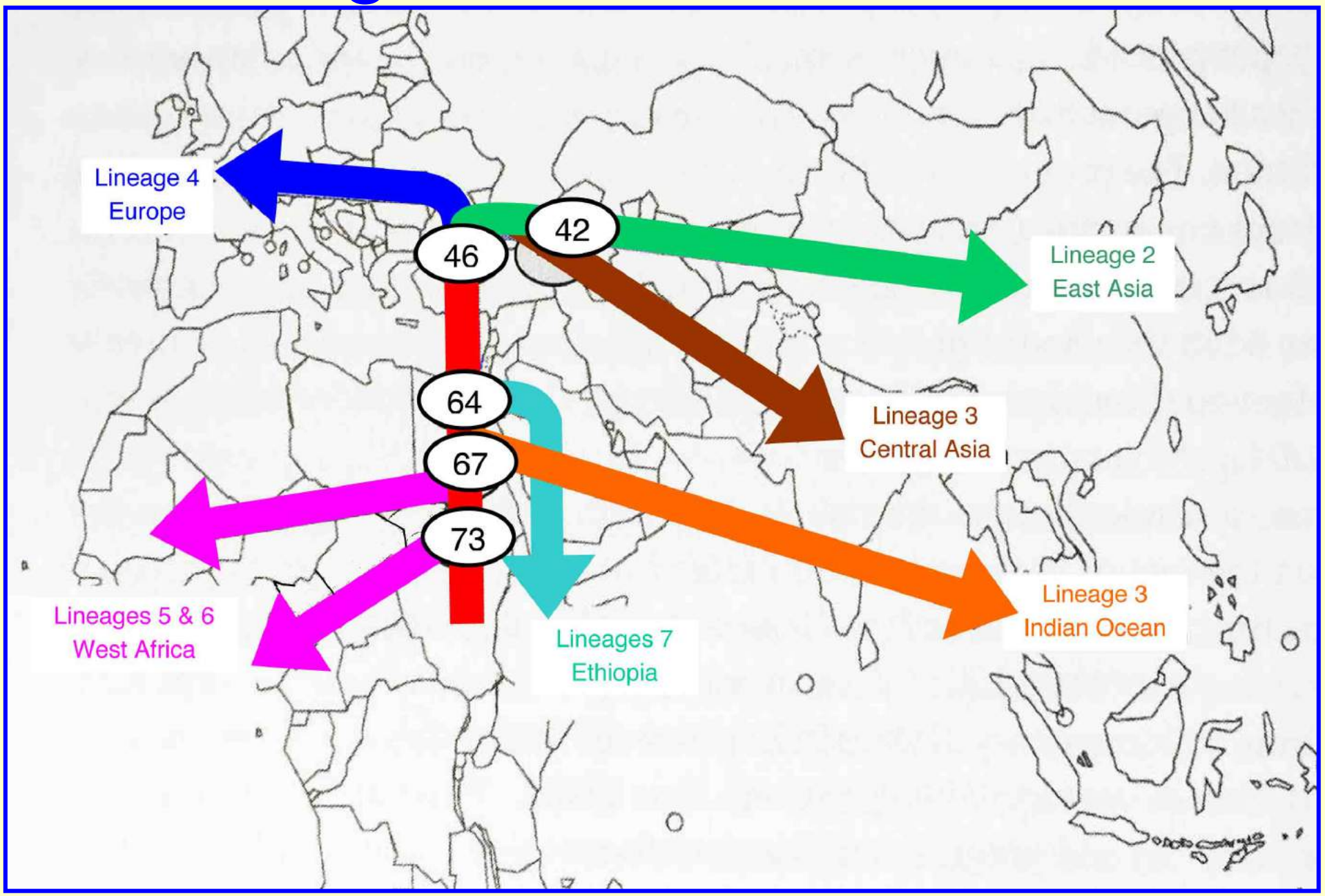
30 million people are infected with HIV.
Without ART 3 million people would die every year.

Good news

If you take ART you will live forever and you will not infect your partner
In Malawi ART costs just $66/year or $0.18/day

Questions?

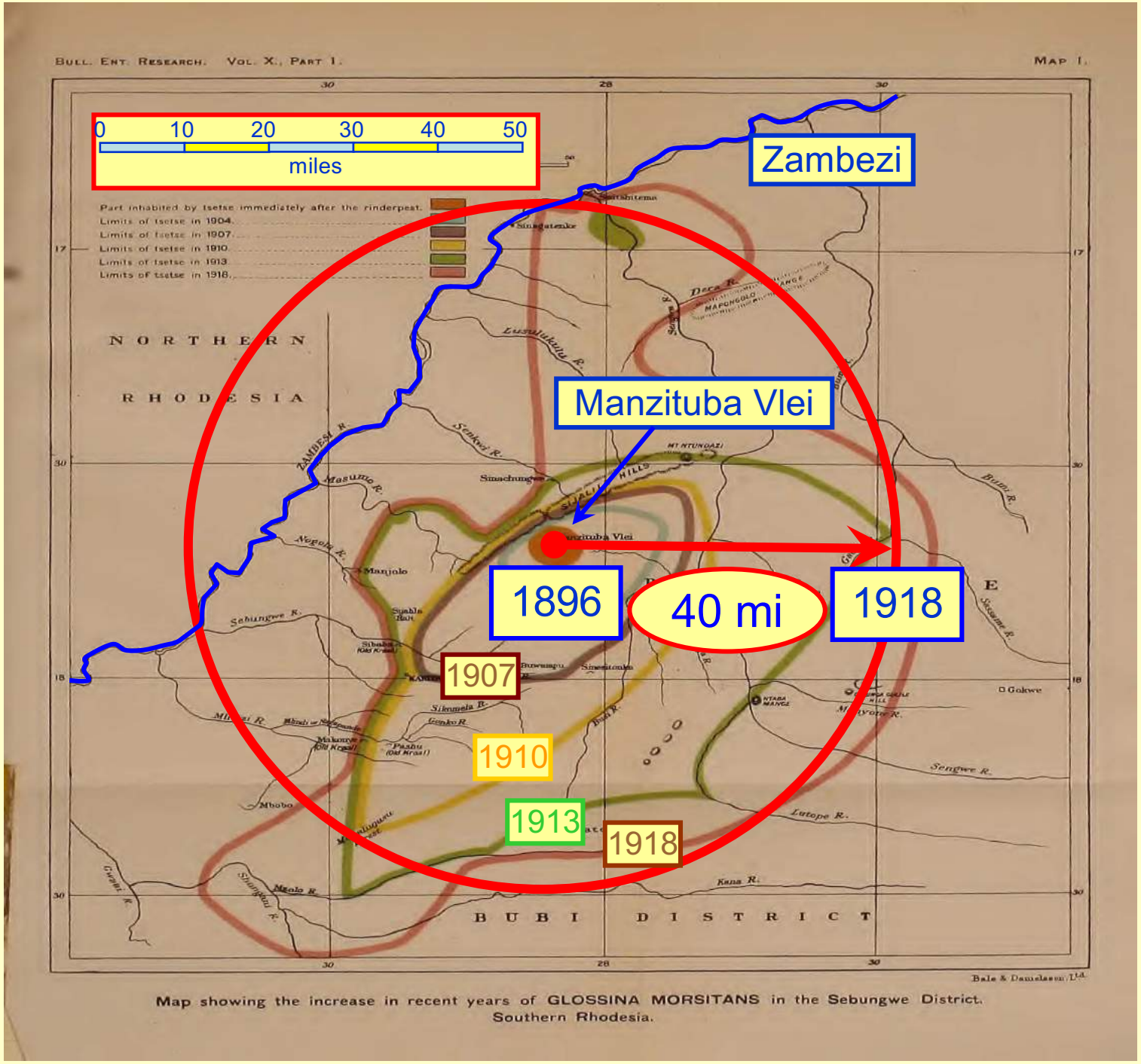
TB originated in Central Africa



Phylogenetic branching. Splits: thousand of years ago

Dye C *The population Biology of TB* (2015) *p. 10.*

Tsetse fly dispersal after the rinderpest in1896



Map showing the increase in recent years of GLOSSINA MORSITANS in the Sebungwe District. Southern Rhodesia.

Tsetse flies move on average about 500m per day. Why did it take them 22 years to spread out over 40 miles?

Jack, R.W. Bull. Ent. Res.X

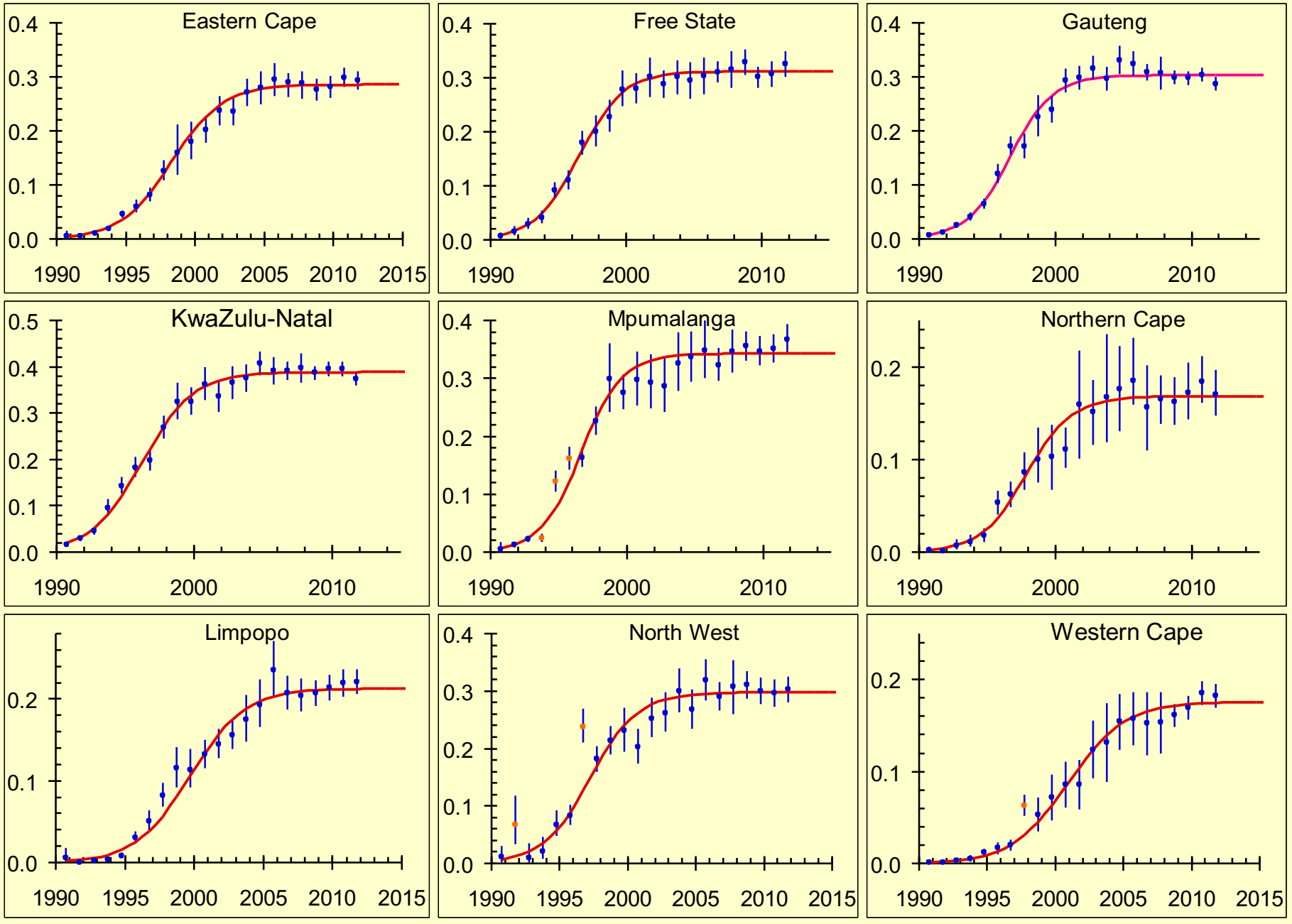
Why is the prevalence of HIV so variable?

Country	Rate/k adults
North India	2
Vietnam (low risk women)	4
Brazil	7
South India	15
Western Cape Coloured	20
West Africa	30
East Africa	50
South Africa	210
Western Cape Black	220
Vietnam (IDU)	400

Why are the nine worst affected countries in the world all in southern Africa?

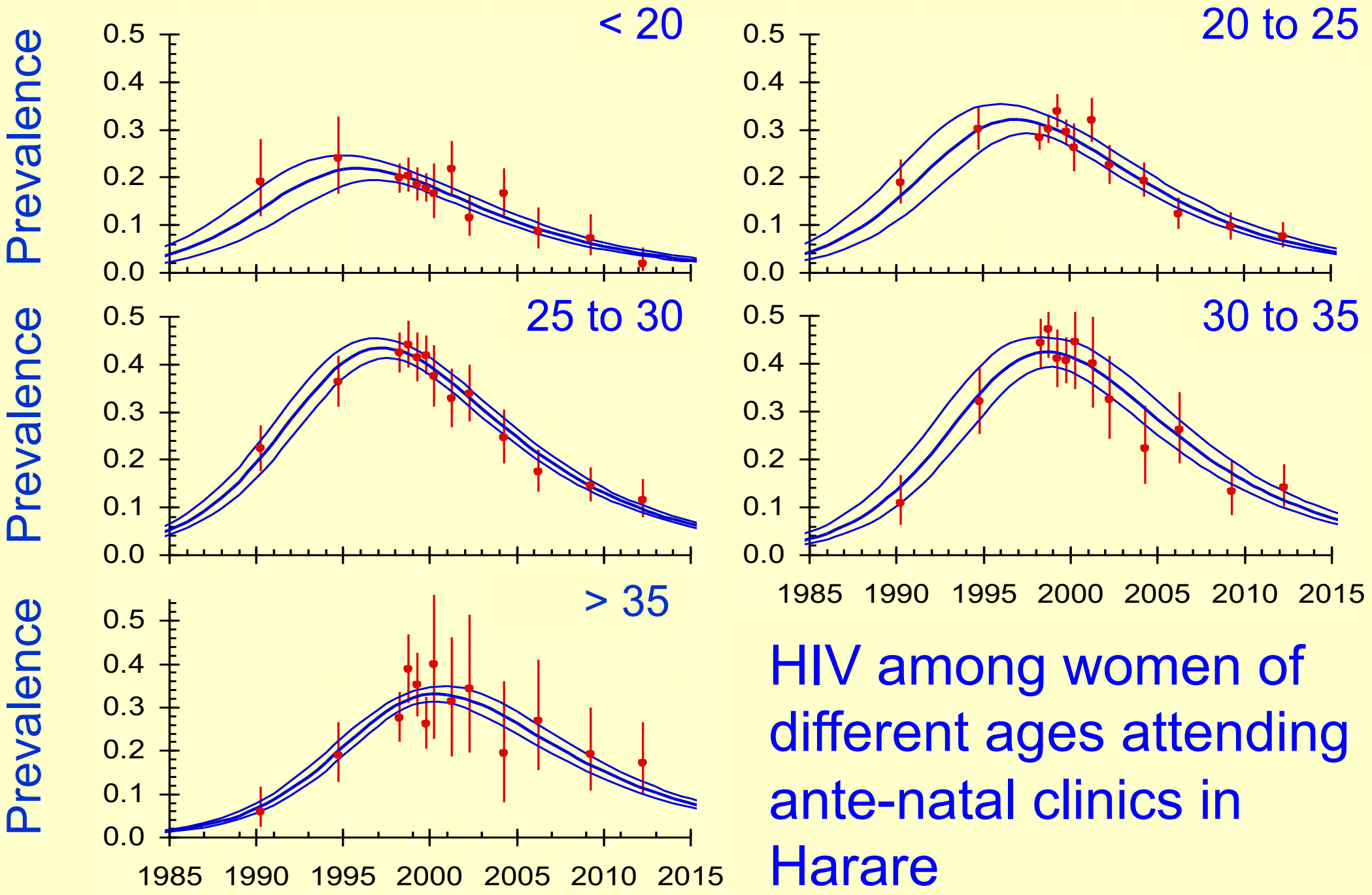
South Africa, Swaziland, Lesotho, Malawi, Botswana, Zimbabwe, Namibia, Zambia, Mozambique

HIV has remained stable in South Africa



Kustner *S Afr Med J.* 1994;84:195-200. National Antenatal Sentinel HIV and Syphilis Prevalence Survey in South Africa, 2012. Department of Health, South Africa.

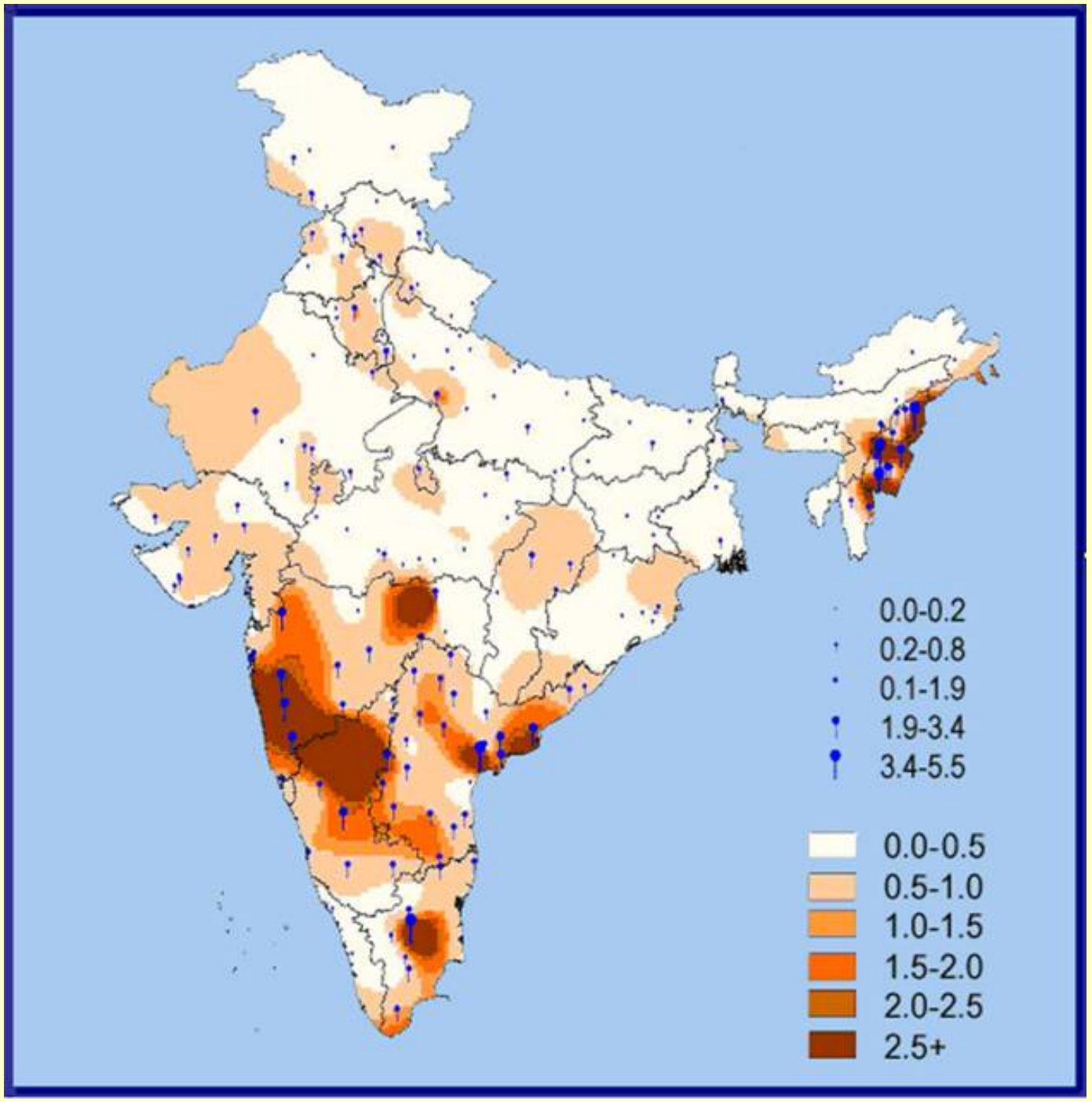
… but not in Harare



HIV among women of different ages attending ante-natal clinics in Harare

Hargrove, J. Personal communication

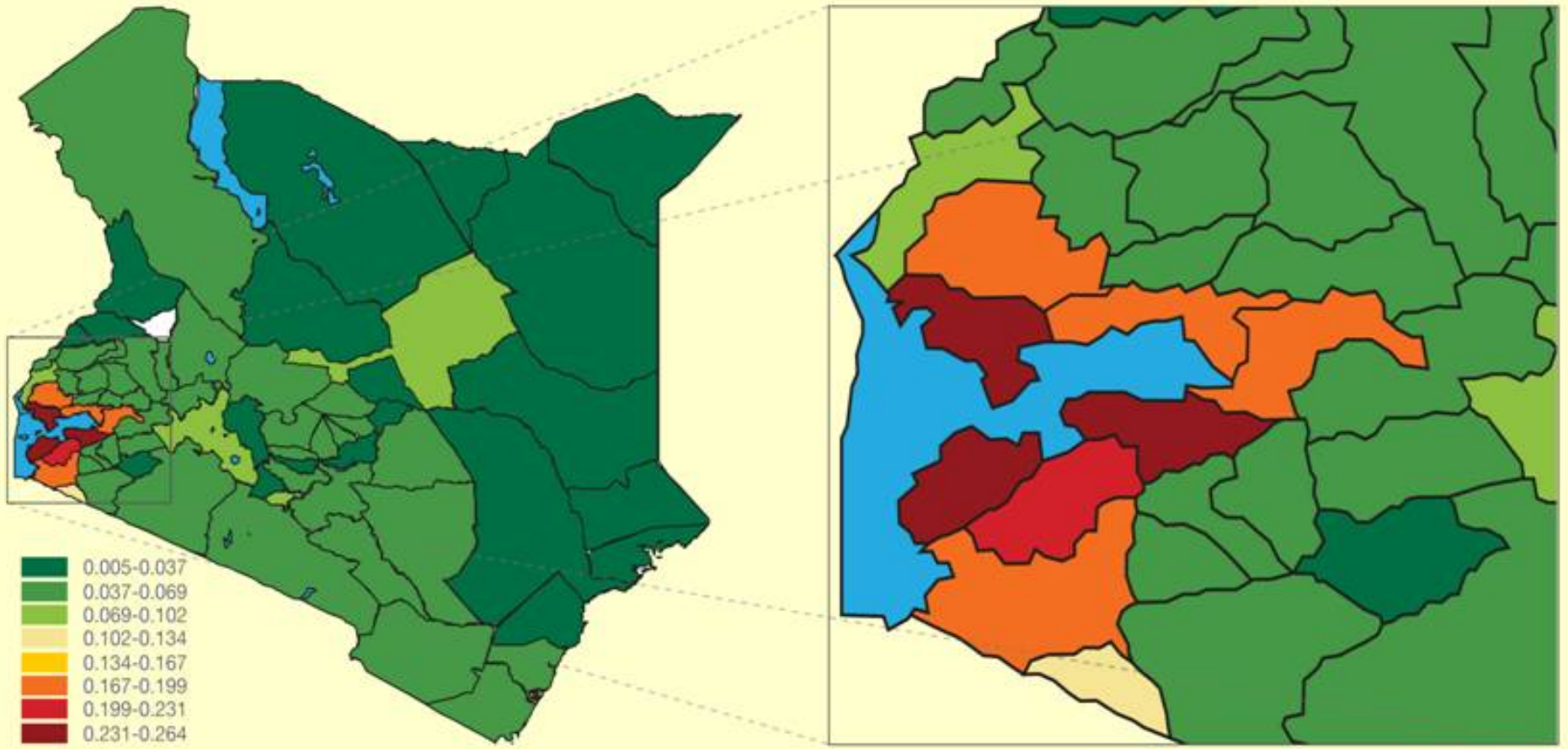
HIV in India



Concentrated in the far east: Manipur and Nagaland;
and in the south: Maharashtra, Karnataka, Andhra Pradesh, and Tamil Nadu, but not Kerala

Williams *PNAS* (2005) 102: 9619-24.

HIV in Kenya

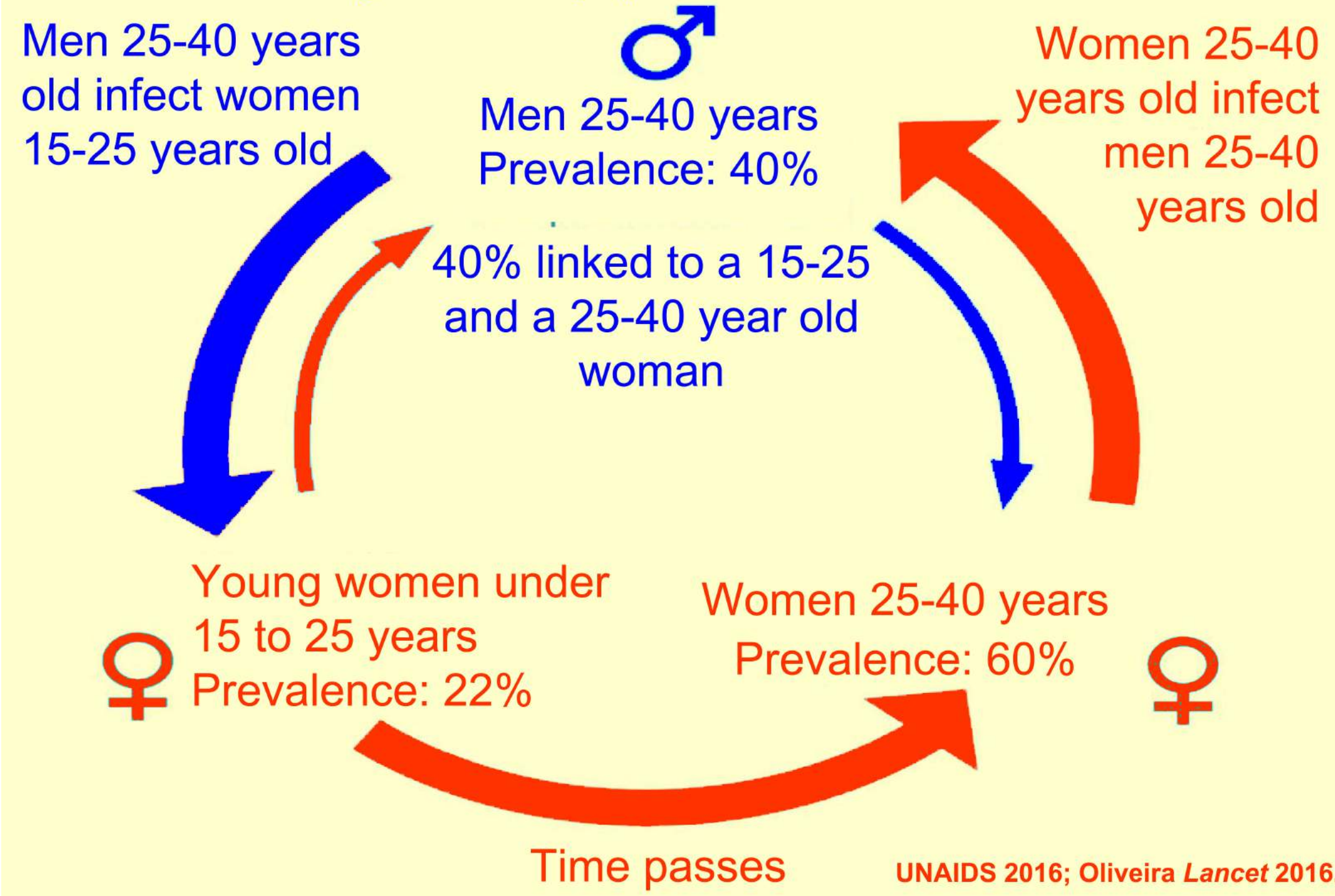


Concentrated in eight districts of Nyanza province bordering Lake Victoria but not Busia (light green, extreme west).

WHO. A Brief History of Tuberculosis Control in Kenya. Geneva: World Health Organization, 2009.

Answers?

Life cycle approach to AIDS



UNAIDS 2016; Oliveira *Lancet* 2016.

Age disparities and the spread of HIV

Sexual partnering between young women and older men, who might have acquired HIV from women of similar age, is a key feature … driving transmission [of HIV]. … strategies that … address age-disparate sexual partnering is crucial to … ending AIDS as a public health threat.[1]

Partner age disparity did not predict HIV acquisition in a rural community in KwaZulu-Natal [addressing] age-disparate sexual relationships may not be a cost-effective … in this setting.[2]

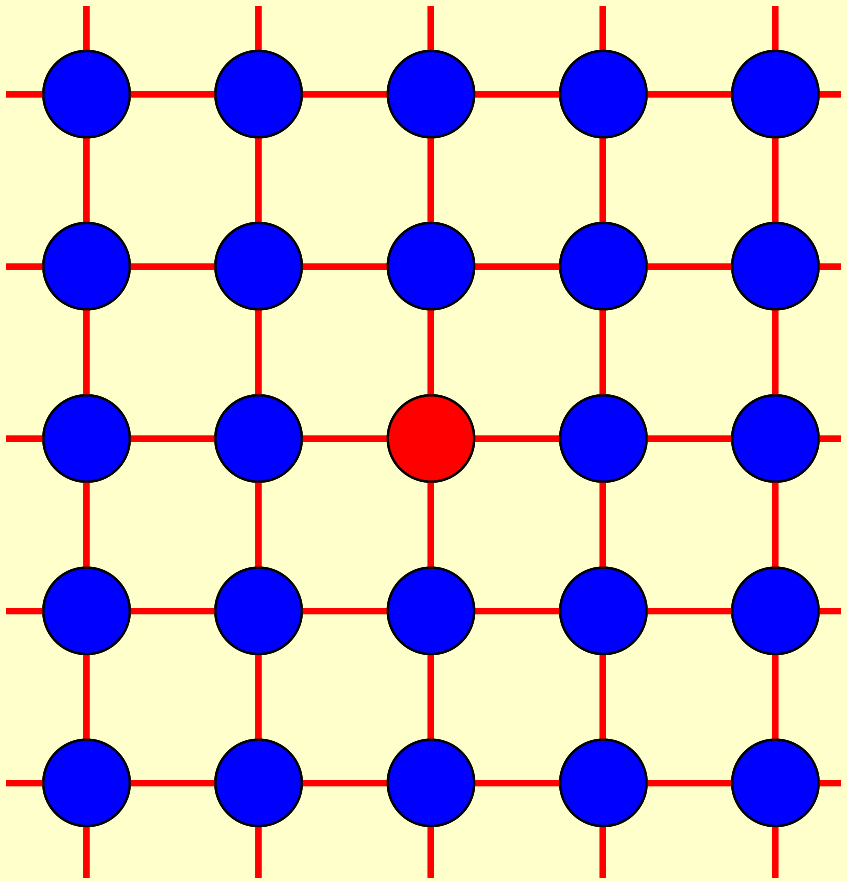
1. Oliveira *Lancet* and Gouws *Lancet* In press 2016; 2. Harling *JAIDS* 2014;

Without connections across space and across ages HIV cannot persist.

Since HIV does persist, what is the minimal level of connectedness needed to sustain an epidemic?

Does this help us to explain different endemic levels of HIV and to find ways to control HIV?

Diffusion on a lattice



$$0 = \nabla^2 \rho$$

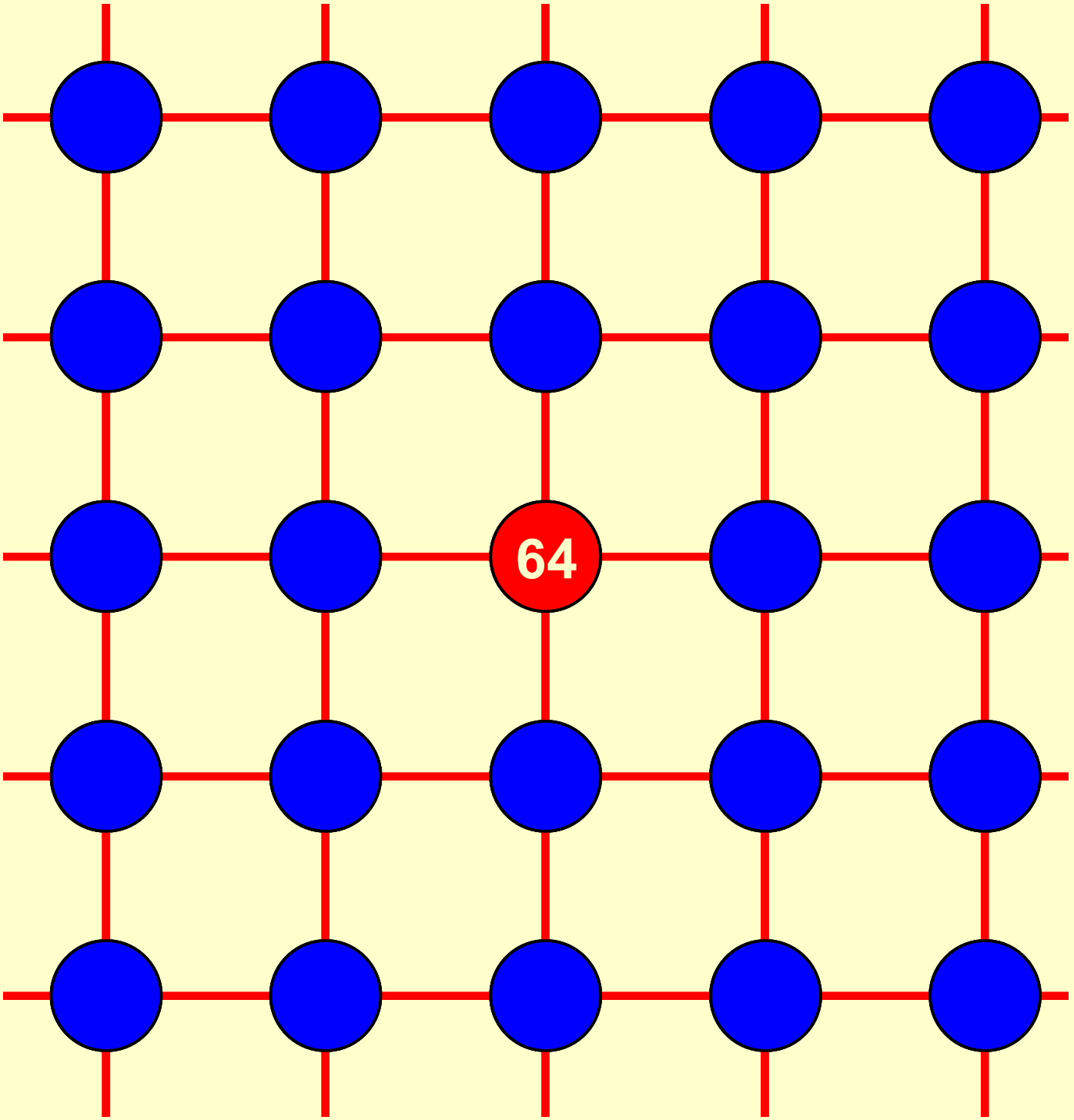
Electrical potential

$$\frac{d\rho}{dt} = \alpha \nabla^2 \rho$$

Diffusion of gases

$$\frac{d\rho}{dt} = \alpha \nabla^2 \rho + r\rho(1-\rho)$$

Tsetse flies, people, HIV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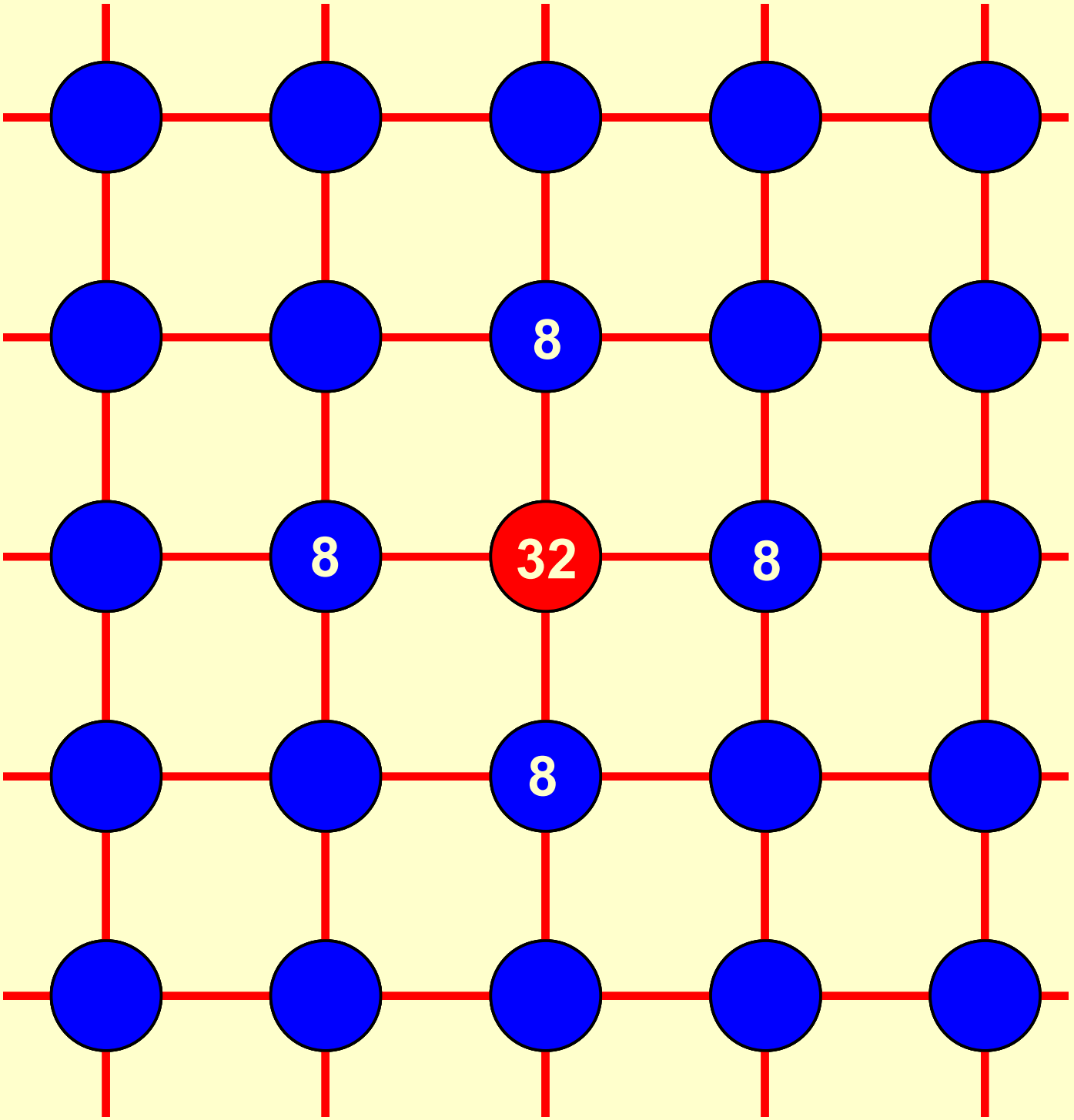
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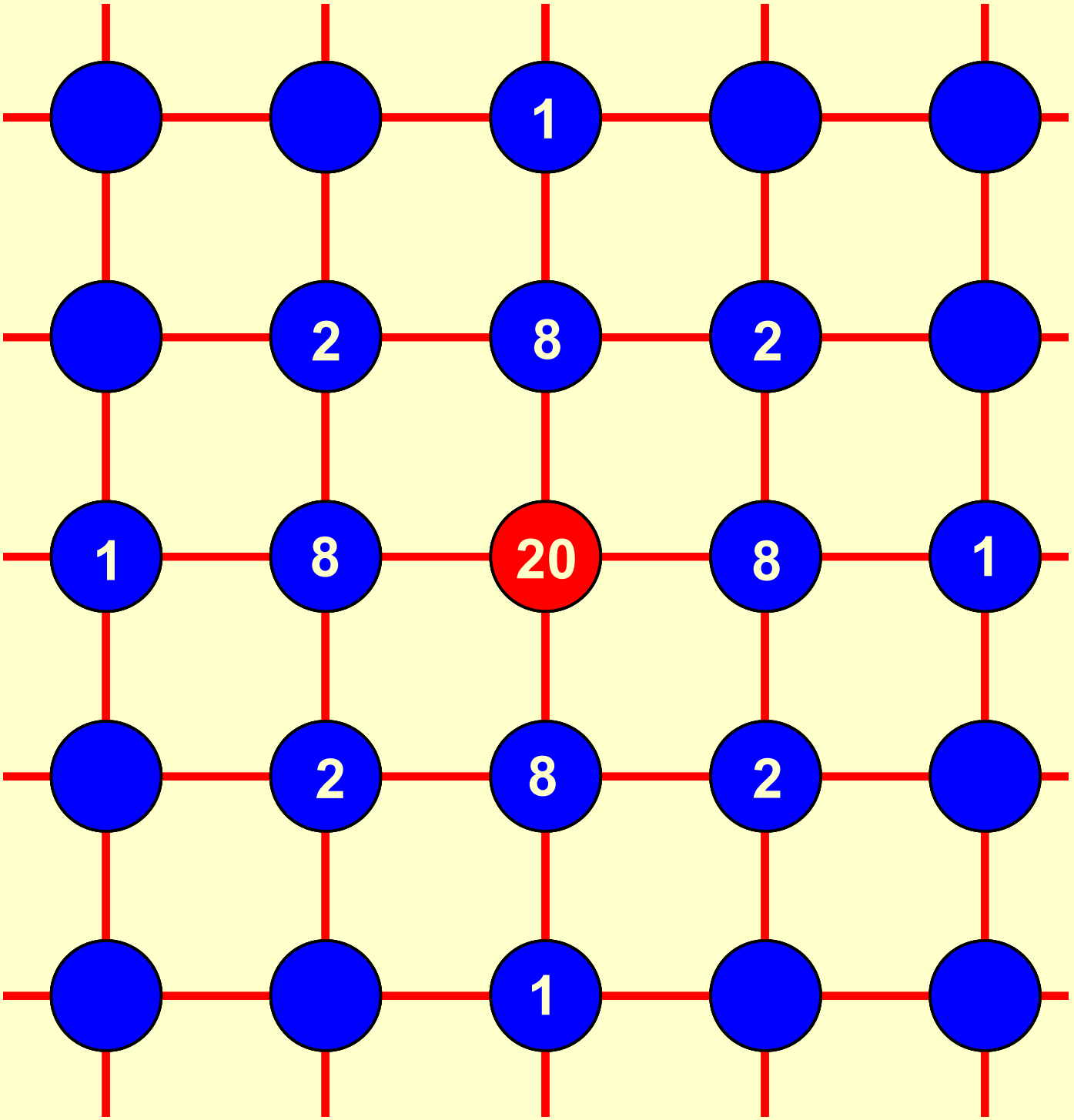
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1

Fisher (1937): Diffusion of genes

Diffusion in one dimension

$$\frac{d\rho}{dt} = \alpha \frac{d^2\rho}{dx^2} + r\rho(1-\rho) - \mu\rho$$

Wave spreading at a rate v

$$v = 2\sqrt{\alpha(r-\mu)}$$

$$R_0 = \frac{r}{\mu}$$

$$\mu = \frac{1}{L}$$

$$v = 2\sqrt{\alpha \frac{R_0 - 1}{L}}$$

Fisher R.A. Ann. Eugenics 1937; Volpert et al. Phys. Life Rev. (2009) 6, 267.

Fisher in space

$$v = 2\sqrt{\alpha \frac{R_0 - 1}{L}}$$

Distance between neighbours, $\alpha^2 \approx 10\text{km}^2/\text{yr}$ $R_0 \approx 5$; $L \approx 10$ years

HIV would spread at a rate of 4 km/year

Fisher with age

$$c = 2\sqrt{\sigma^2 \frac{R_0 - 1}{L}} \qquad \sigma > 0.7\frac{L}{R_0 - 1}$$

σ = standard deviation of the age of sexual partners that a person has in one year.

Spreads out by c years of age per calendar year of time.

$c > 1 \rightarrow \sigma > 1.3$ years: 95% range $\rightarrow$ 5.2 years

Age ranges of sexual partners

Place	Age range (yrs: 95% CI)
Carletonville[1]	20 years
Likoma Island[2]	20 years
Vulindlela[3]:	25 years
Hlabisa[4]:	10 years
Balkus[5]:	Difference not range

Carletonville: MacPhail IJSA 2002; Likoma Island: Beauclair Nature 2016;
Vulindlela: Oliveira Lancet 2016 In press; Hlabisa: Harling JAIDS 2015; Balkus JAIDS 2015

Extreme cases

Mean Field approximation

Everyone is connected to everyone else (with some small probability)

Increase in prevalence is exponential (South Africa and Zimbabwe)

Lattices

Only connected to nearest neighbours

Increase is locally exponential but overall numbers increase linearly (1D) or quadratically (2D)

Spatial Epidemiology of HIV in a 'small world'

Imagine two worlds. In the first world people only have sex with their neighbours. In the second world they have sex with their neighbours but occasionally have sex with someone who lives far away. We will keep everything else the same: the frequency of sex, the number of partners, and the risk of infection. What does playing away from home, or migration, do to the epidemic?'

Doubling time = 1 year; Life expectancy = 10 years
Number of partners = 4; size of population = 16k

Left	Right
Sex only with Immediate neighbours	90% of sex with neighbours, 10% chosen at random

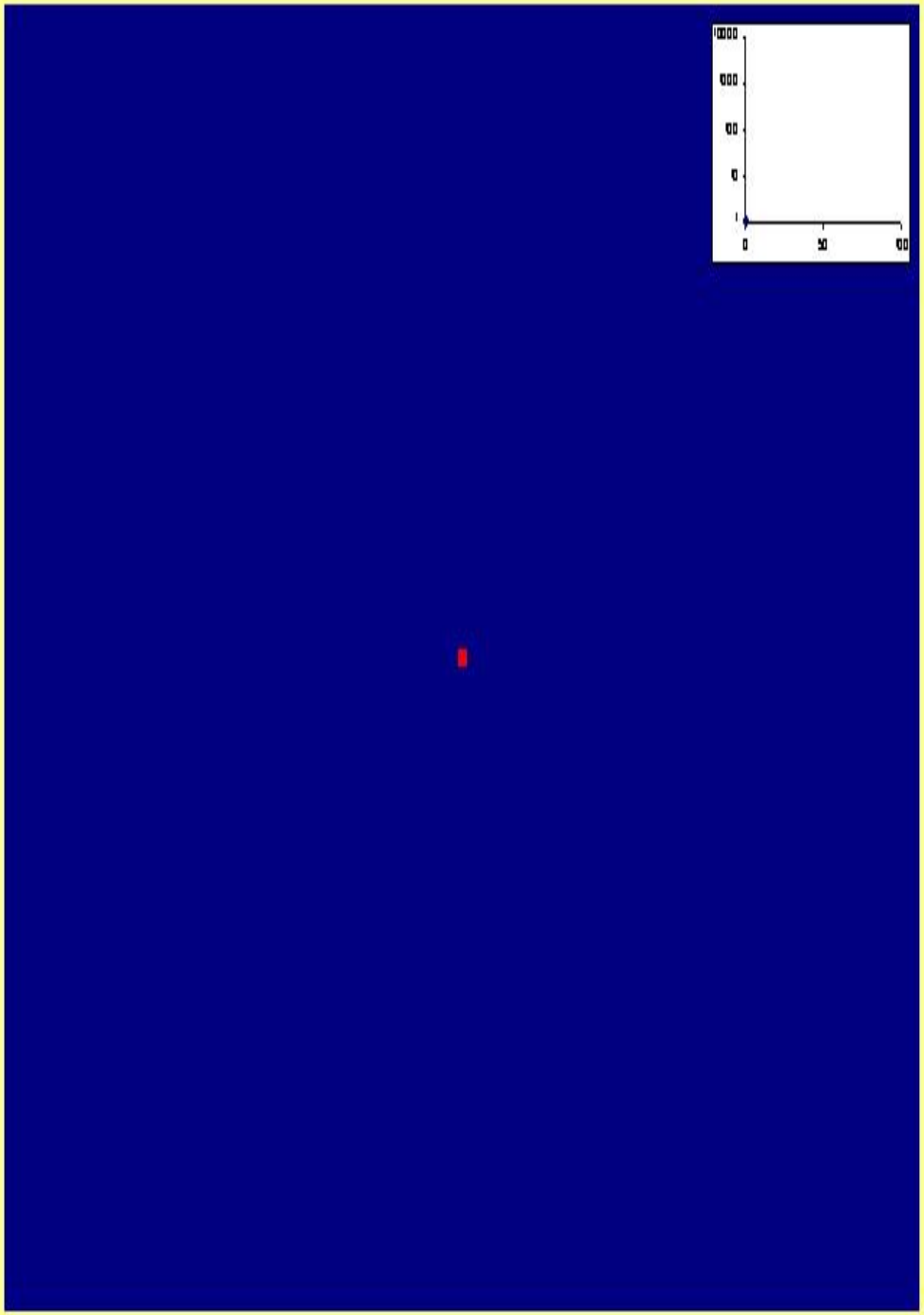
Start with one infected person at in the middle of the screen

Blue: Suscept.

Red: Infected

Yellow: Dead

0



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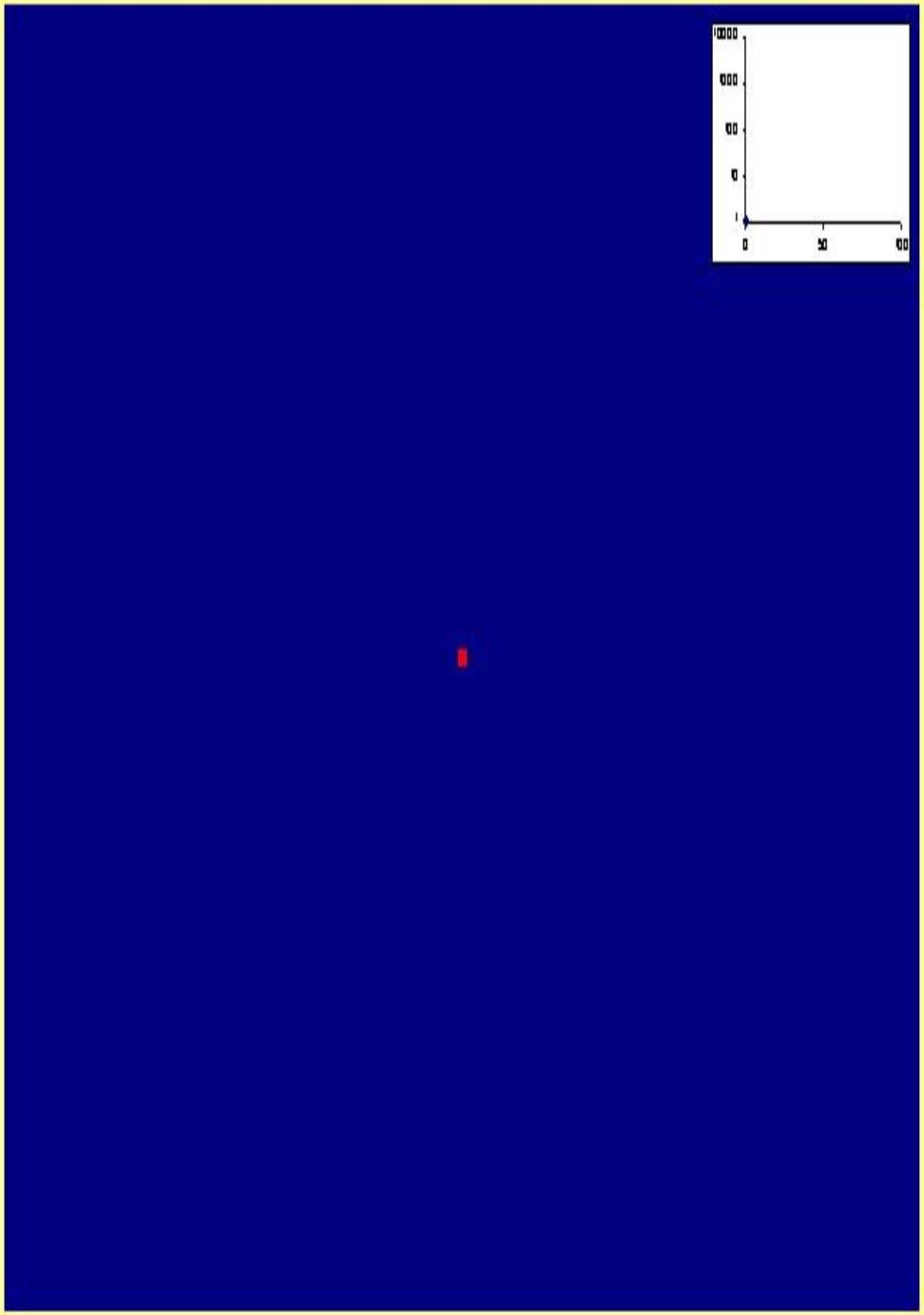

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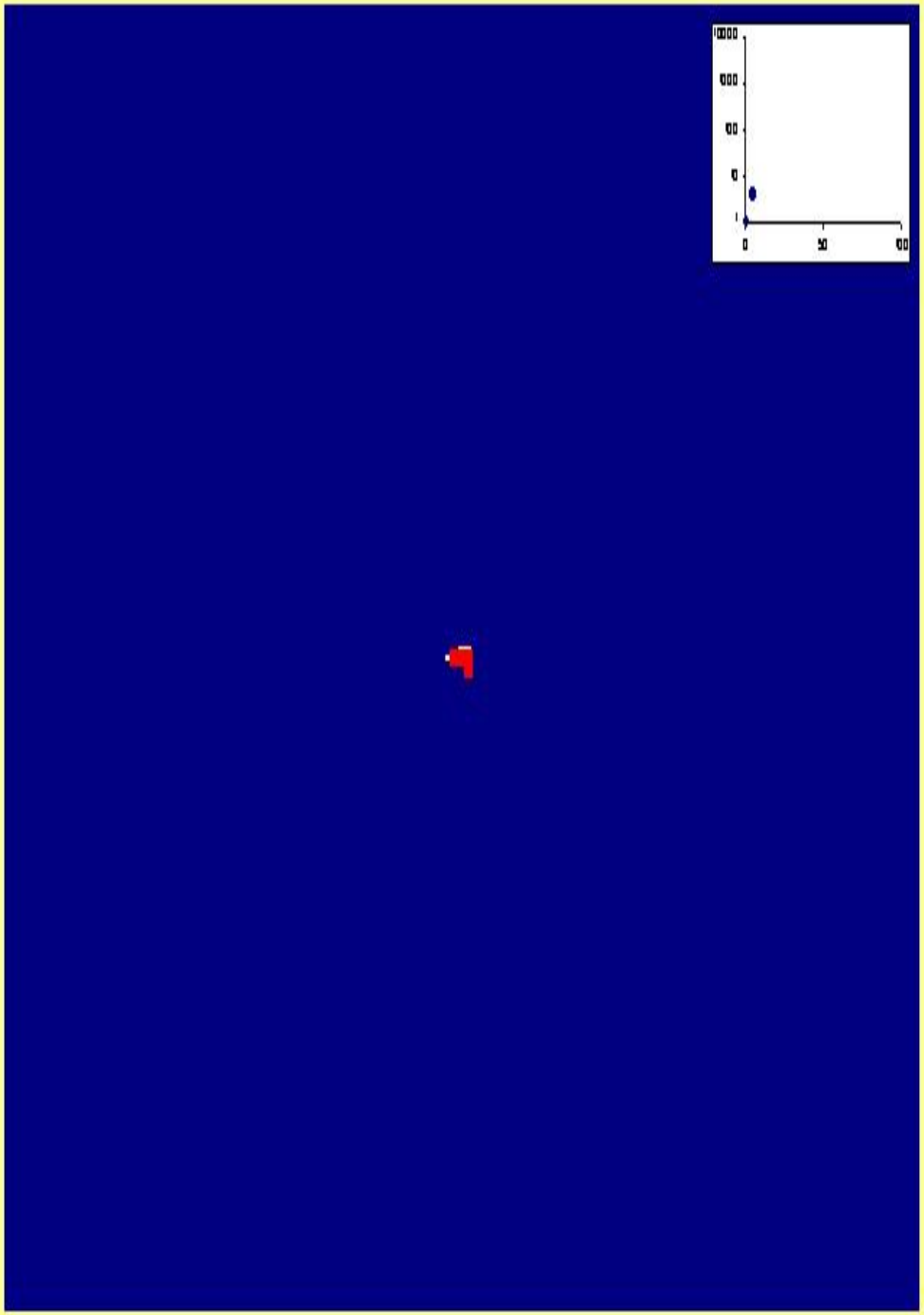

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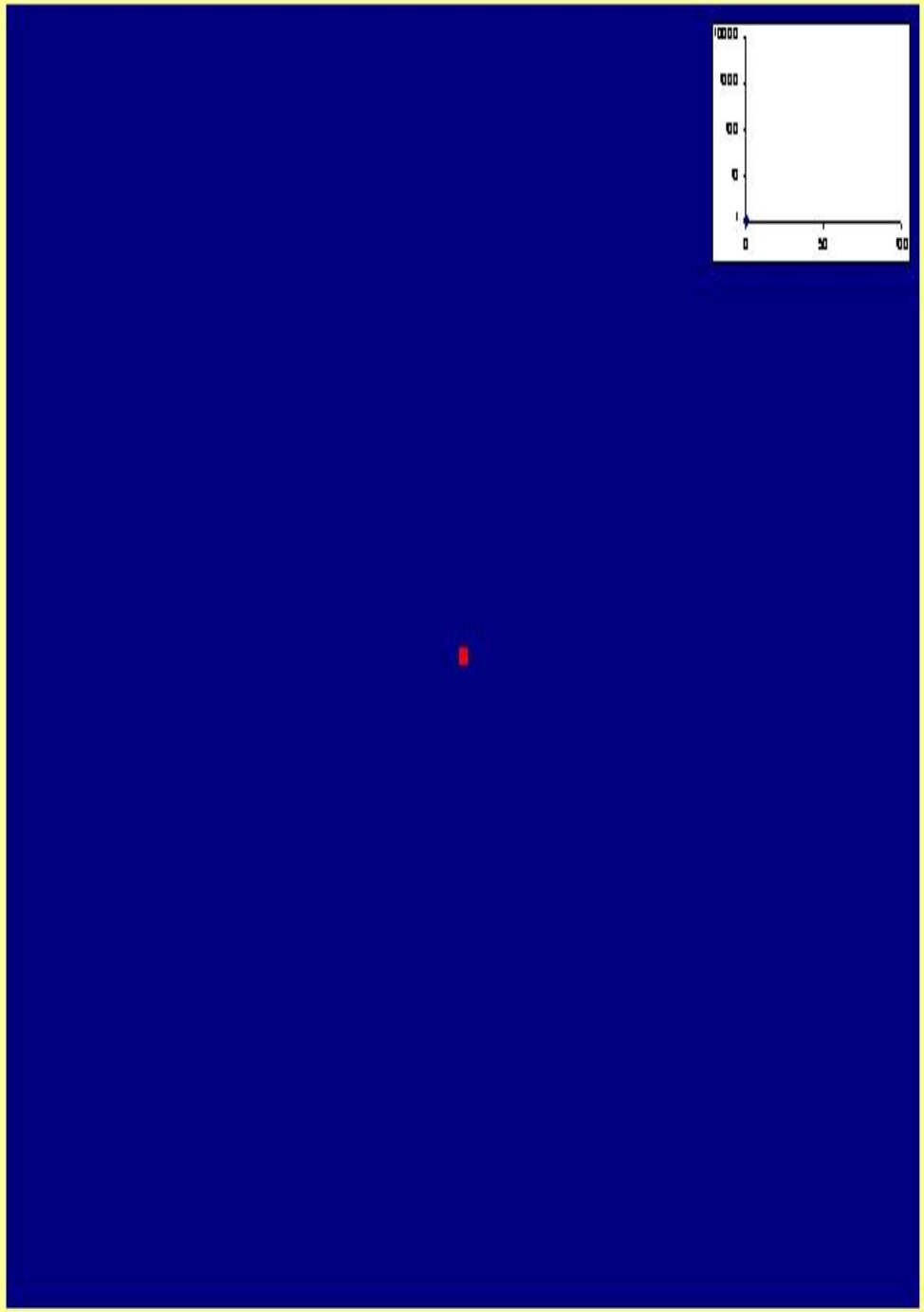

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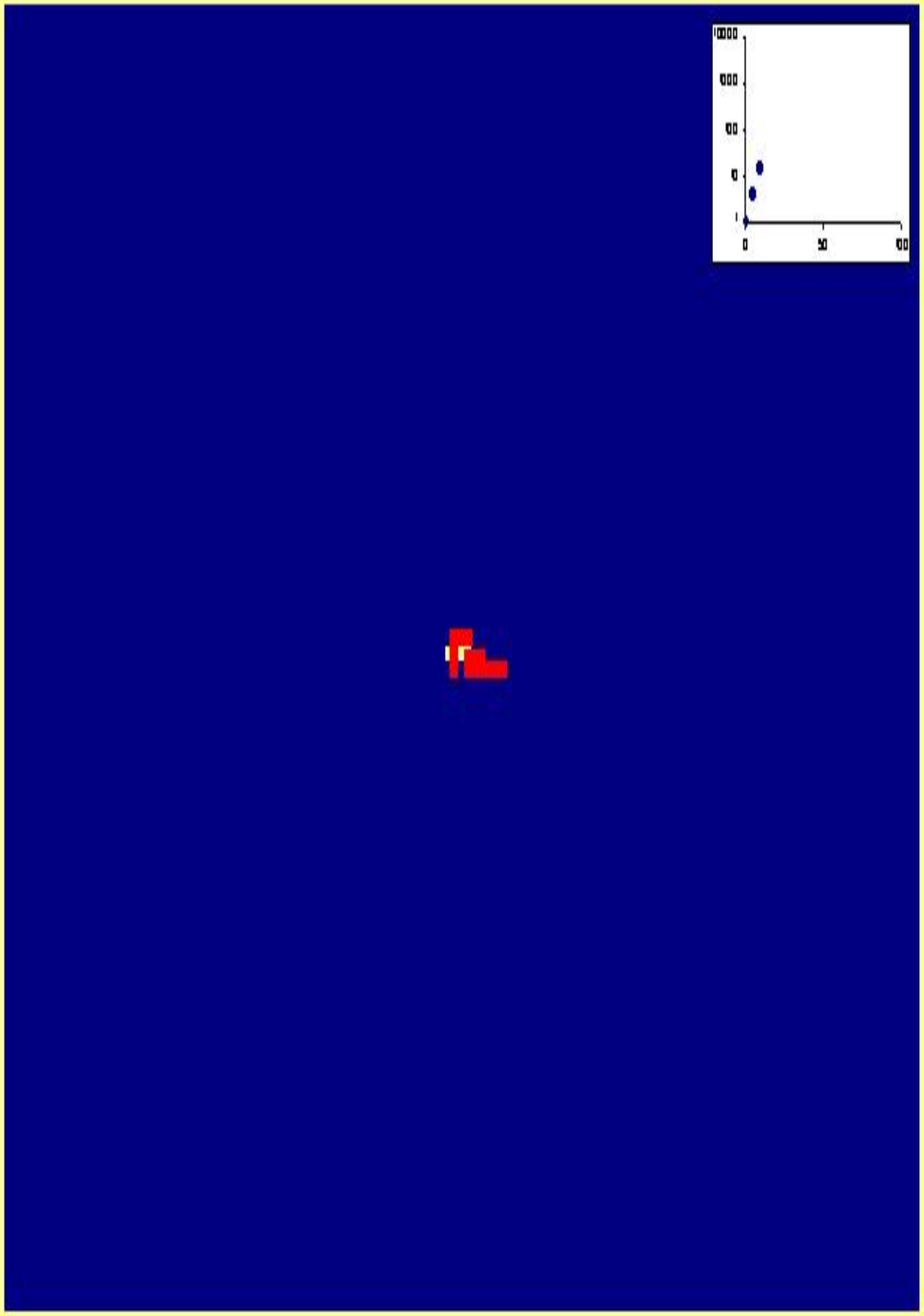

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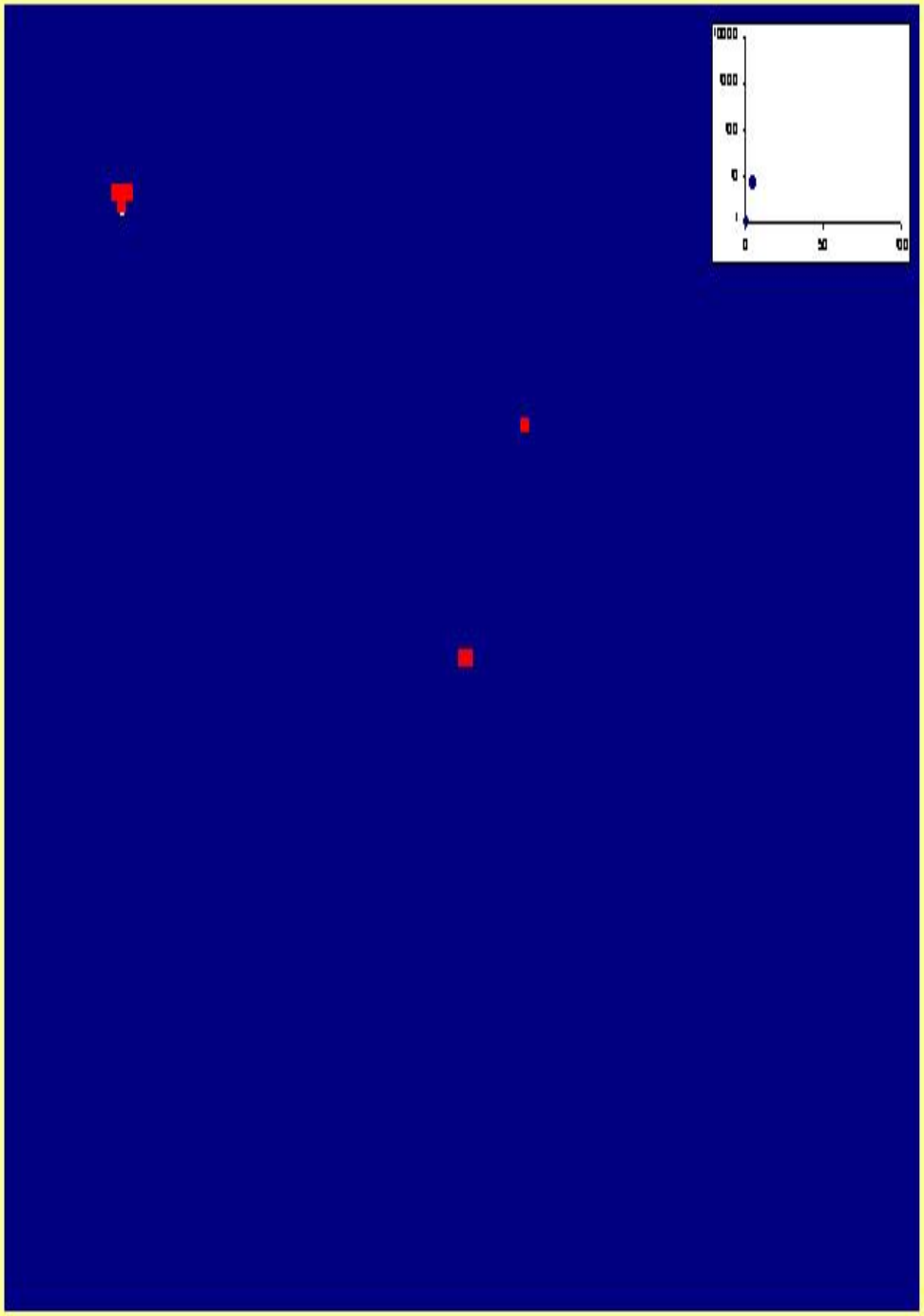

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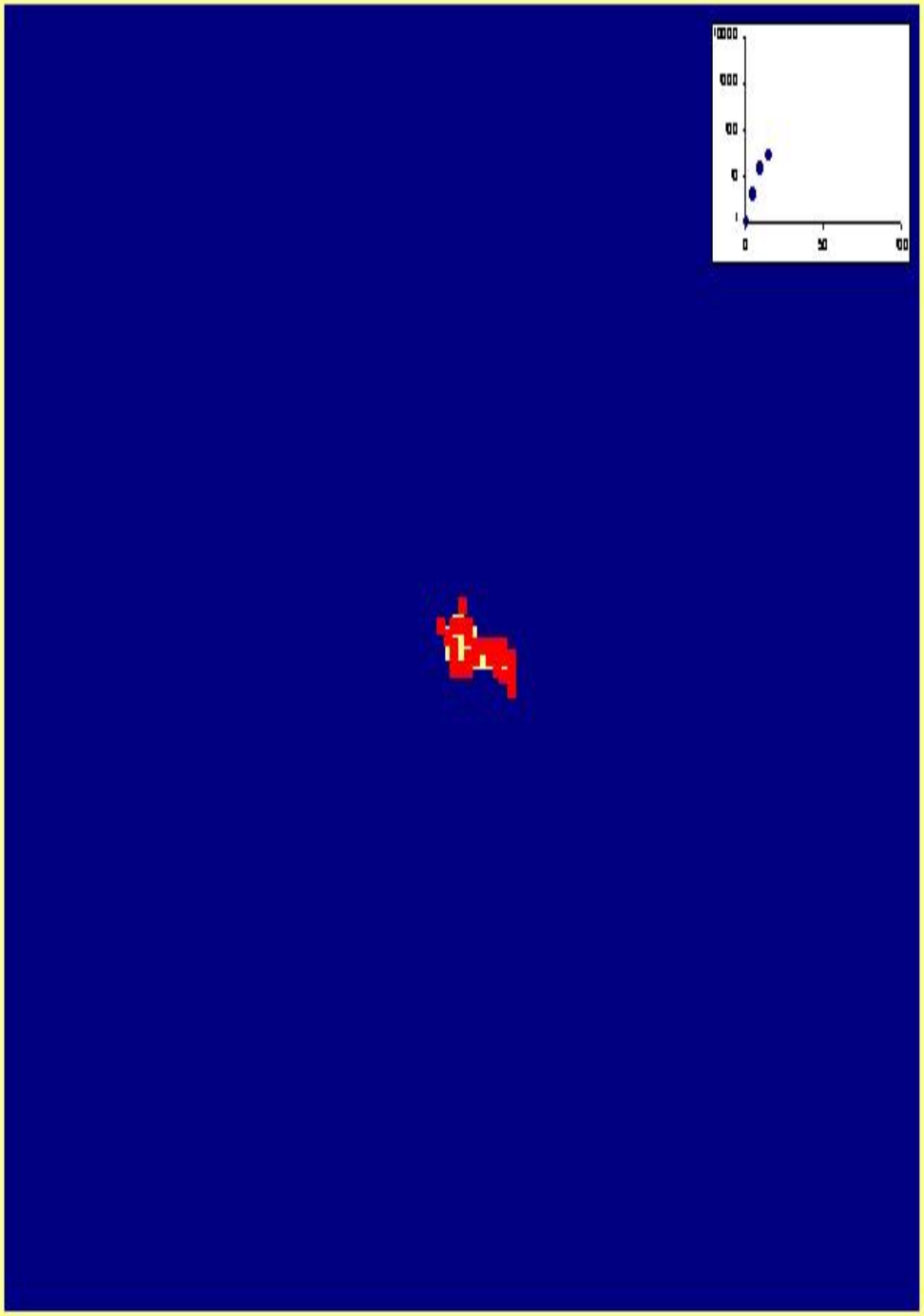

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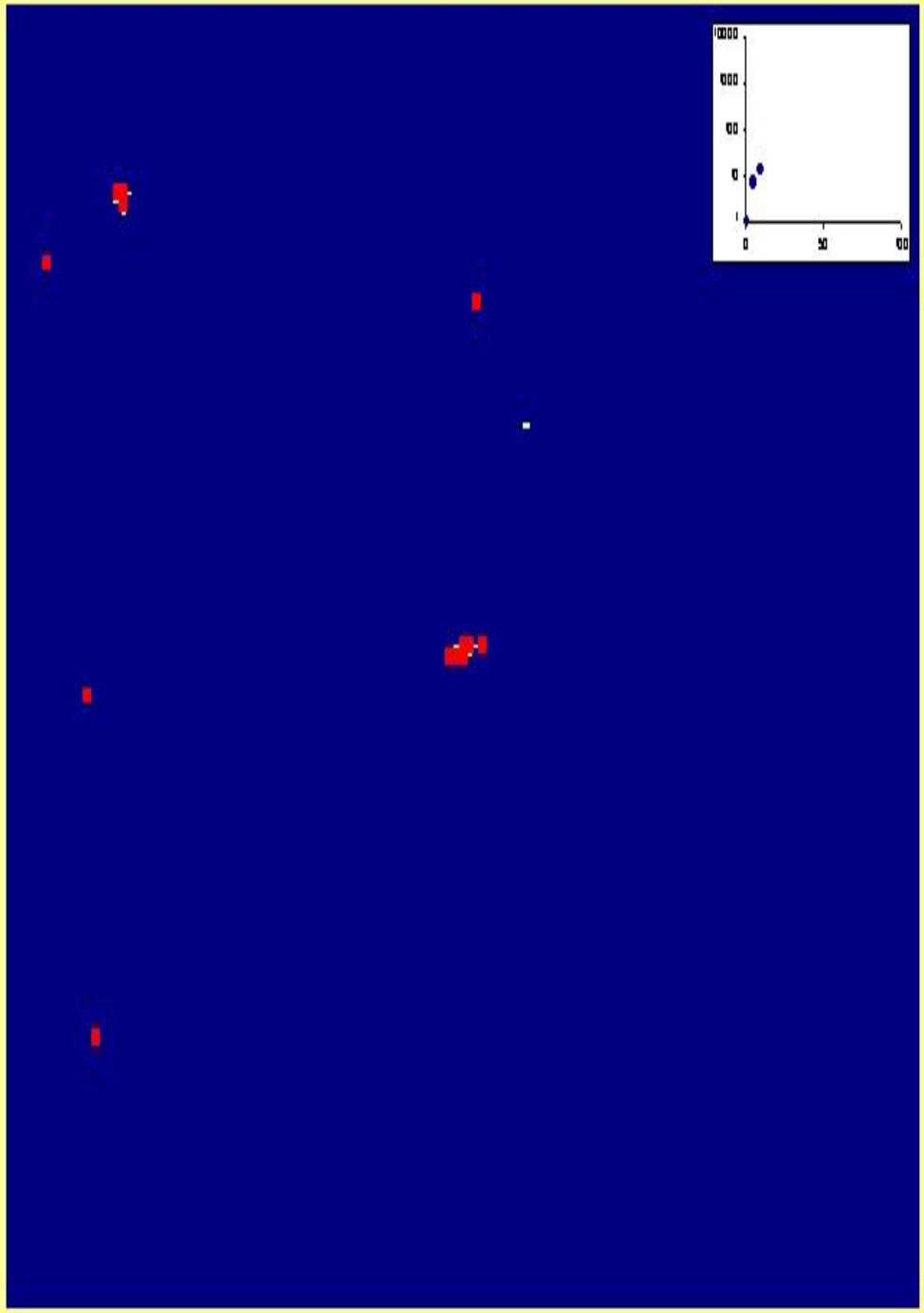

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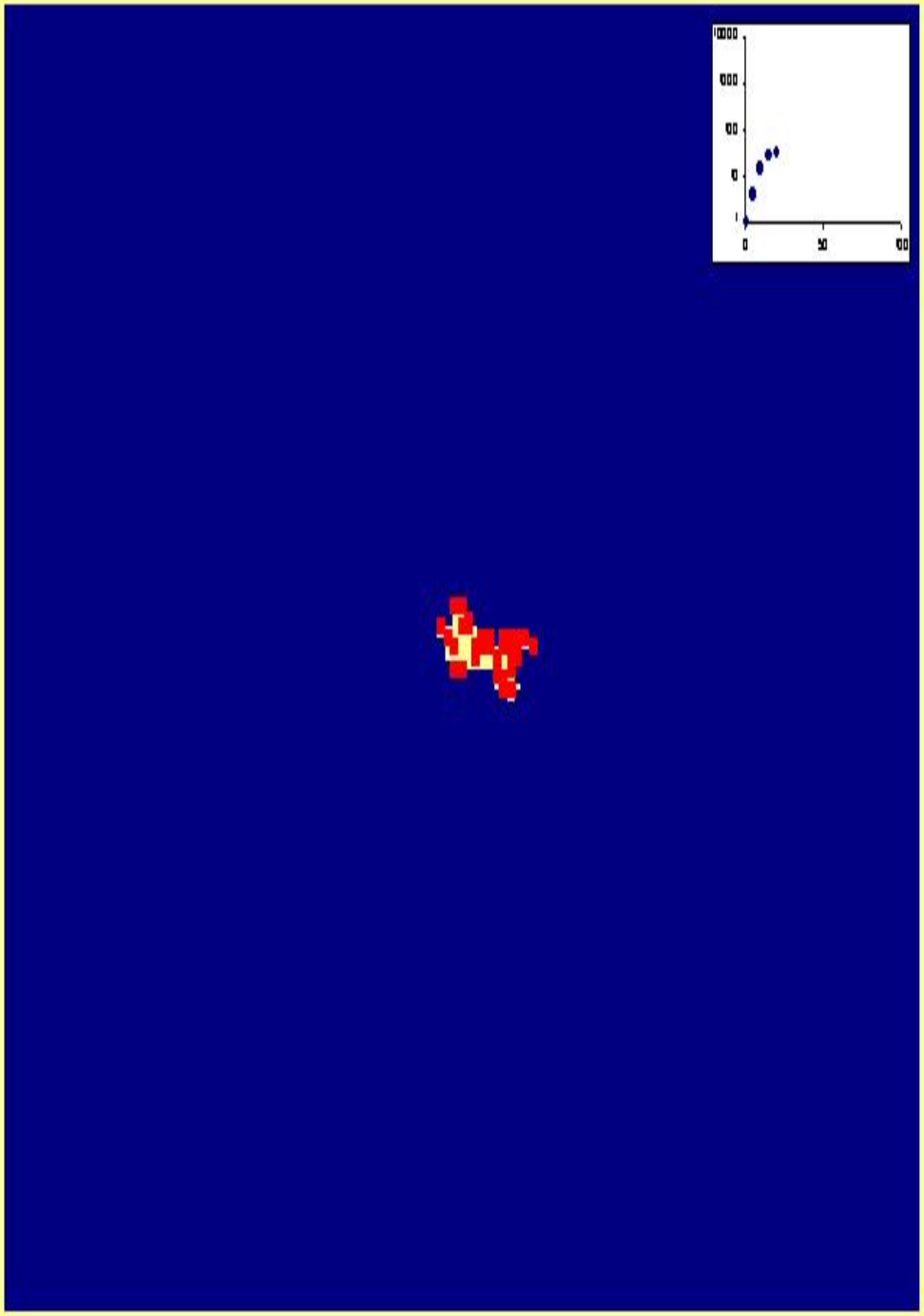

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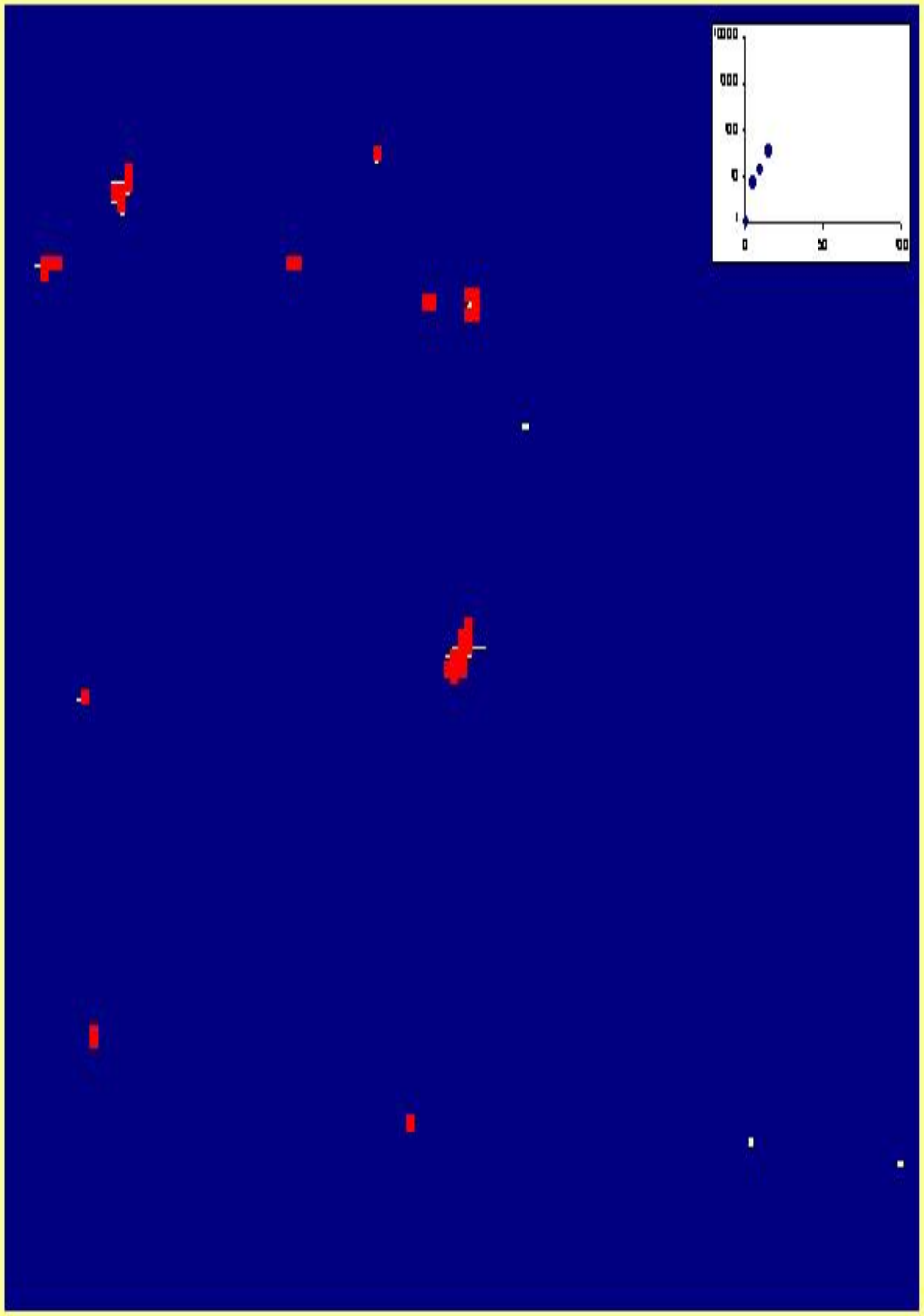

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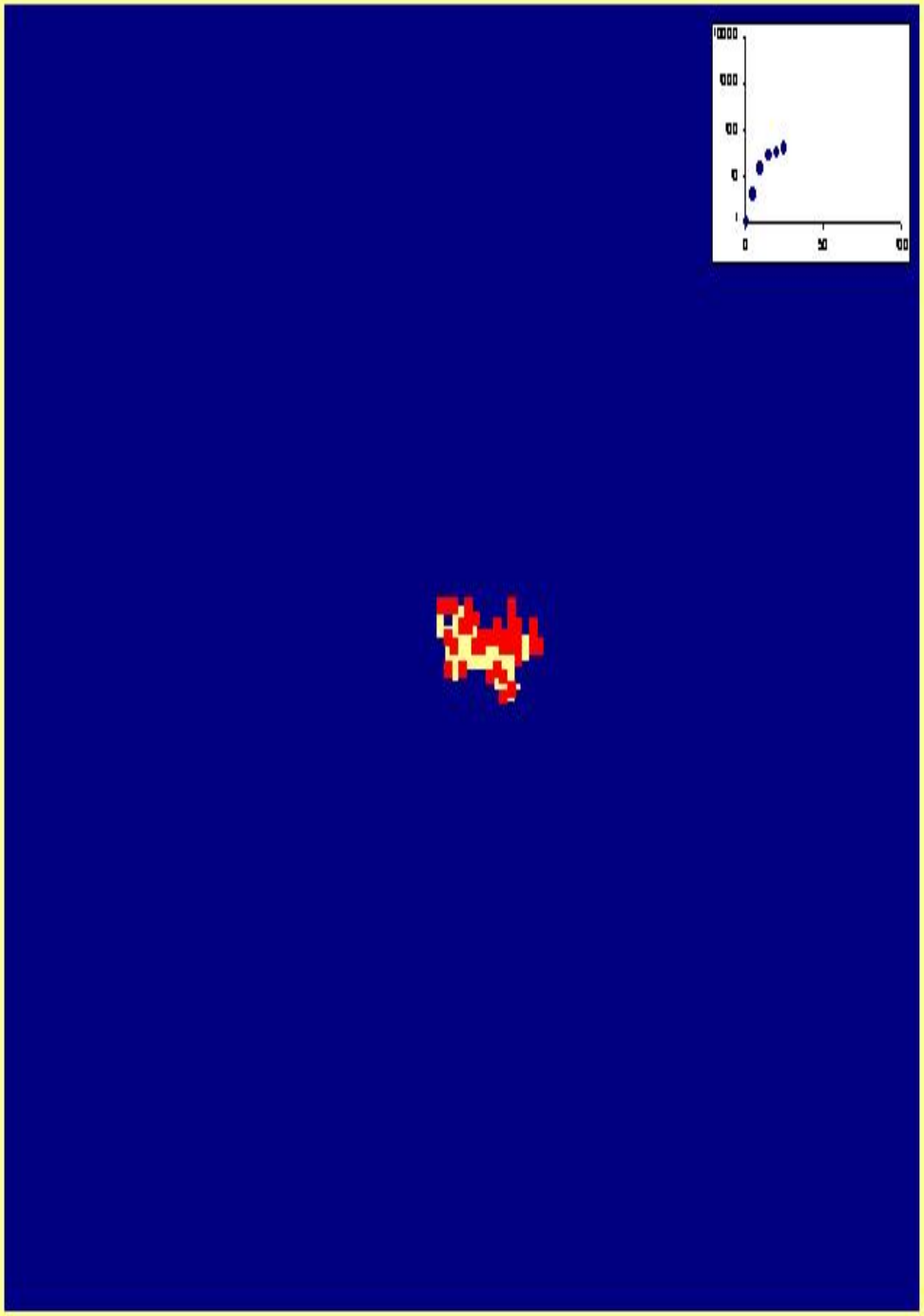

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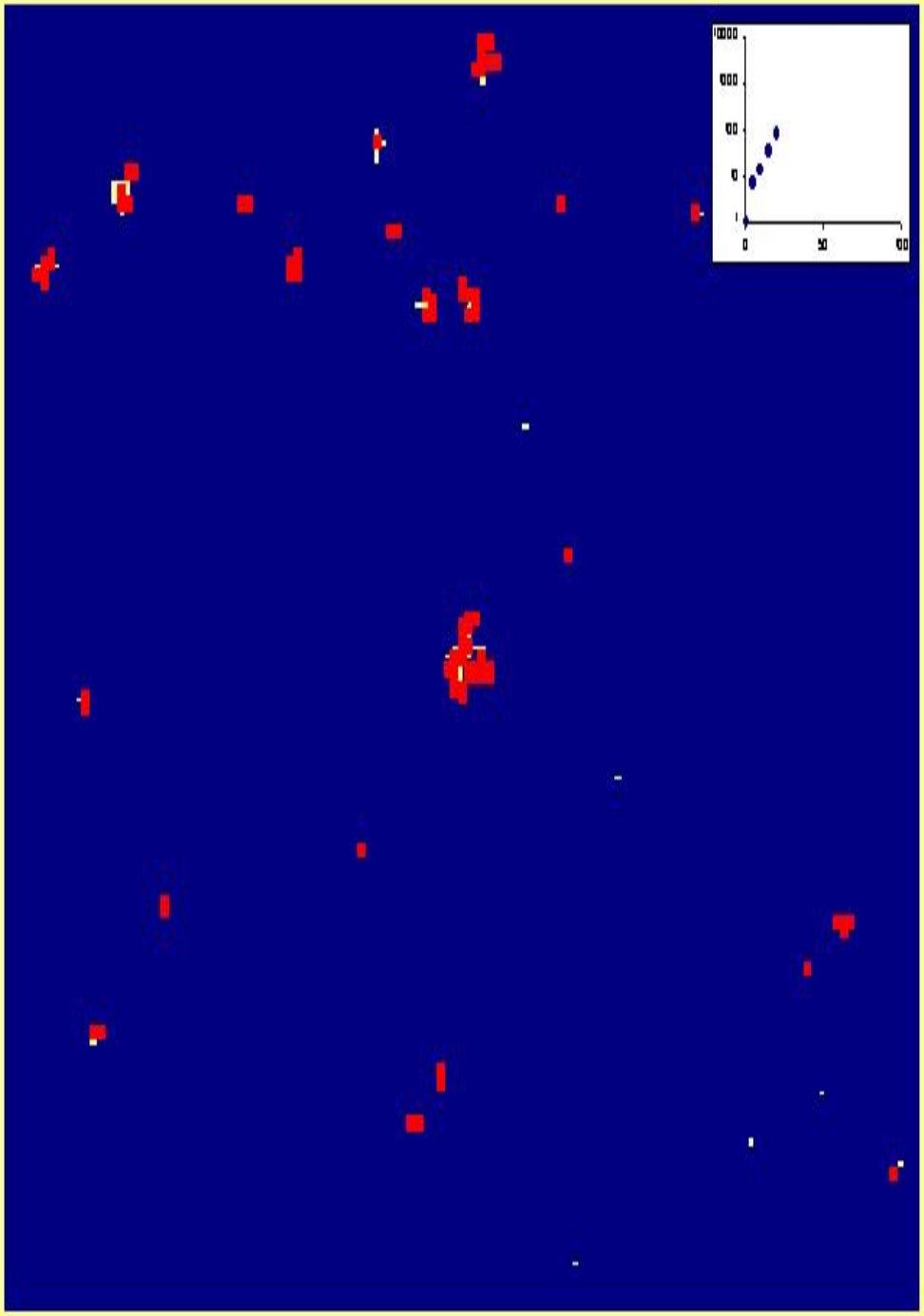

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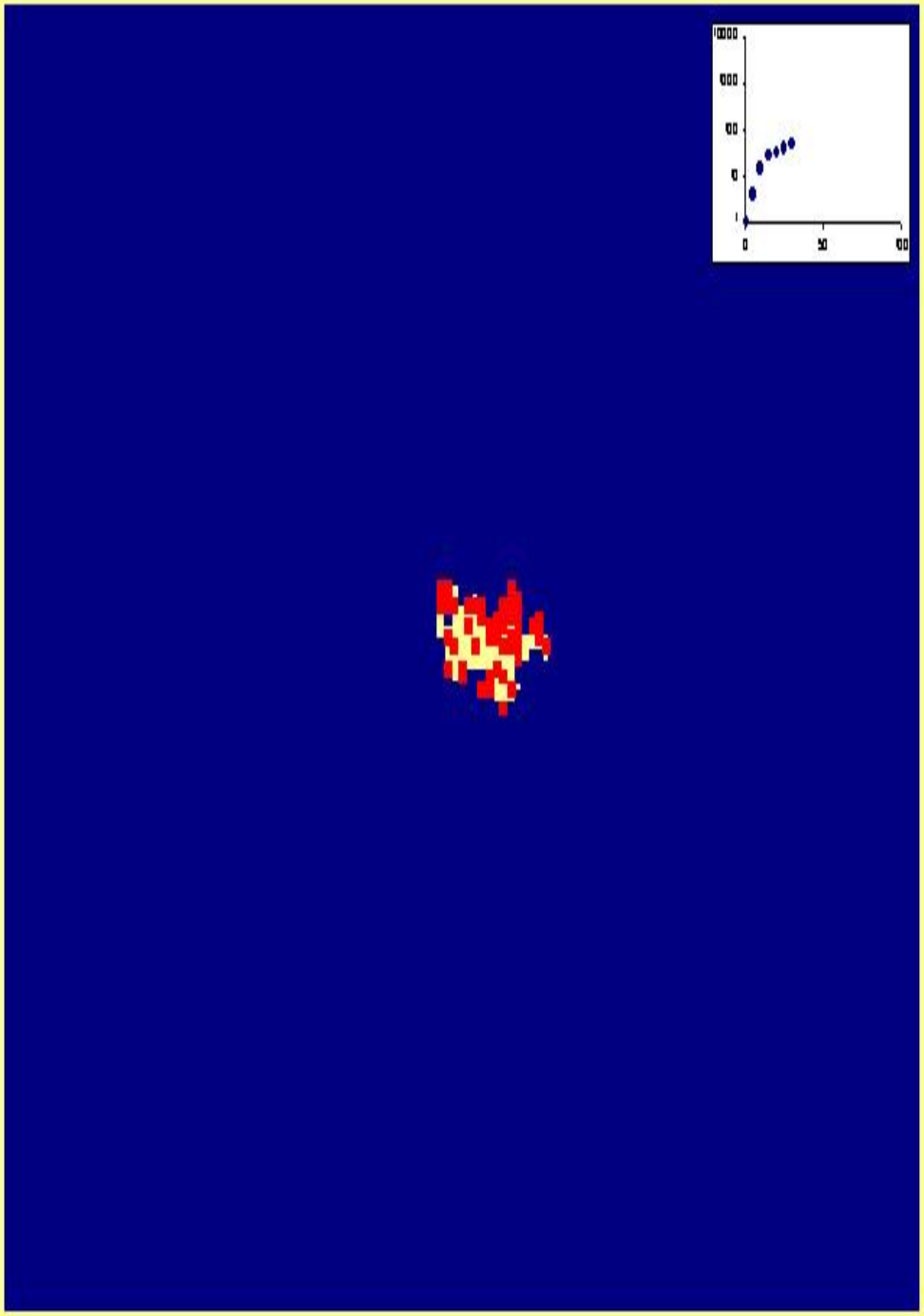

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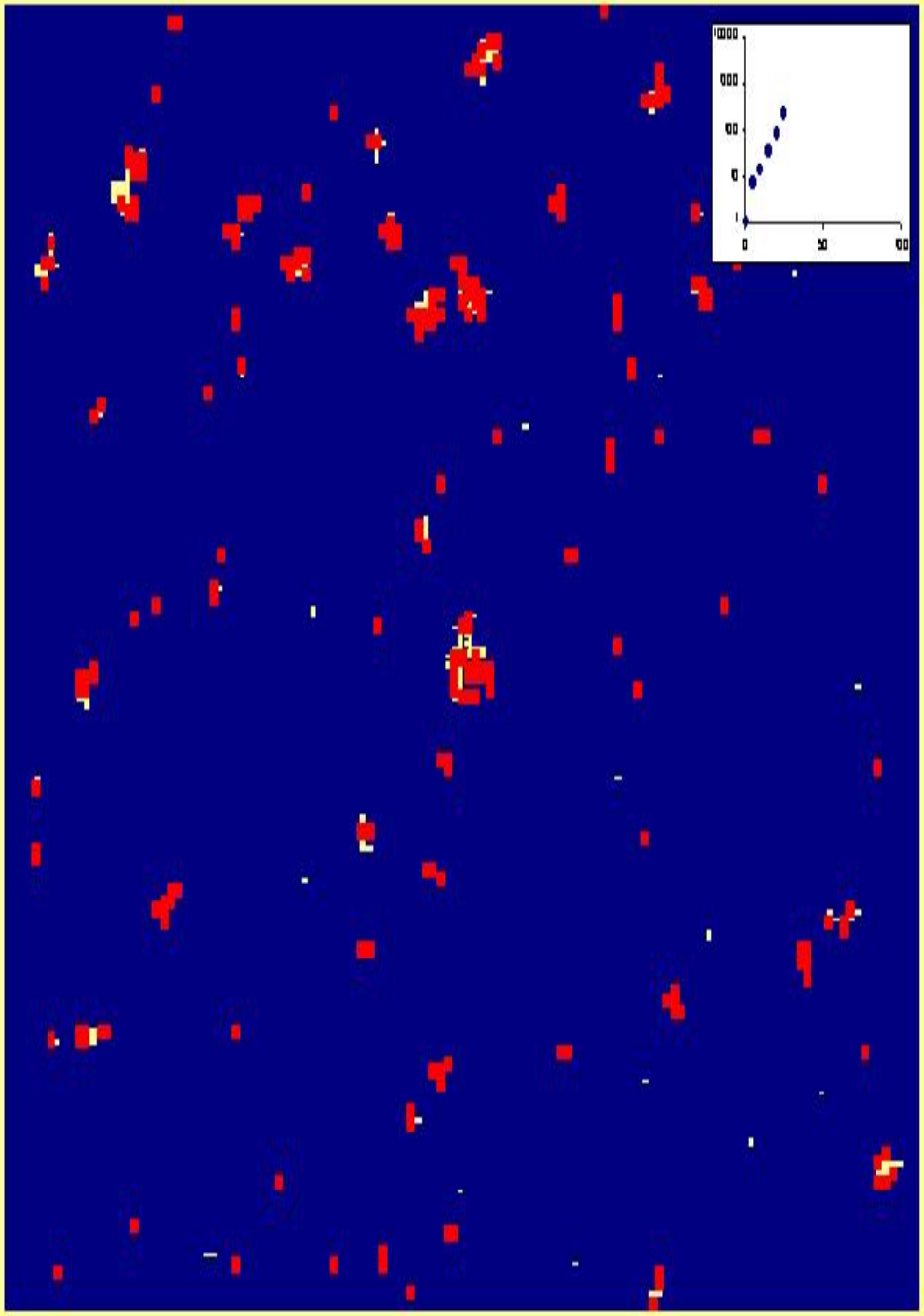

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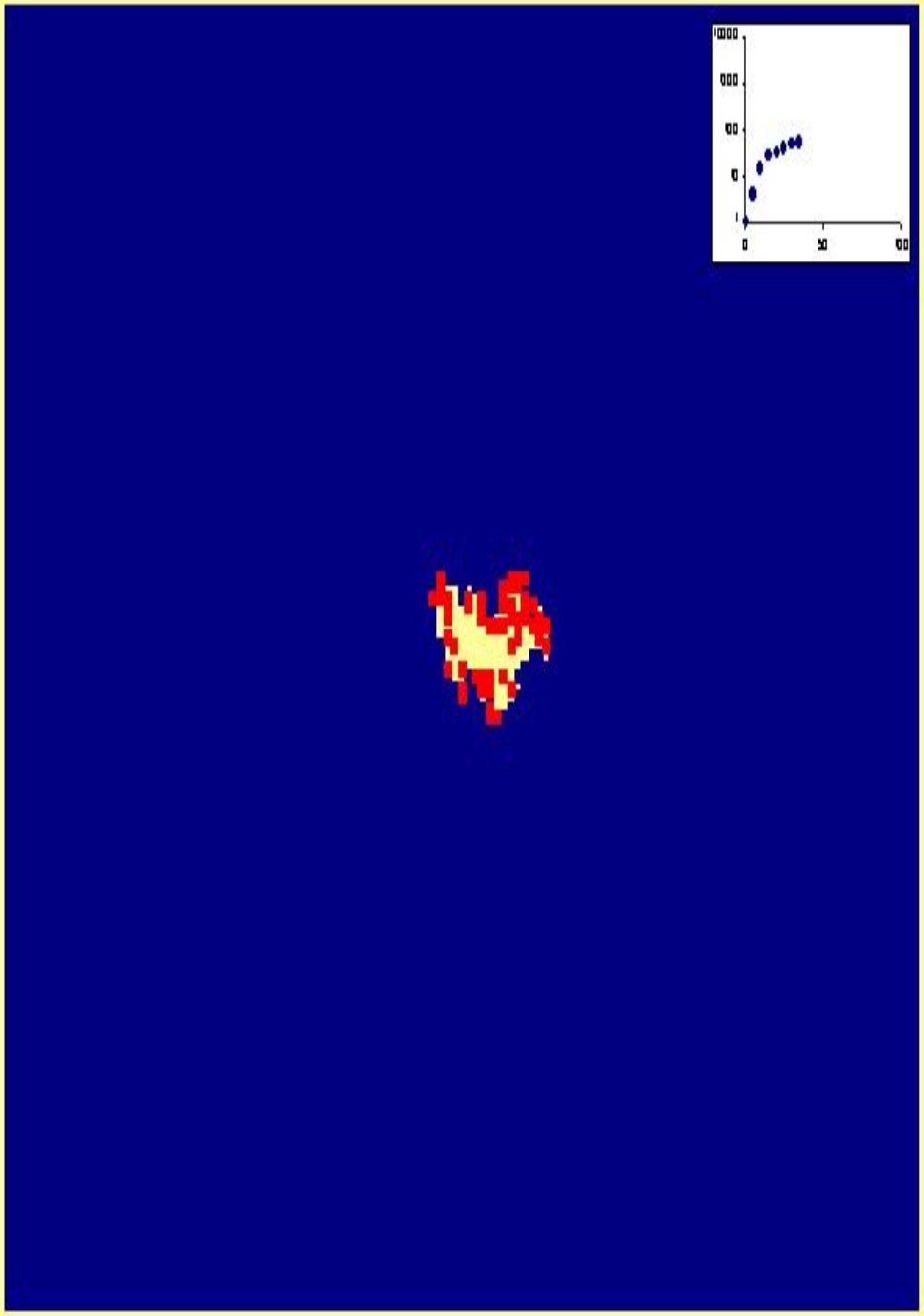

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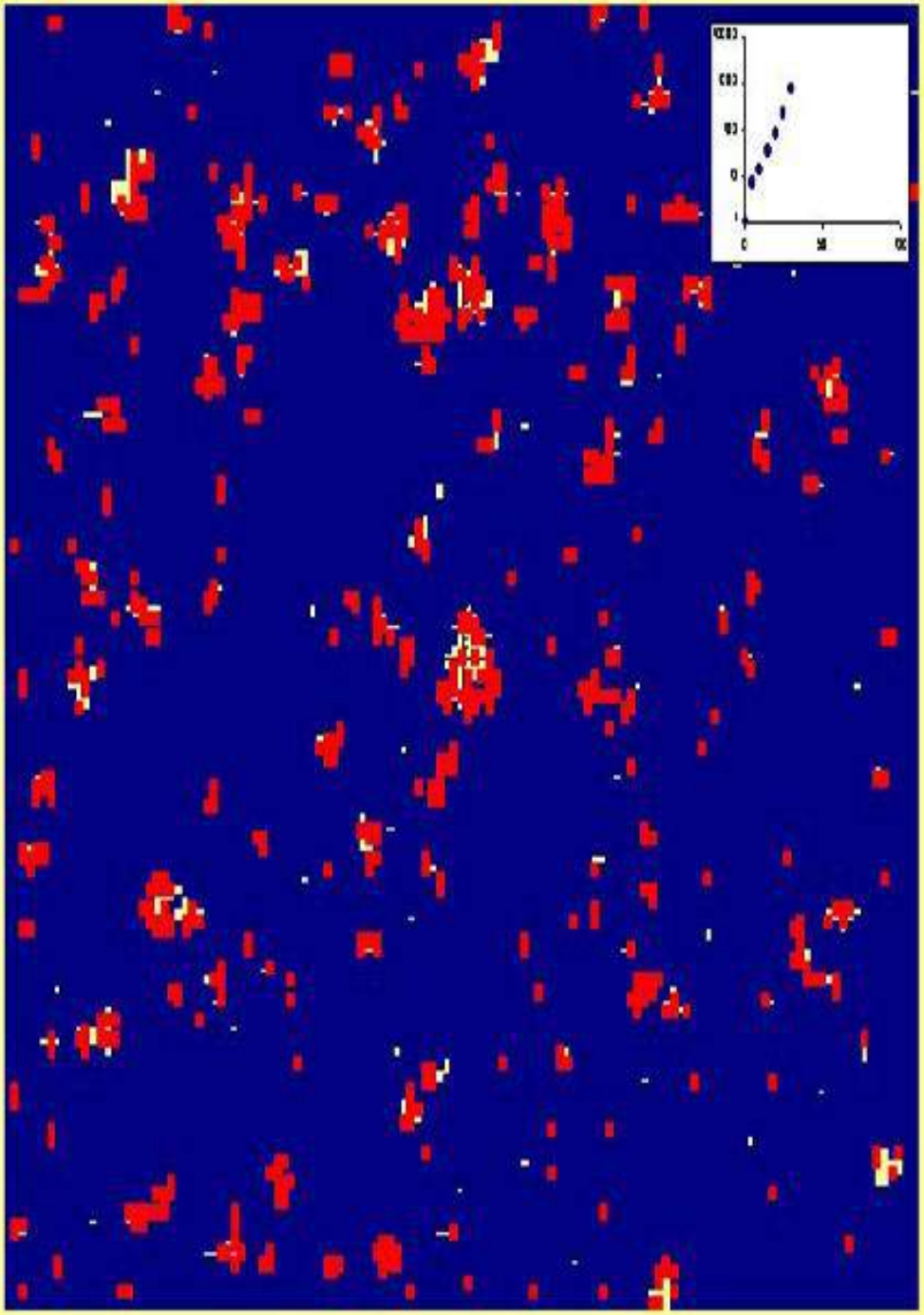

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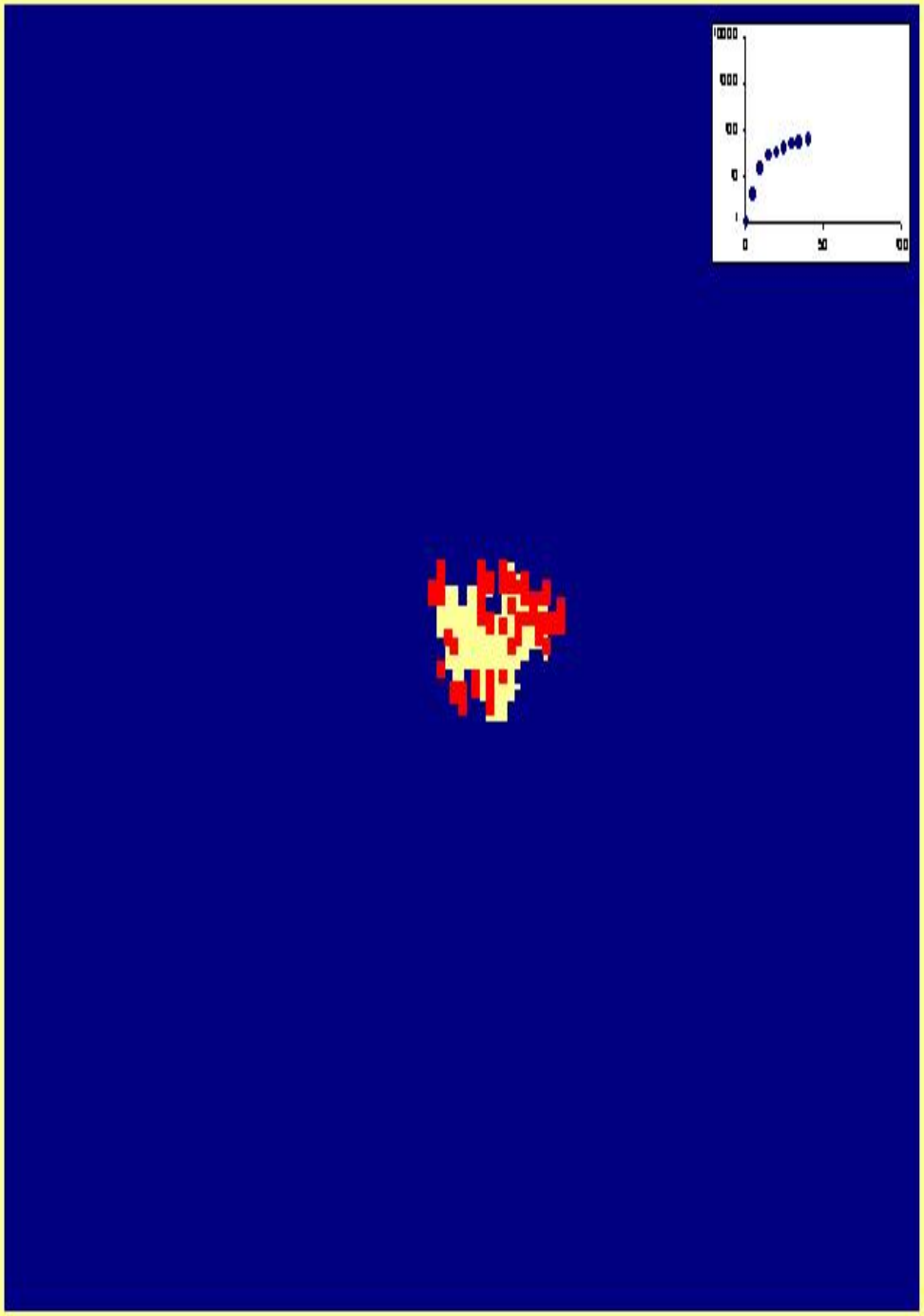

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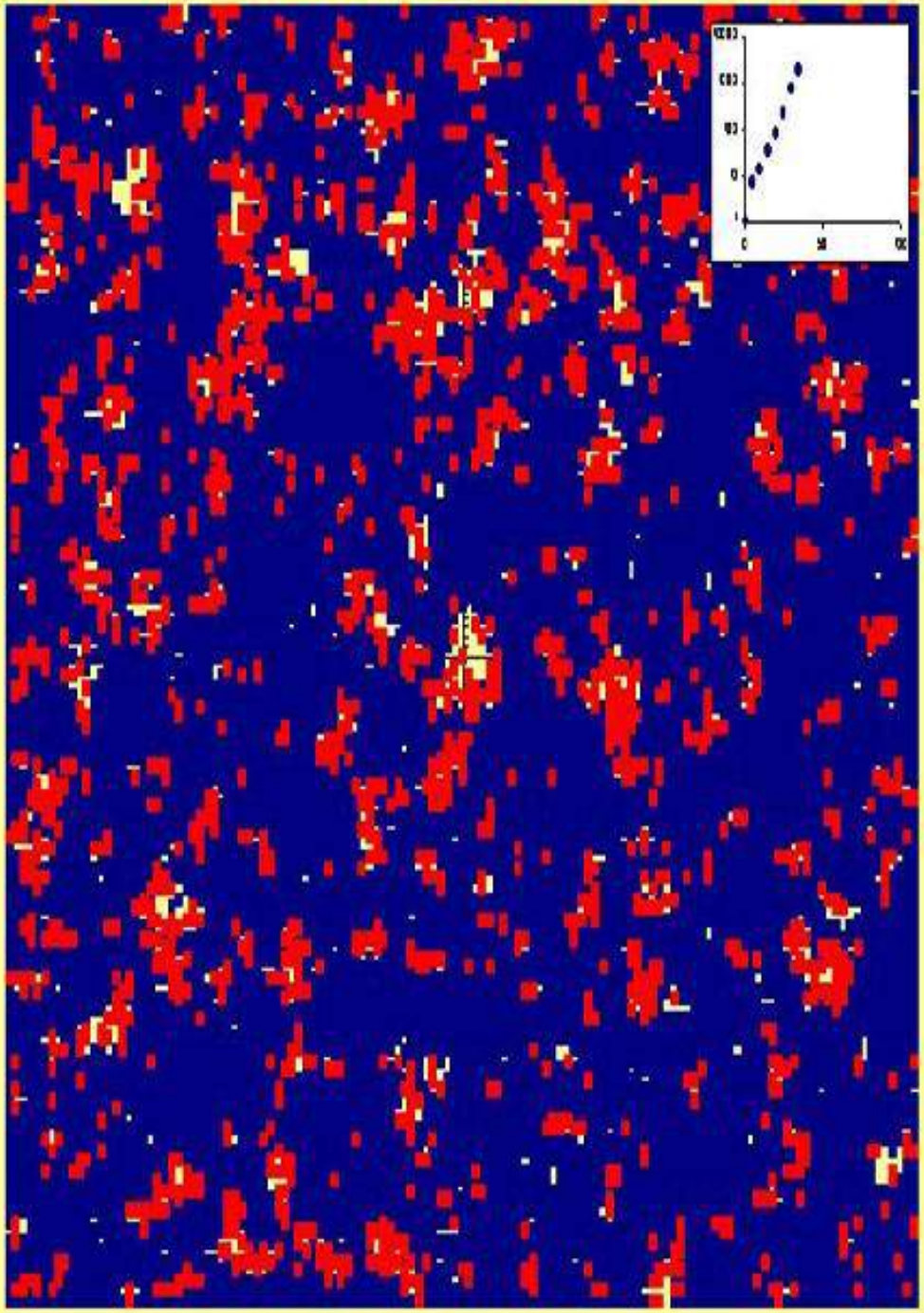

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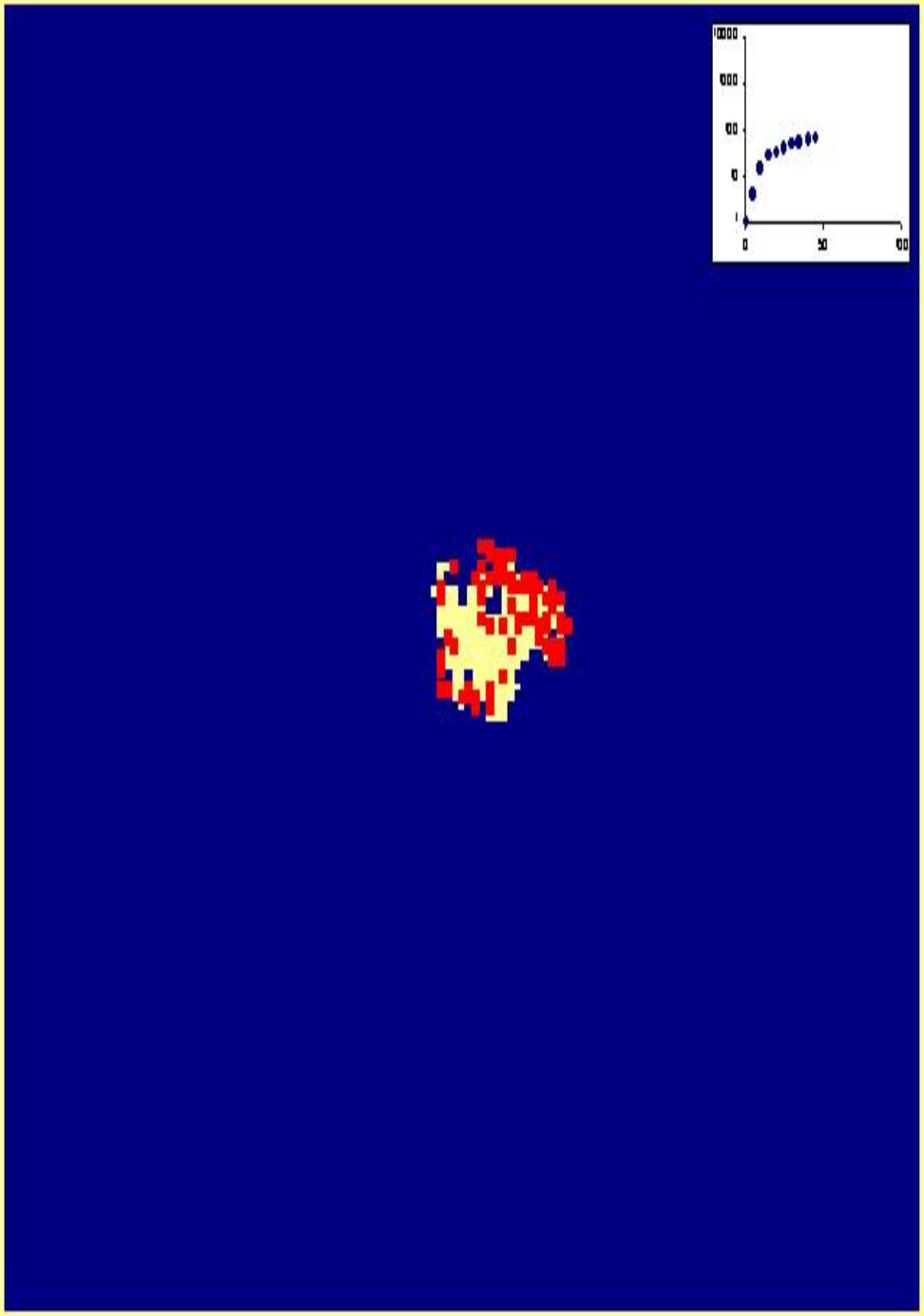

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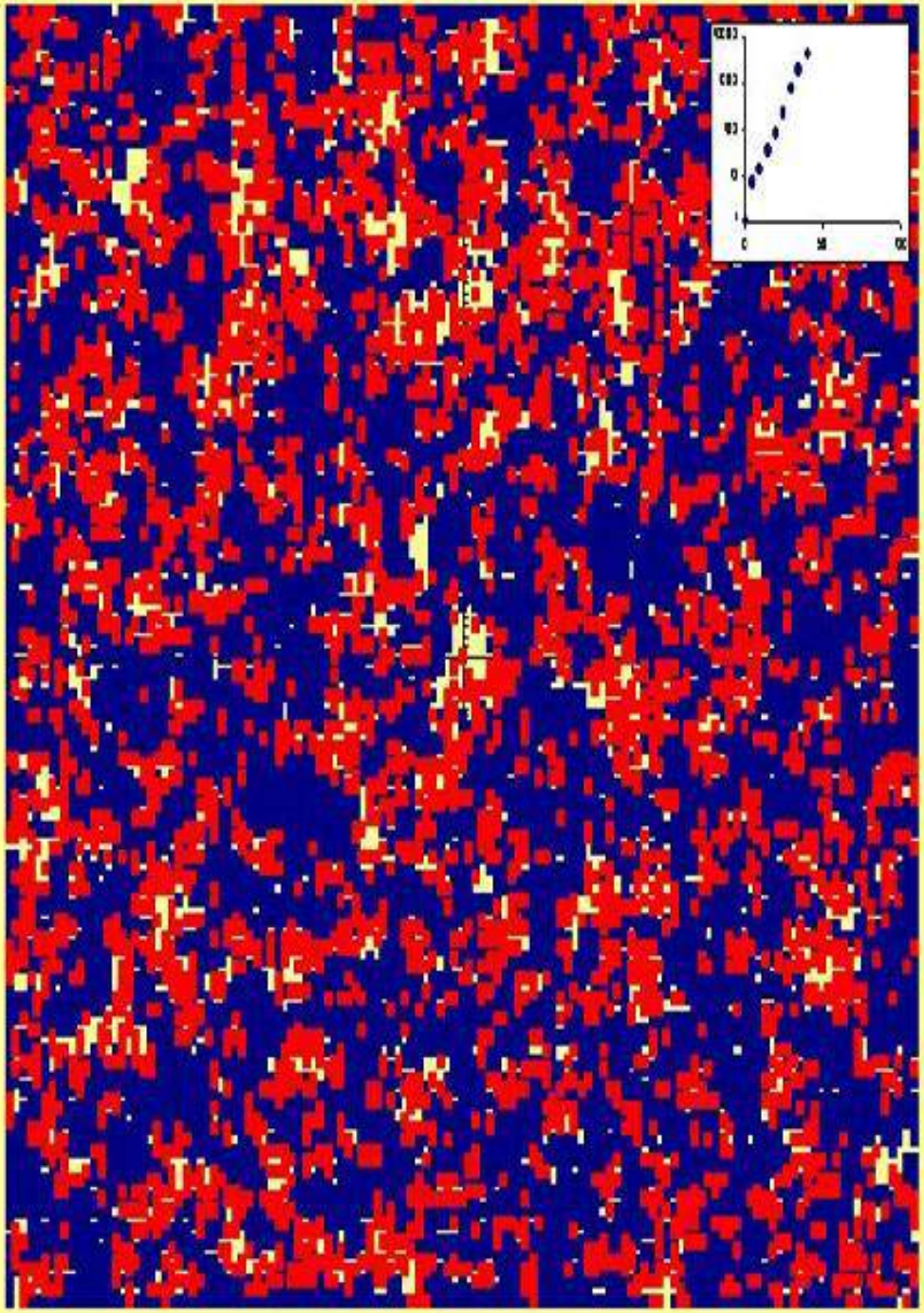

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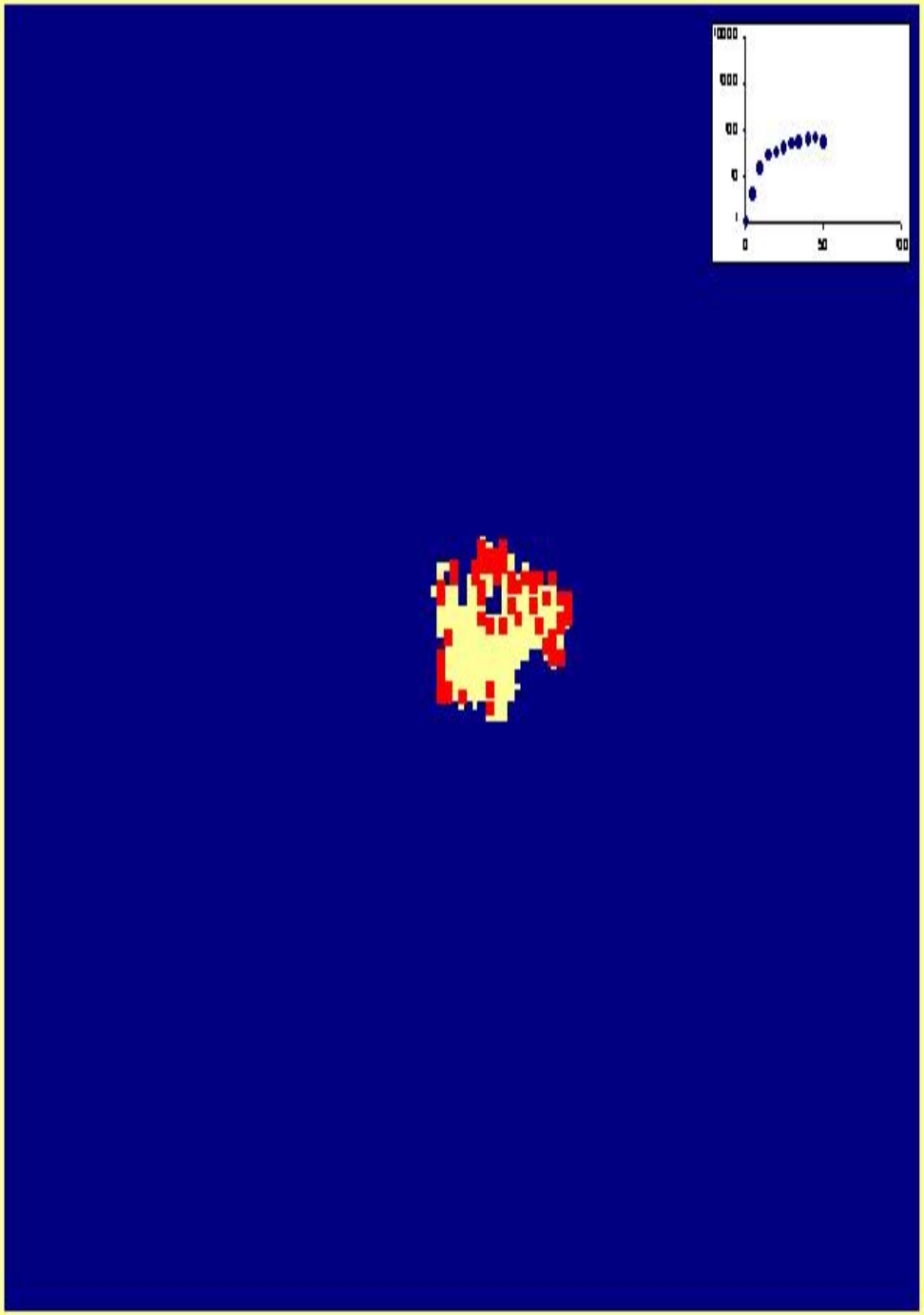

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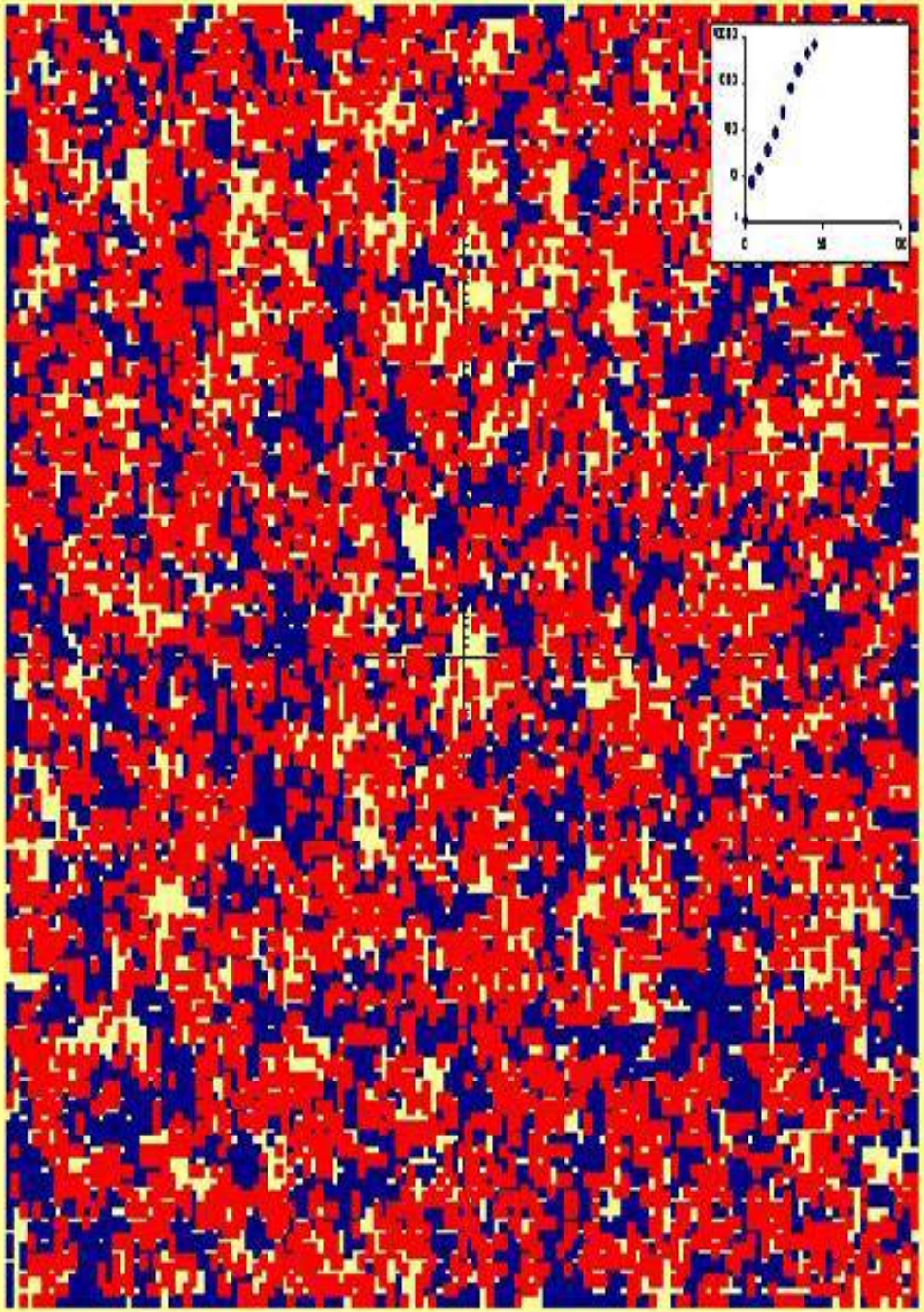

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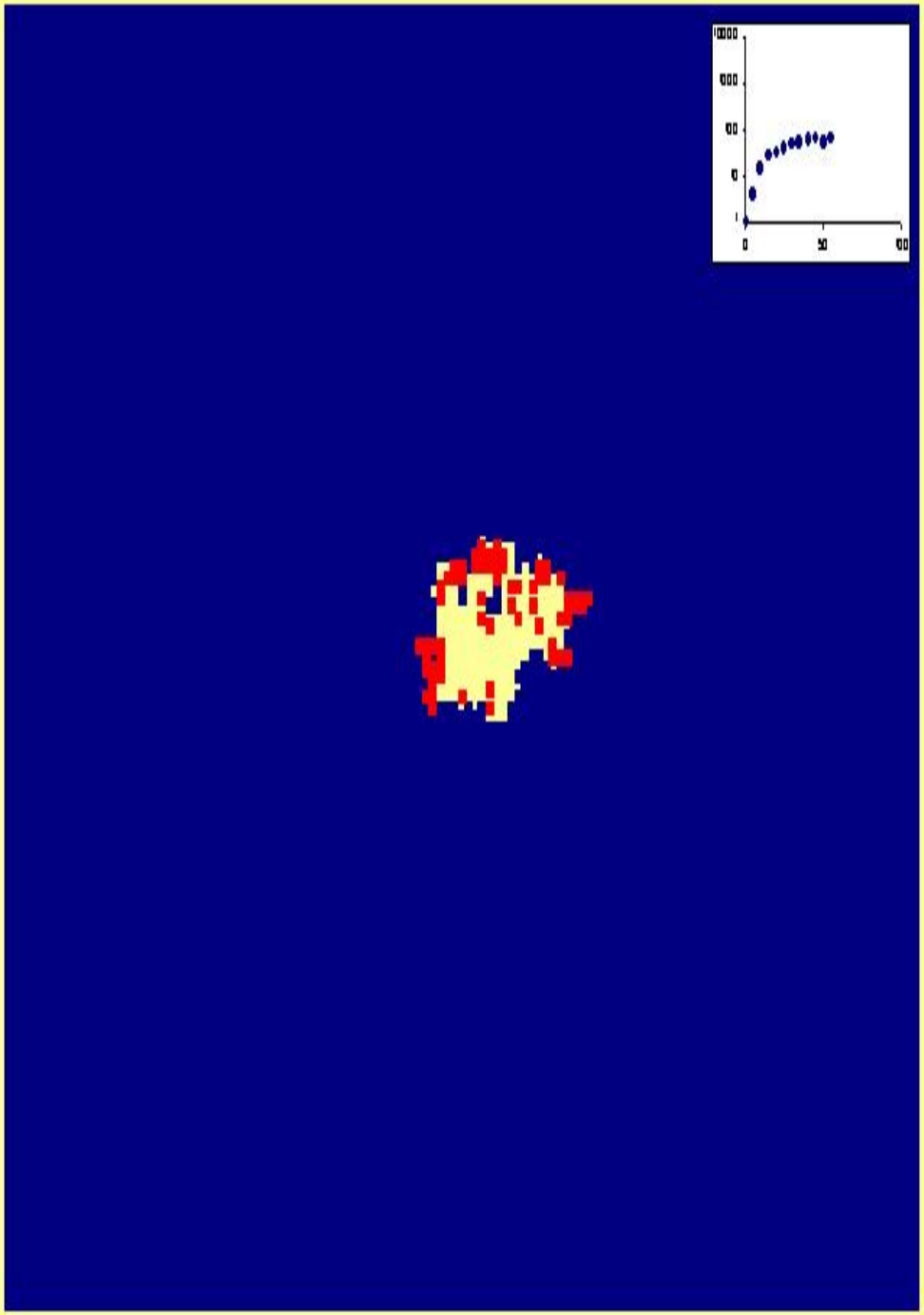

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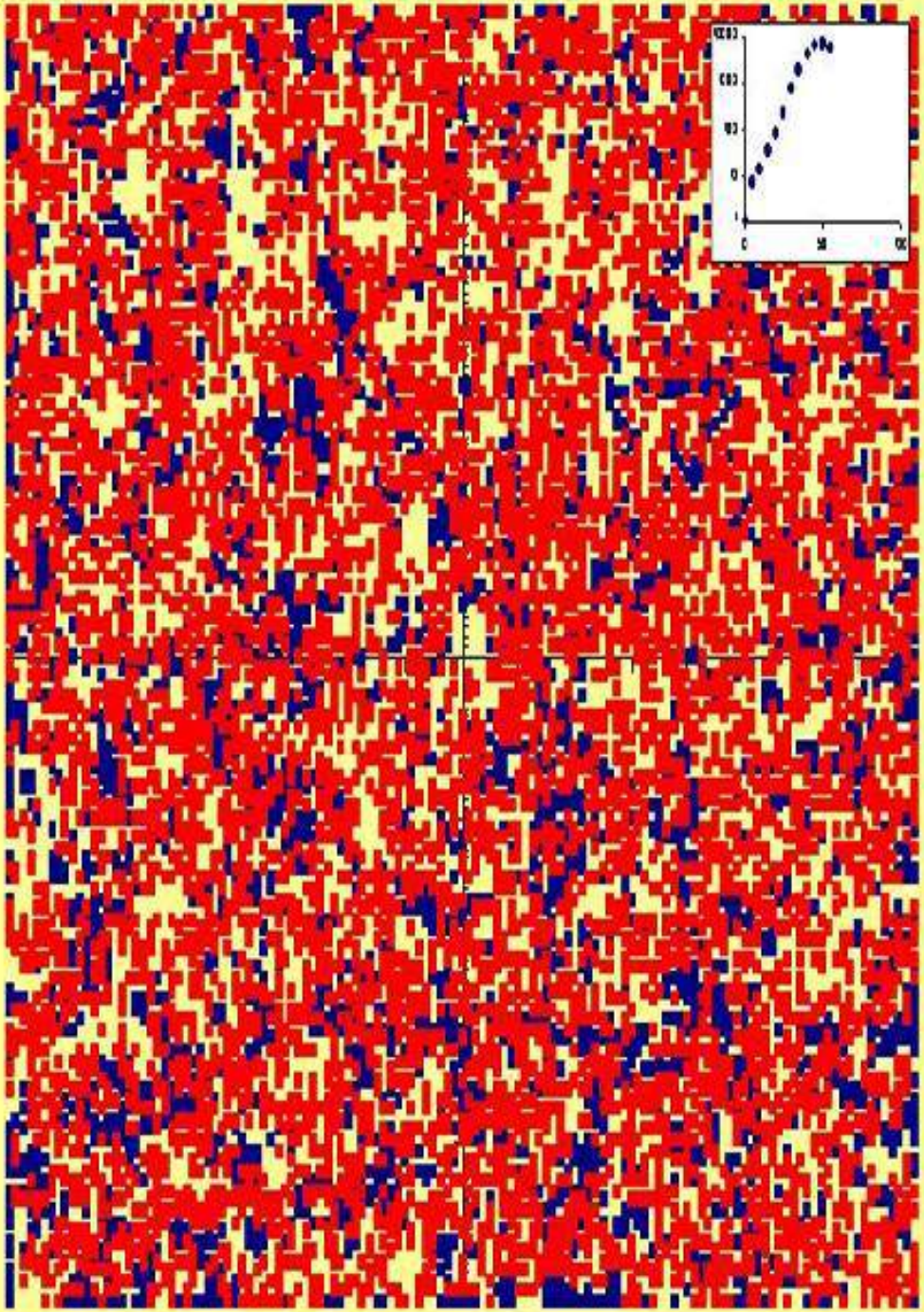

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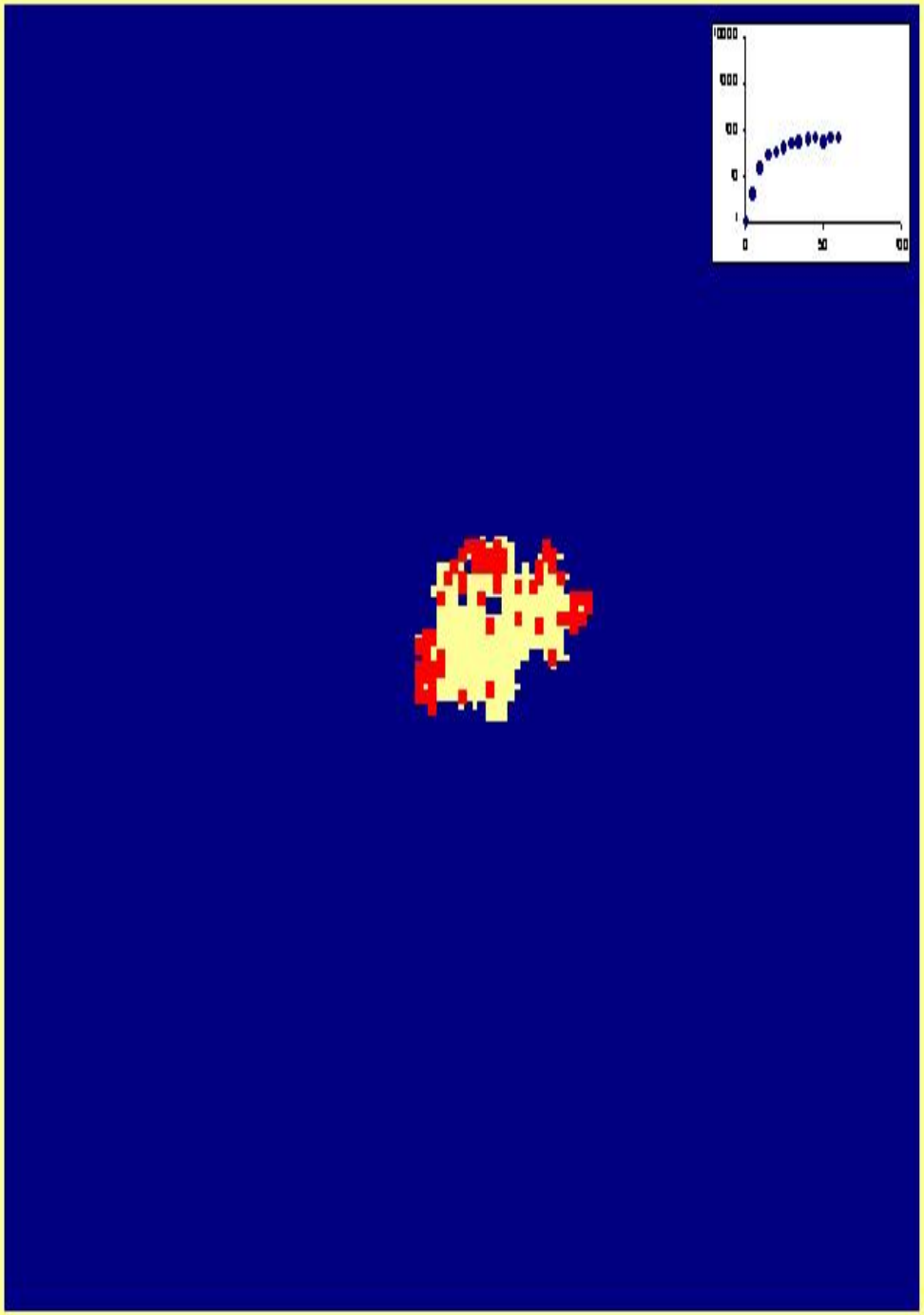

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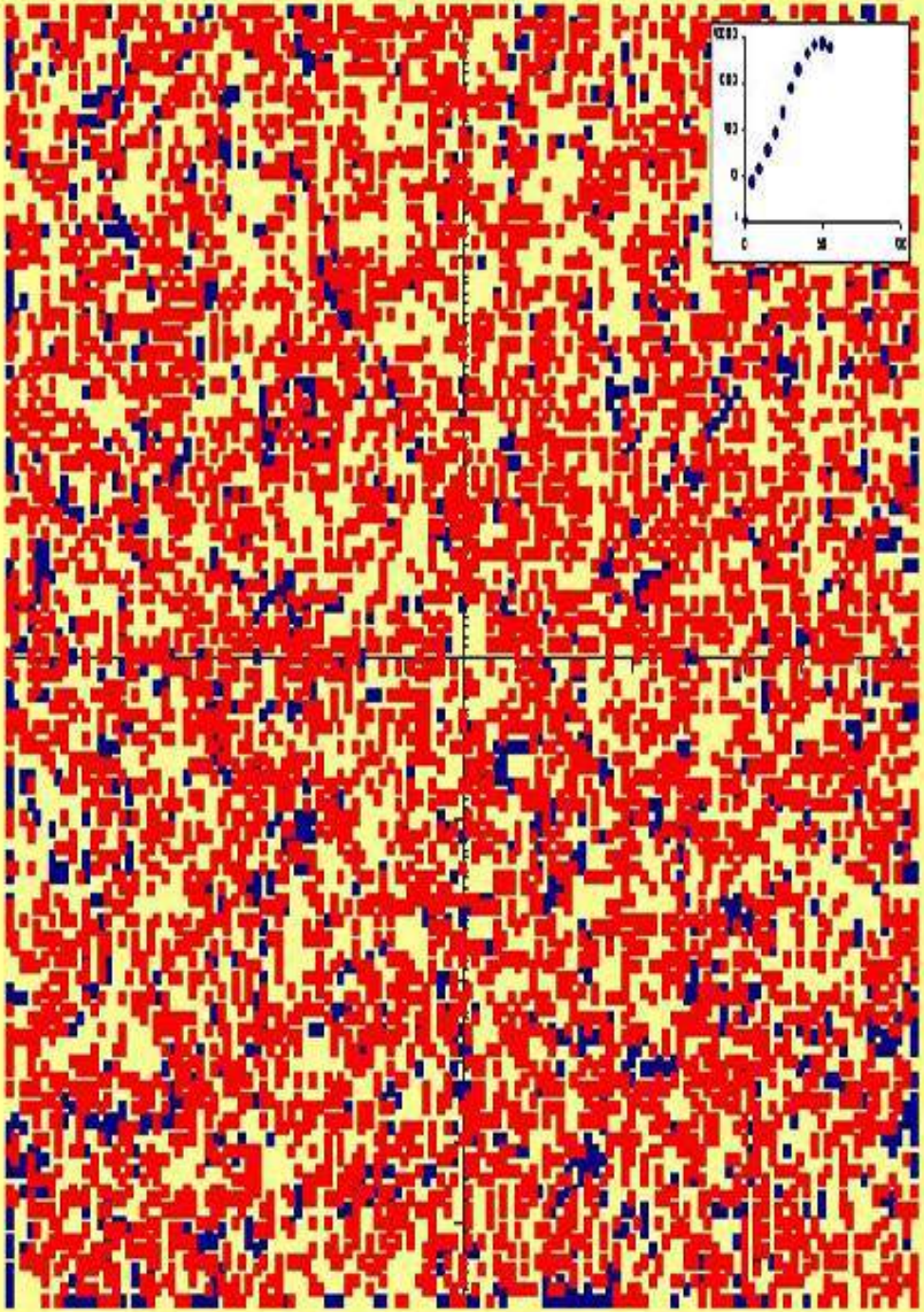

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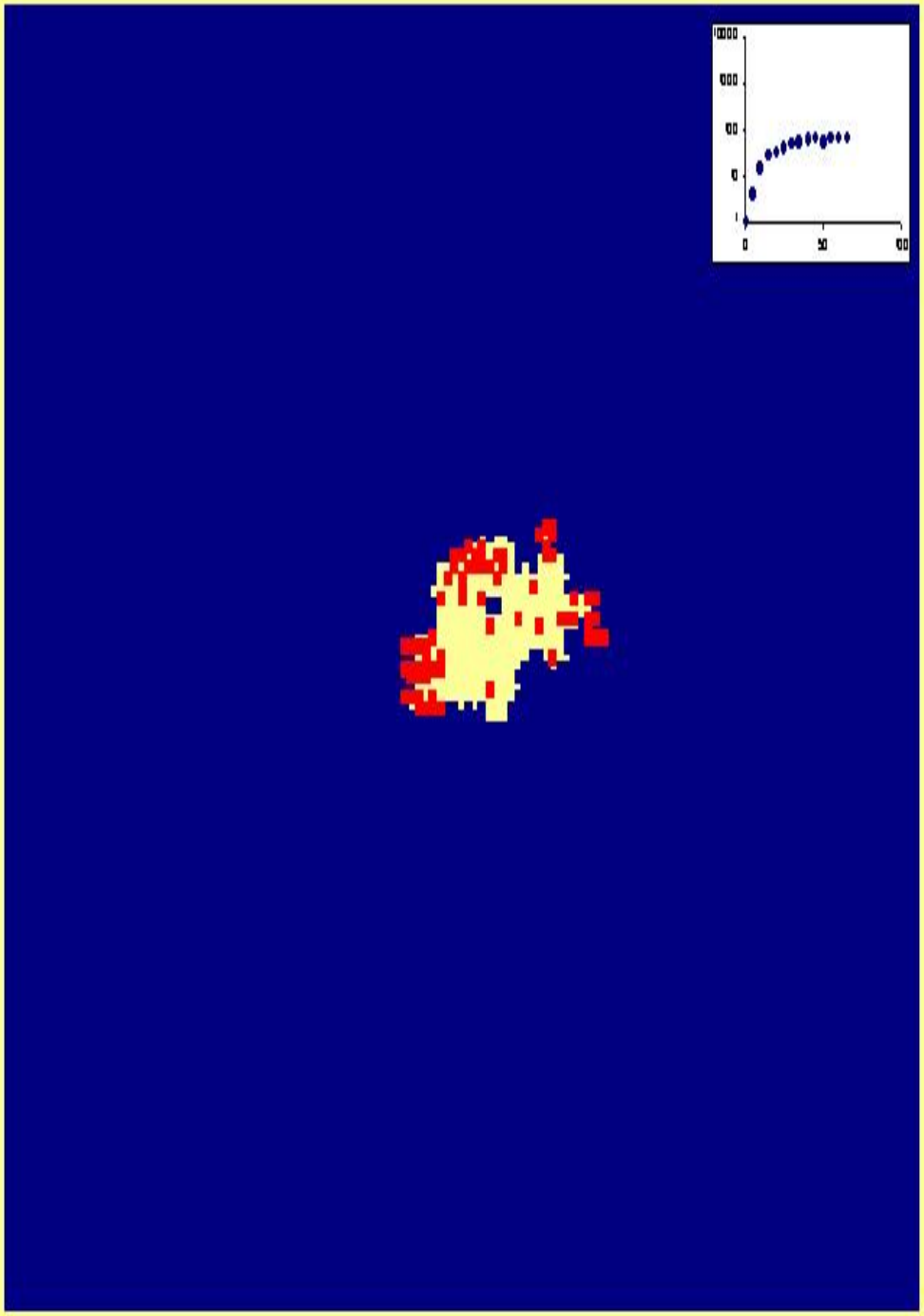

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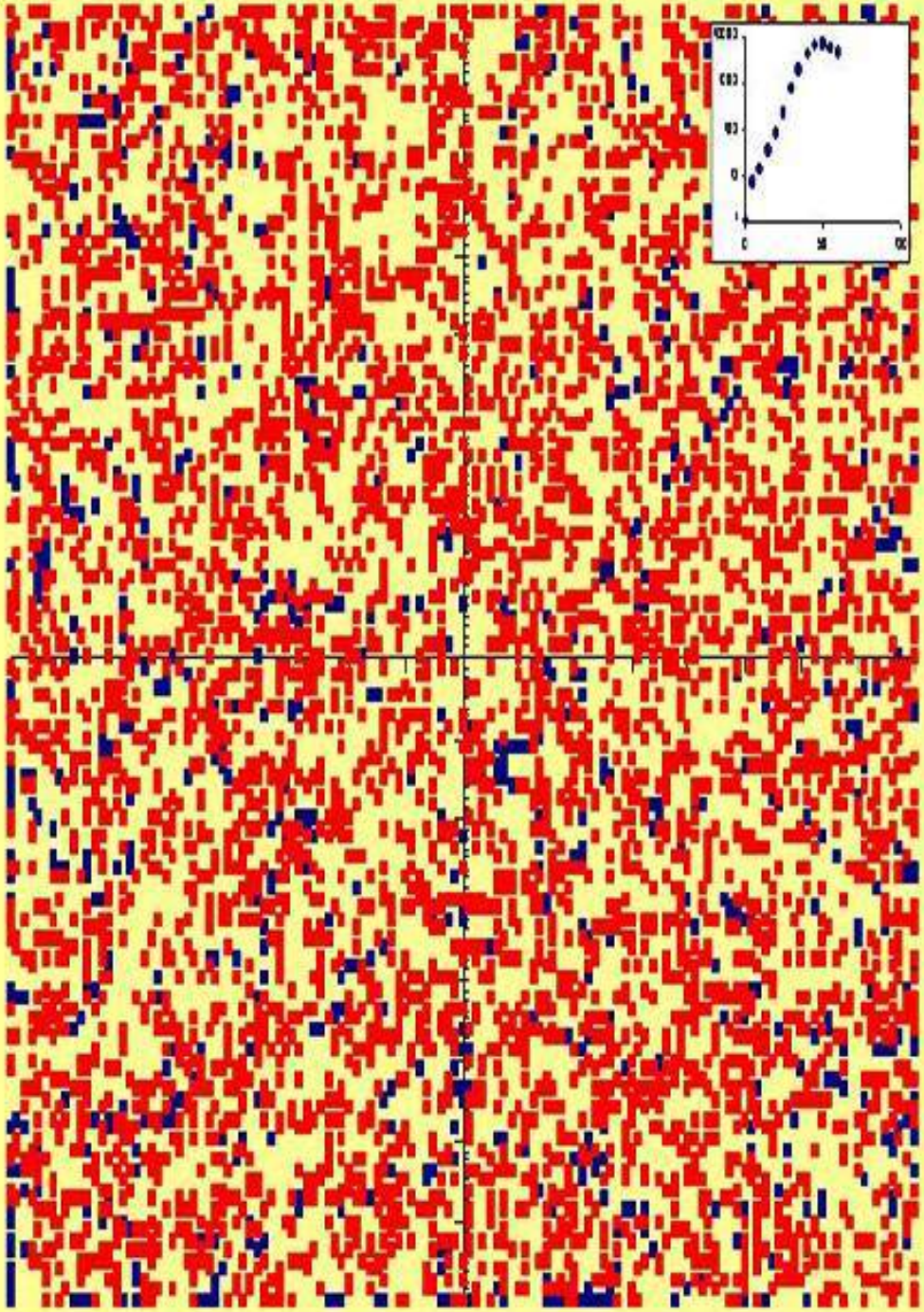

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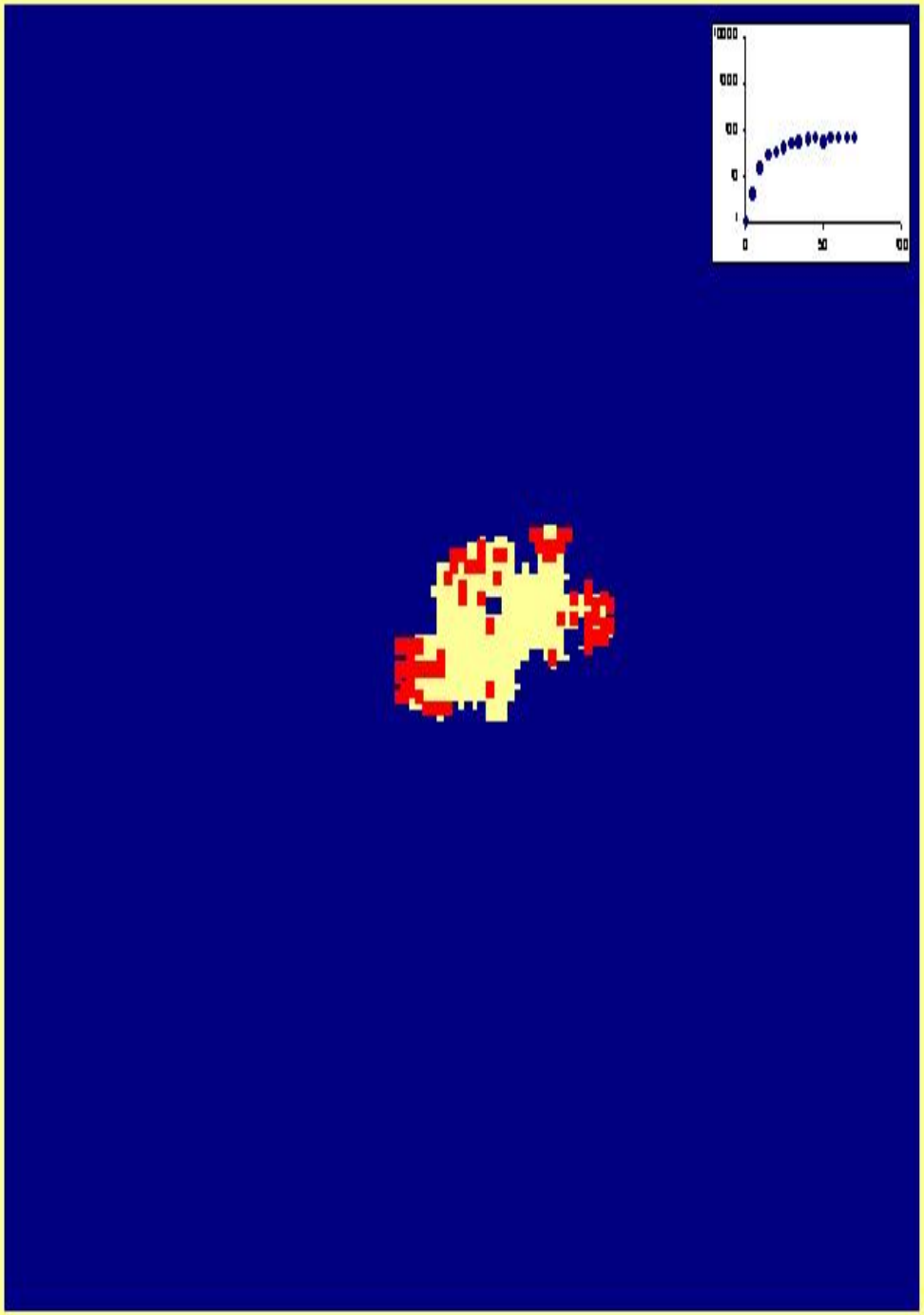

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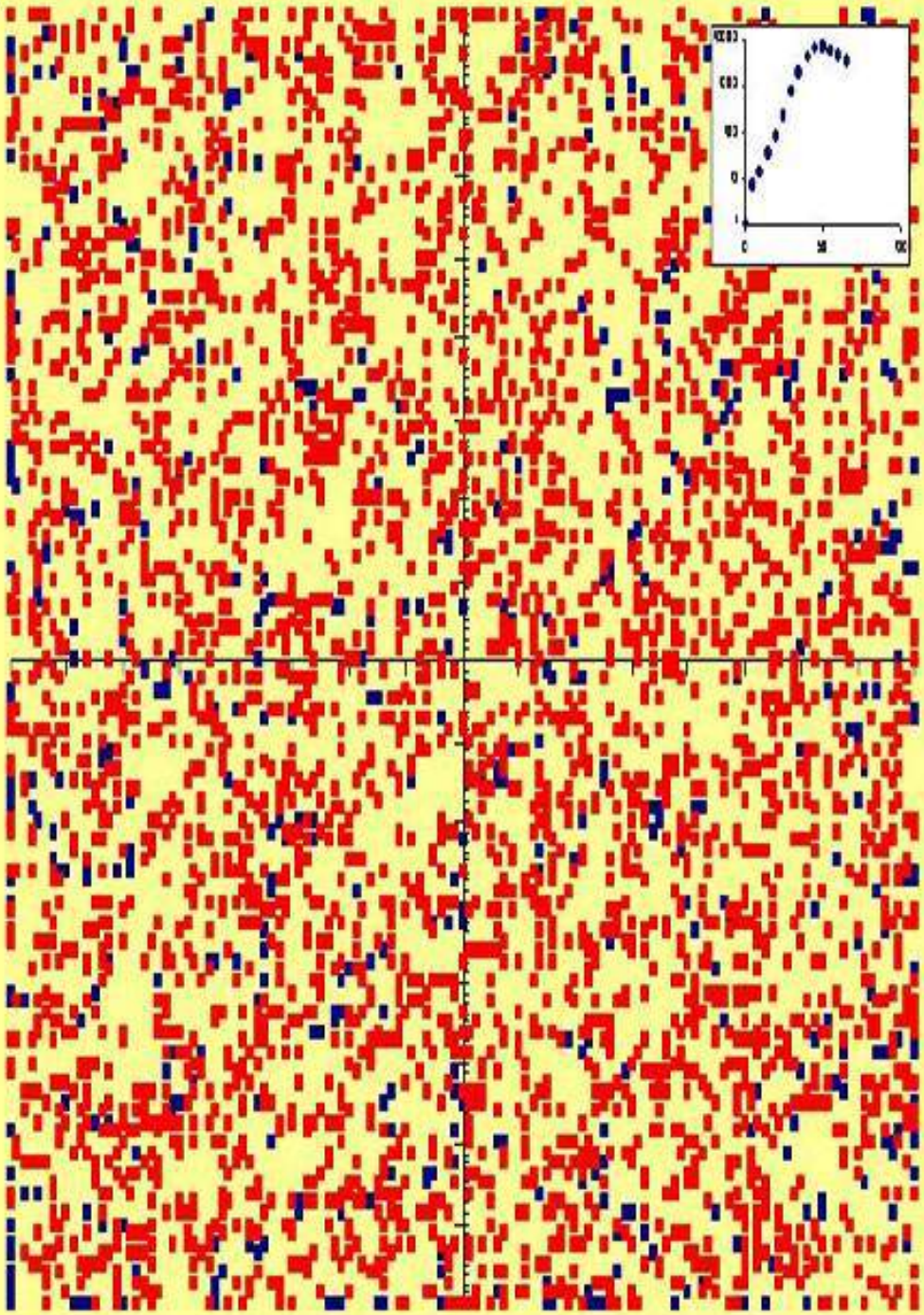

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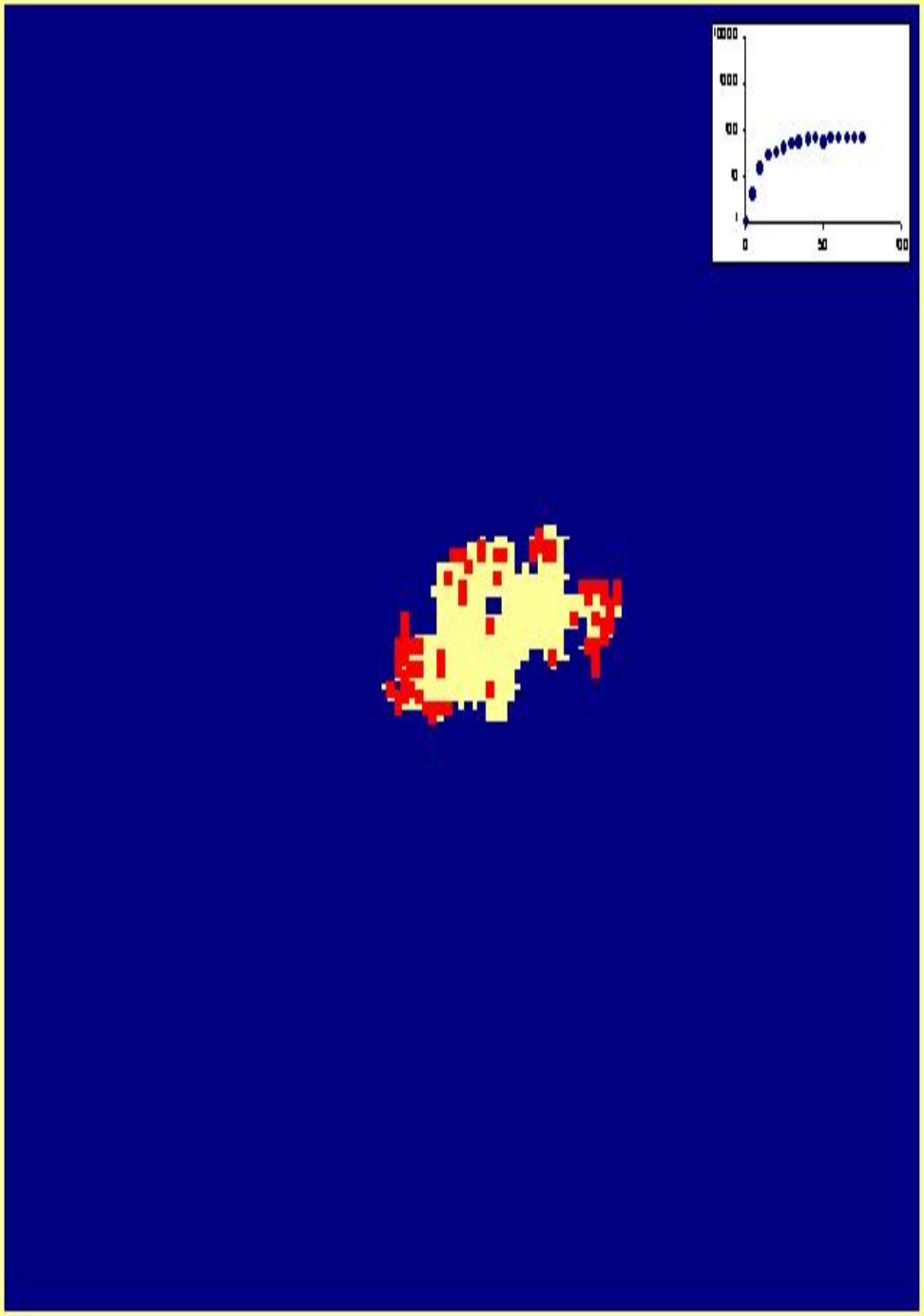

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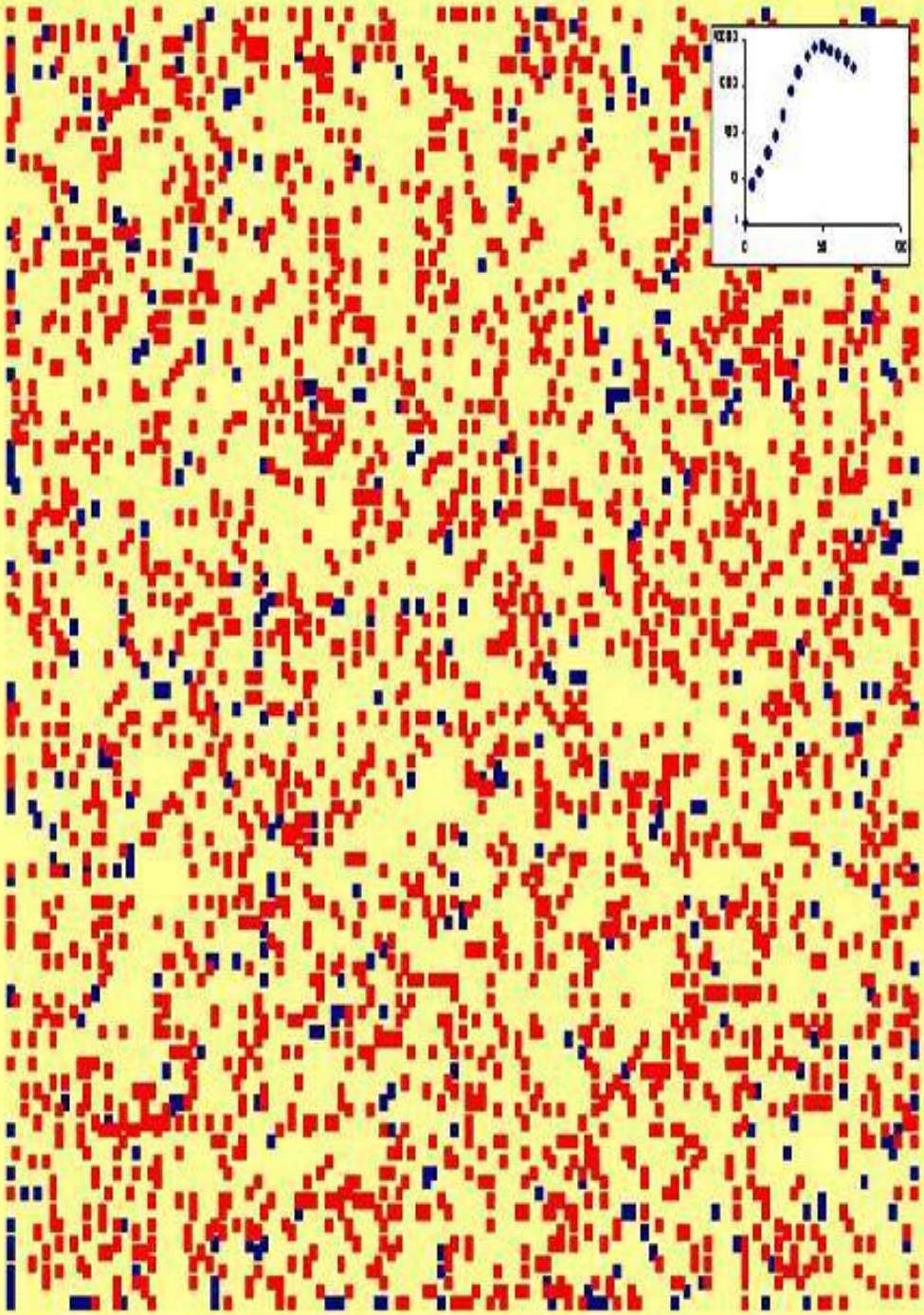

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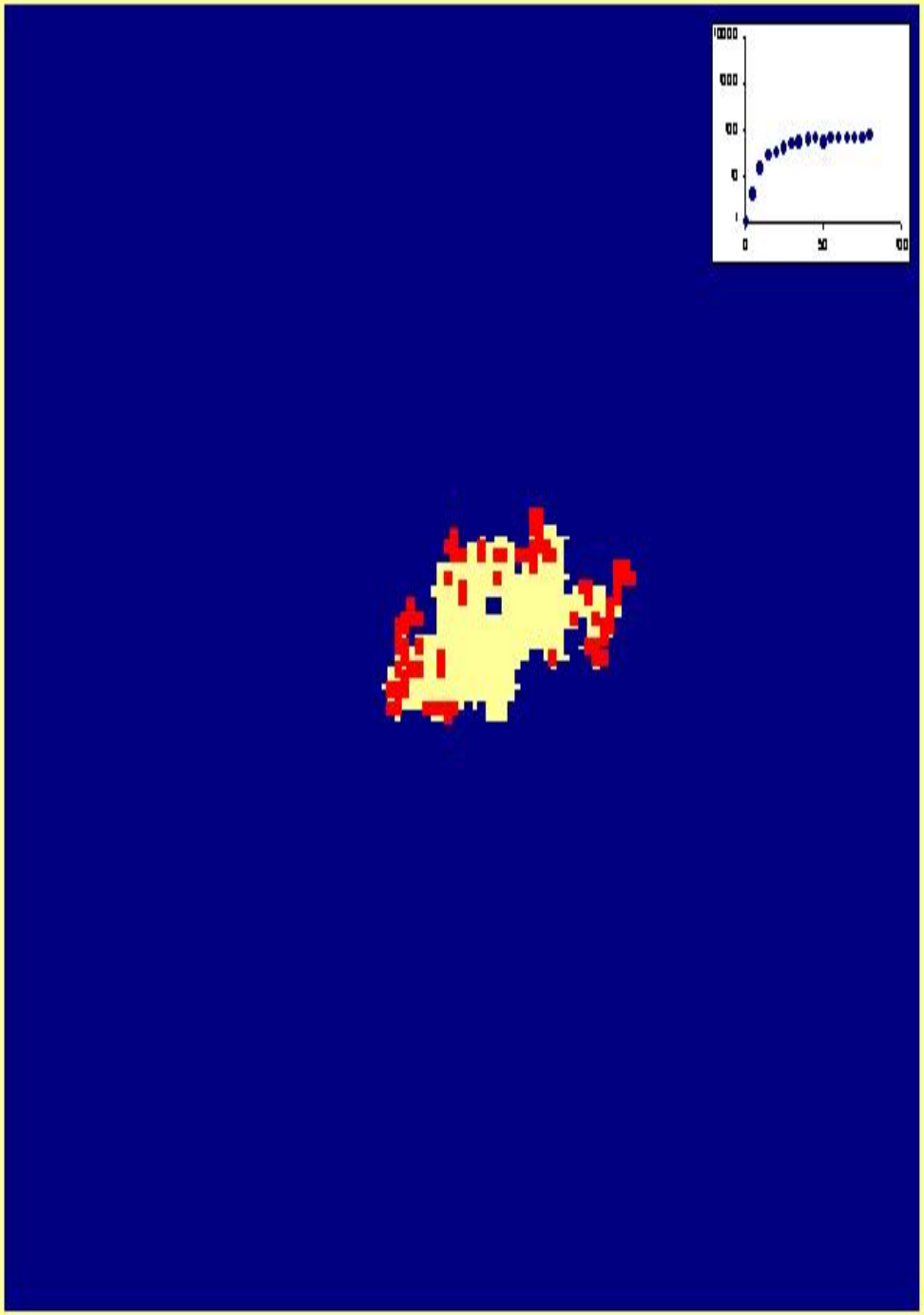

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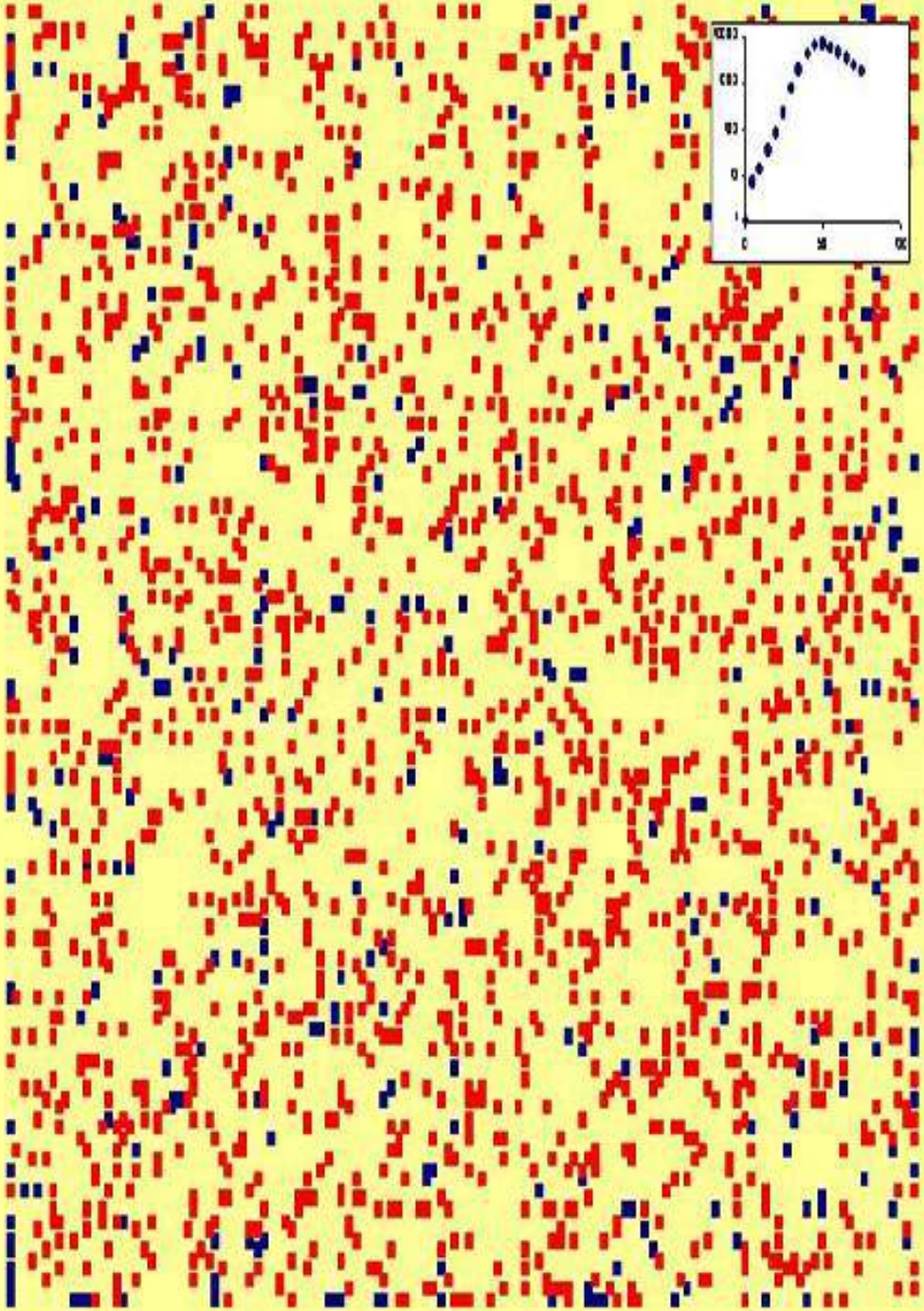

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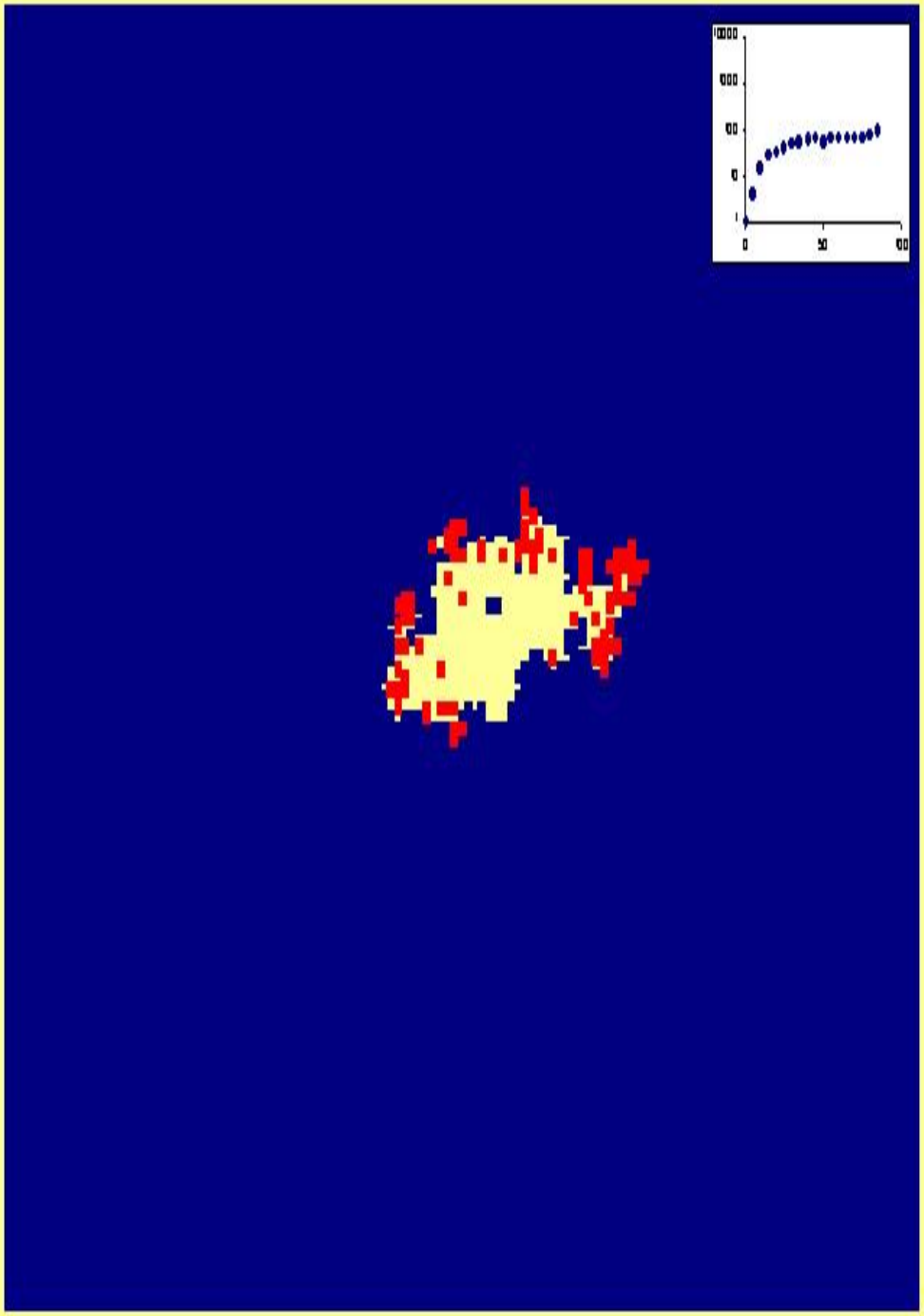

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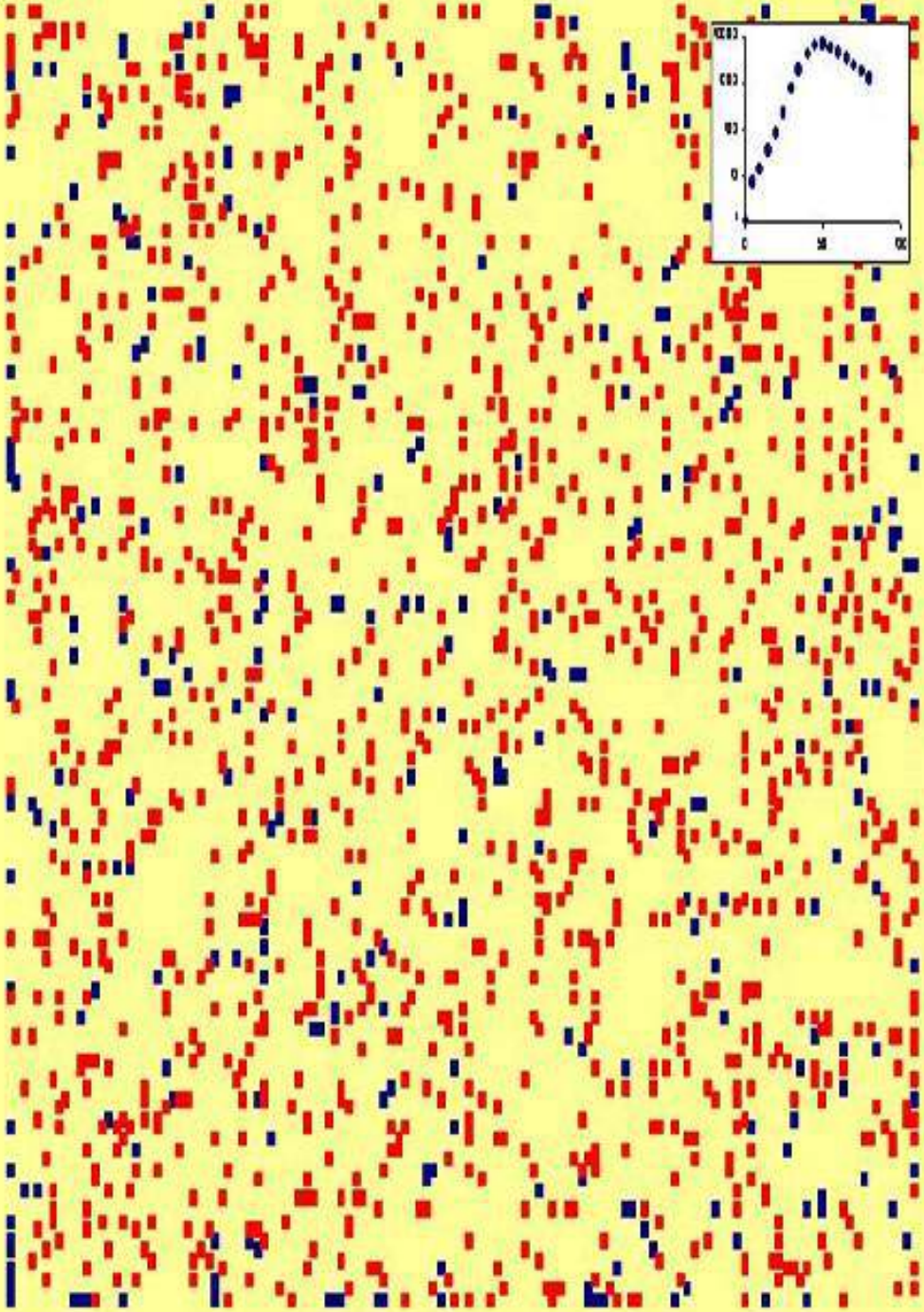

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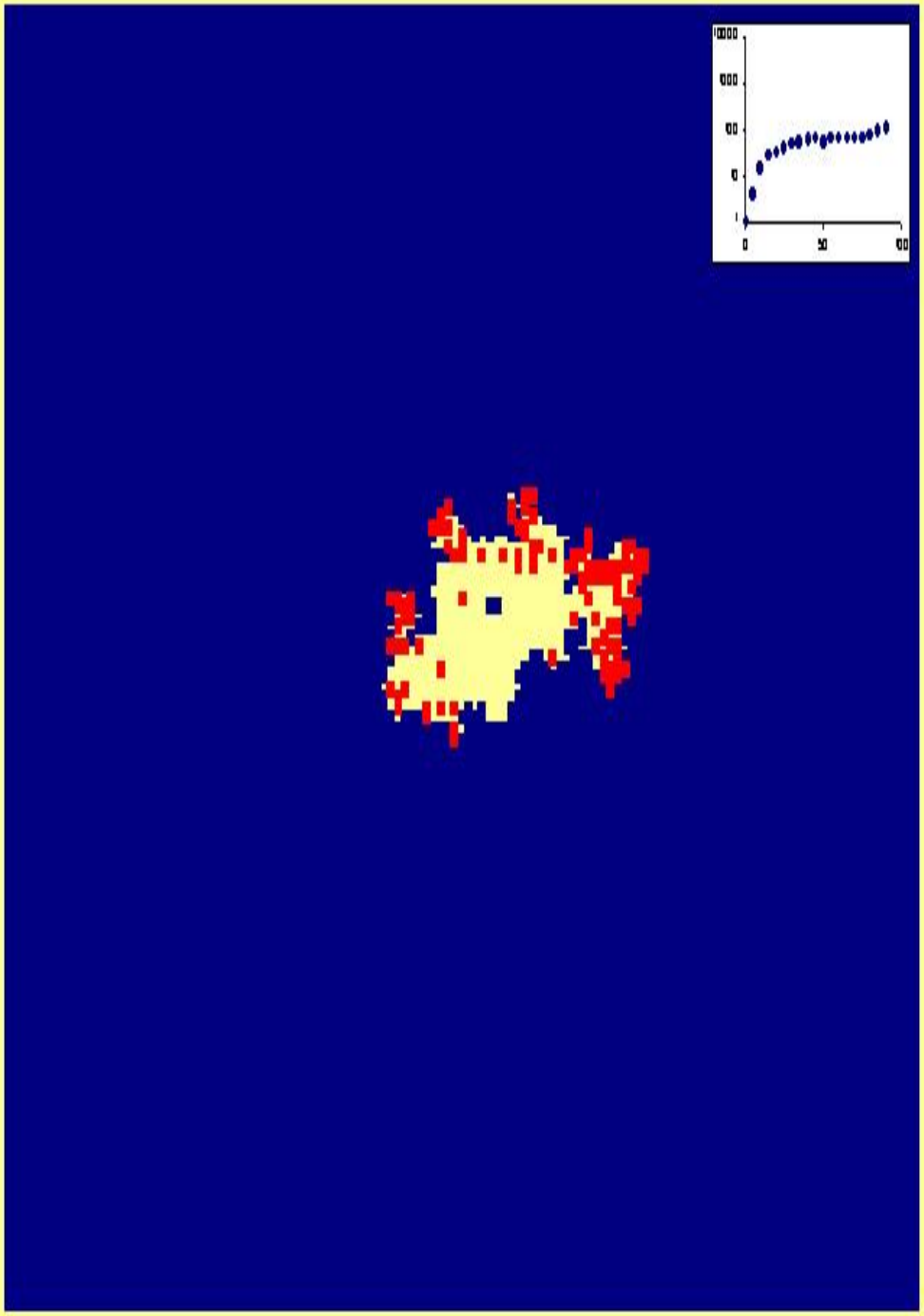

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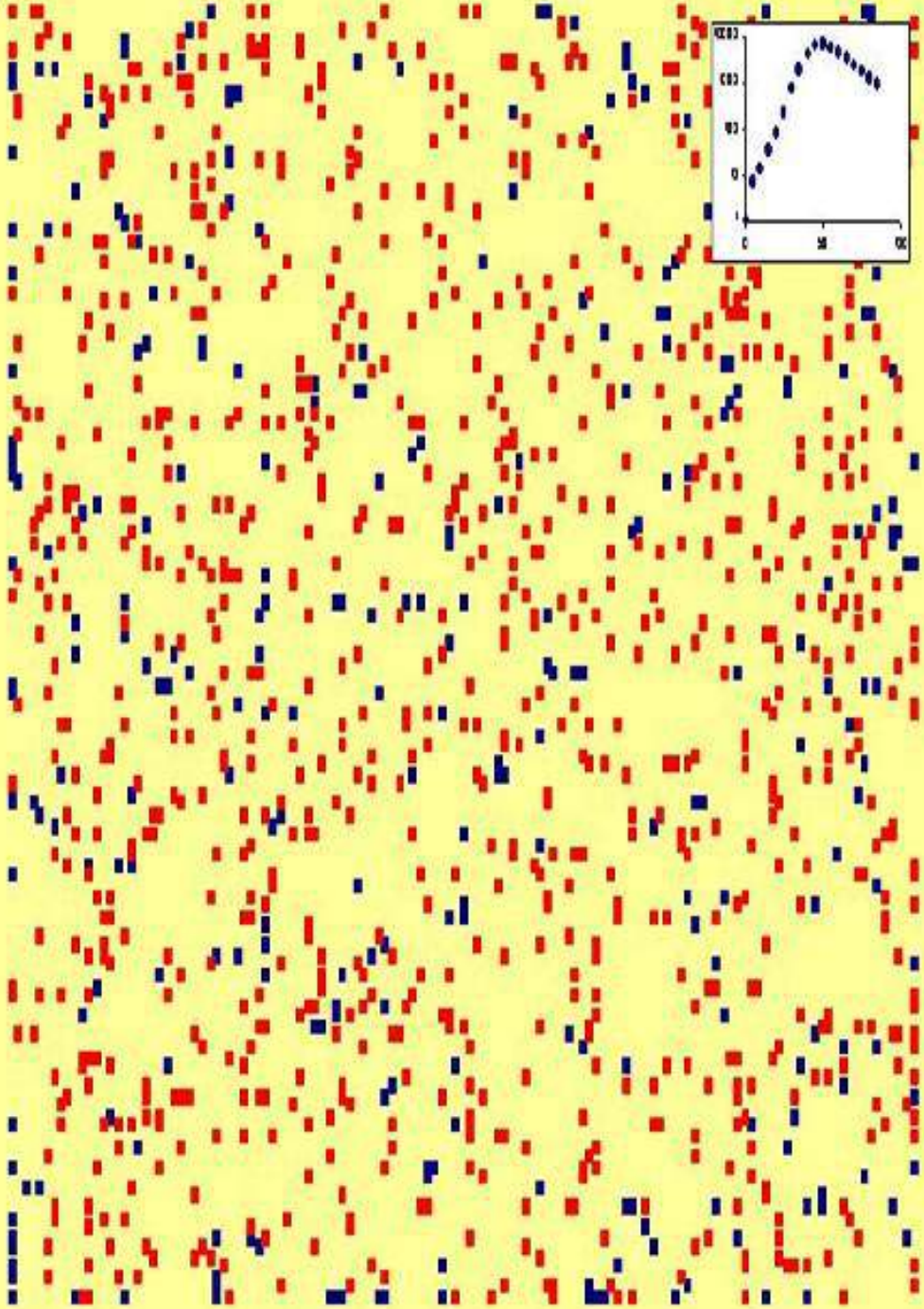

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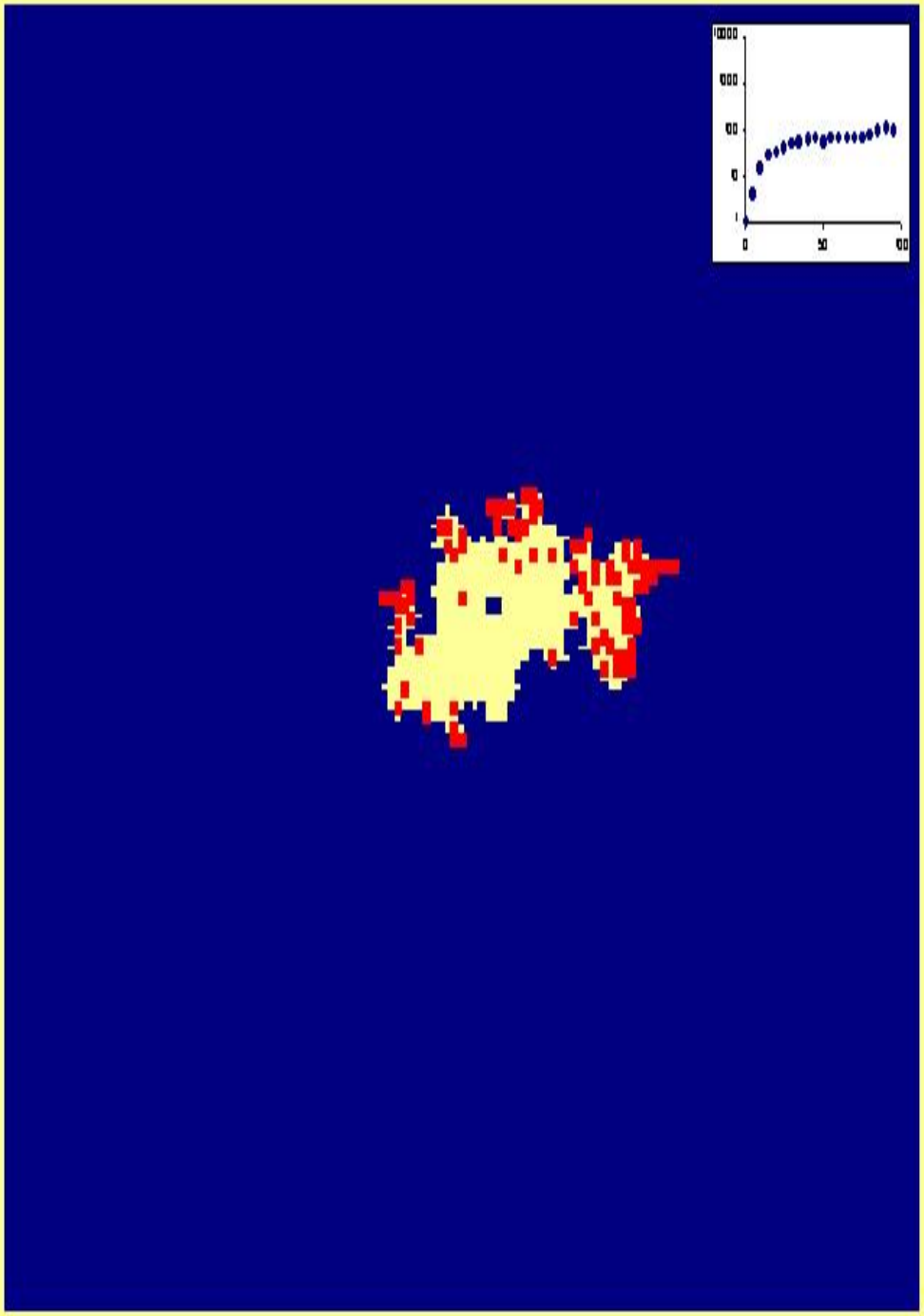

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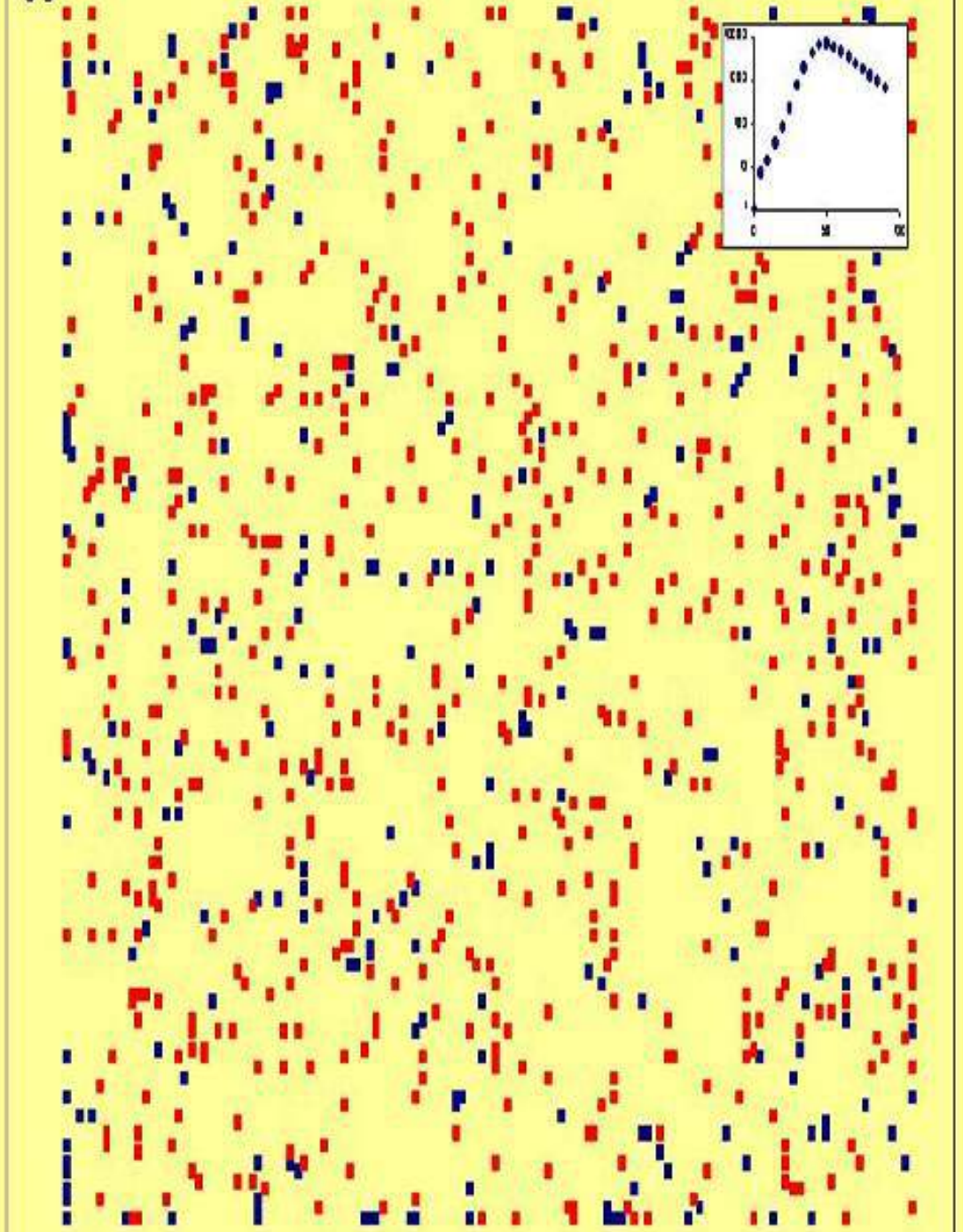

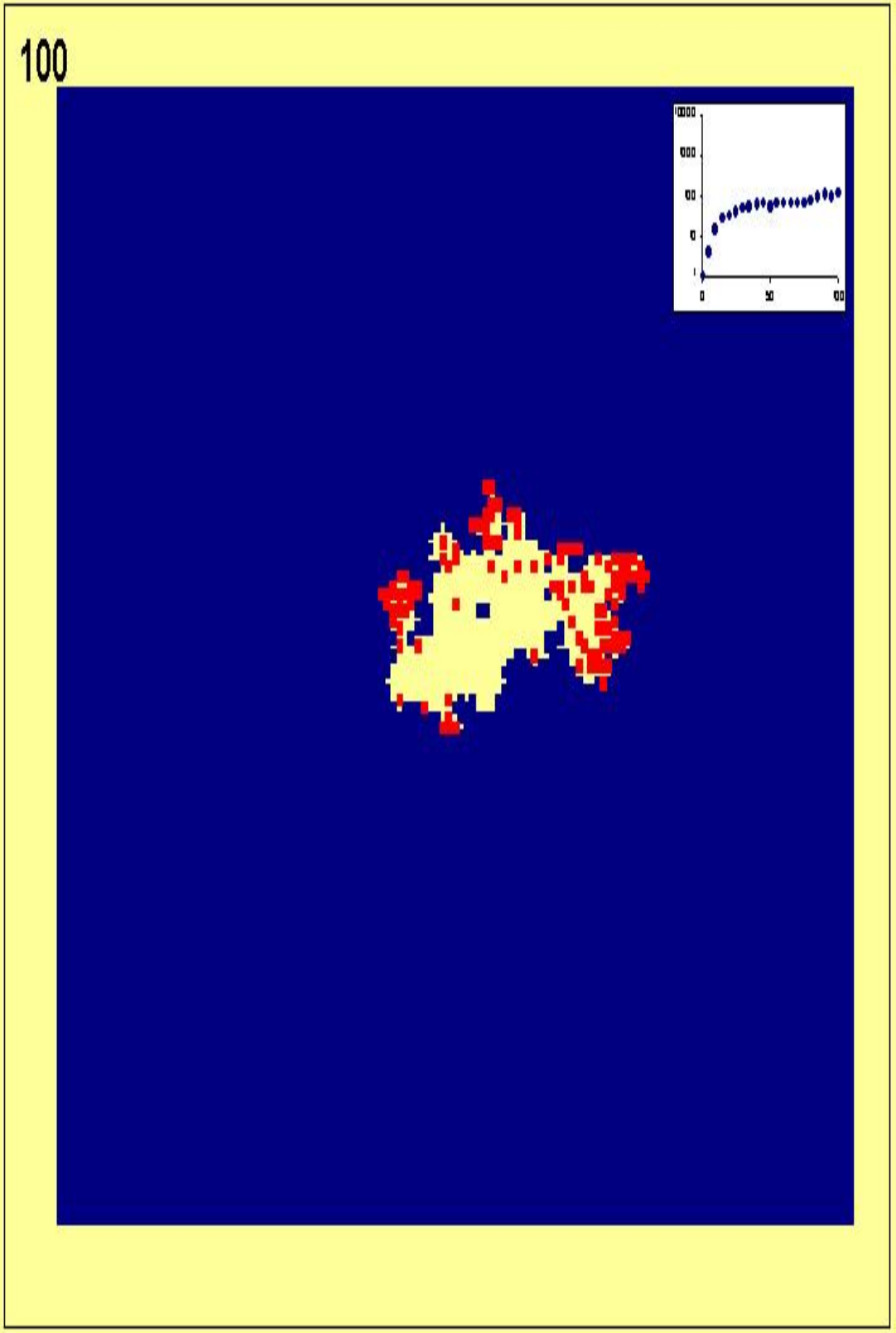
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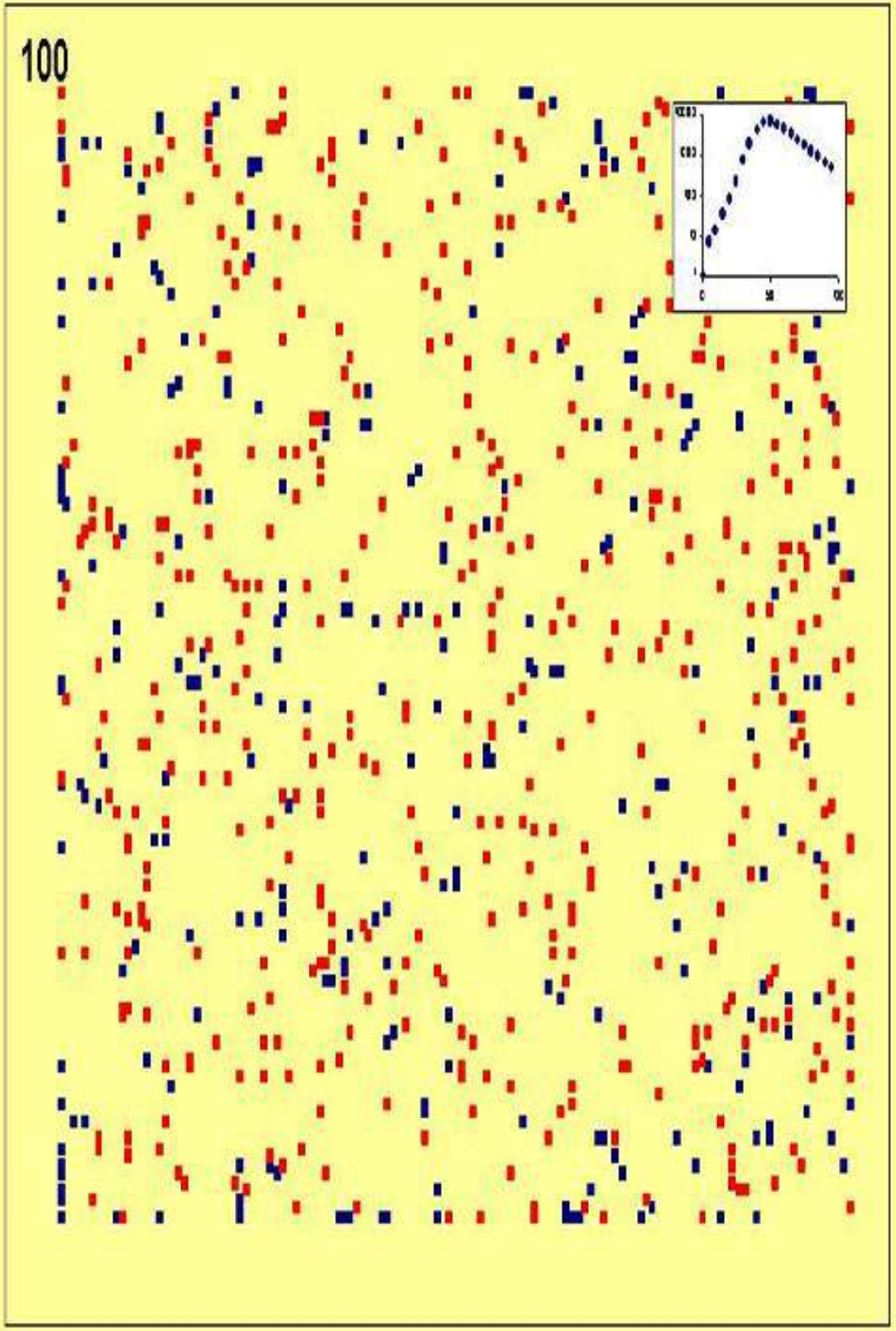

100

Spatial Epidemiology of HIV in a 'small world'

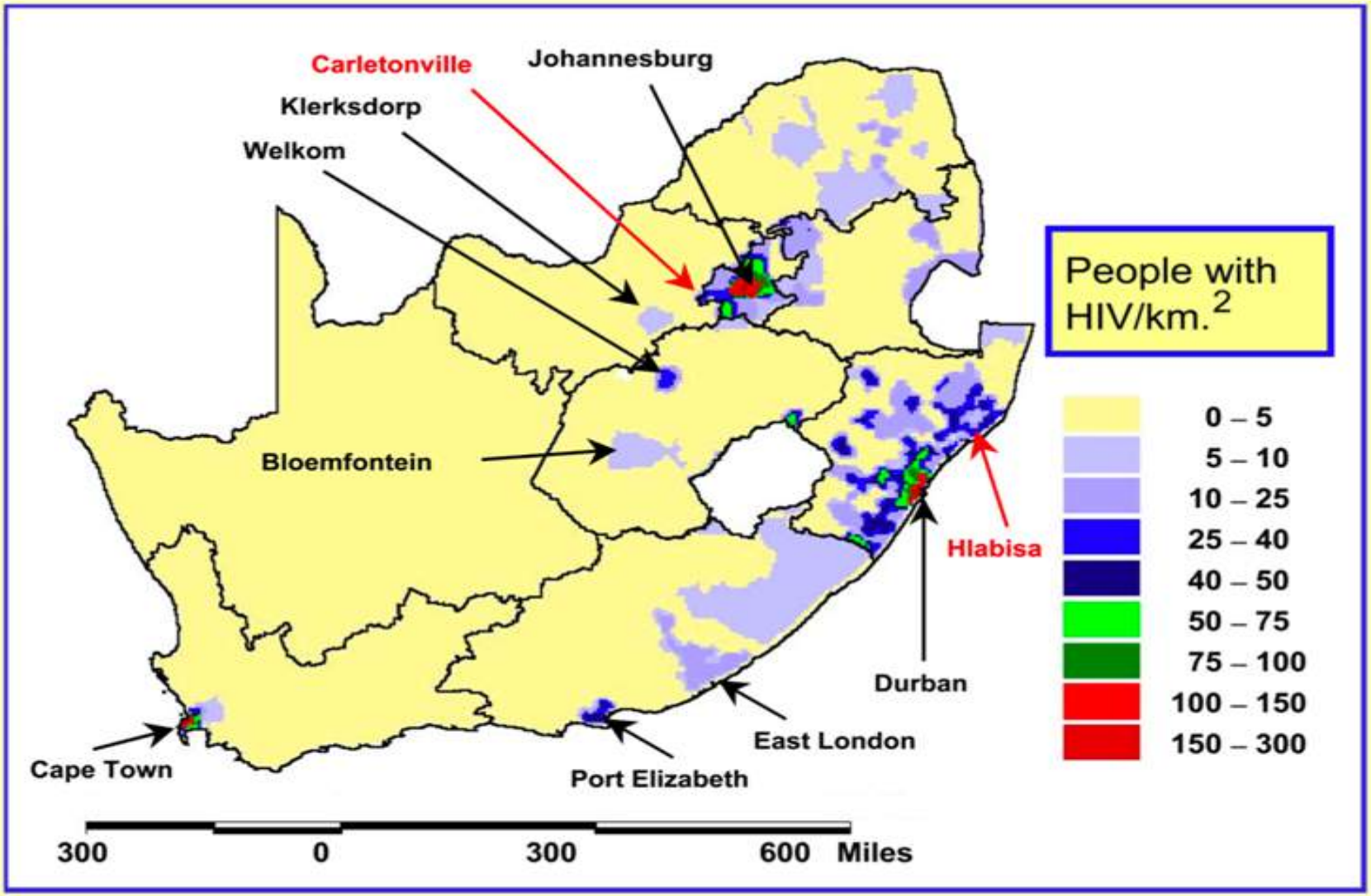
Without migration the epidemic spreads linerly and remains local. With migration the epidemic is constantly seeded in new areas, the prevalence increases exponentially until almost everyone is either infected and eventually dies.

Something that is unique to Southern Africa is what we call ‘oscillating migration’.

Created by the mining industry at the very beginning of the 20th century.

Very deep mines needed large amounts of unskilled labour, preferably disposable. Provided the economic basis for Apartheid

HIV in South Africa



Concentrated in major urban and mining centres. KwaZulu-Natal Cape Town

Williams *Phil Trans Roy Soc* 2001

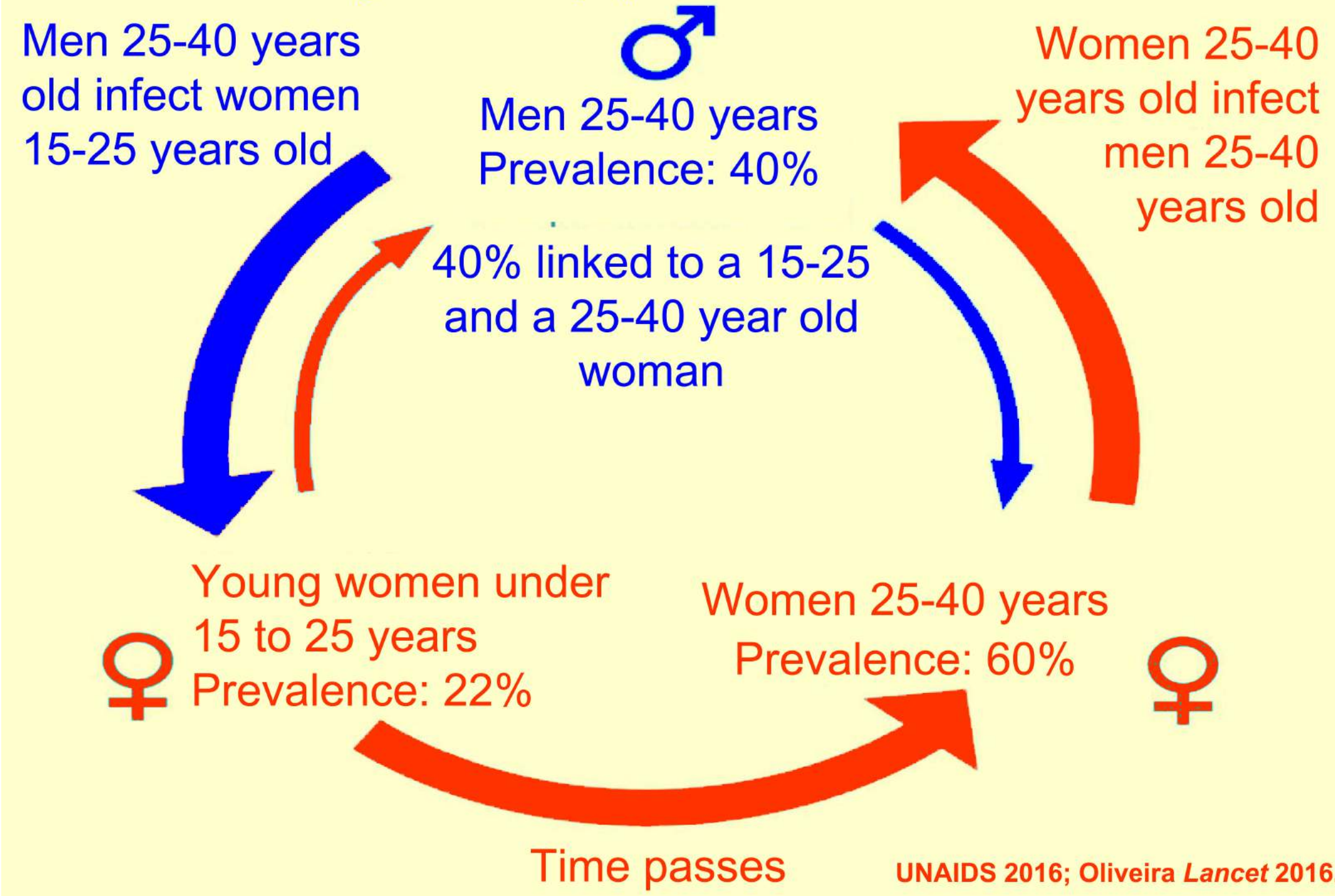
Age disparities and the spread of HIV

Sexual partnering between young women and older men, who might have acquired HIV from women of similar age, is a key feature … driving transmission [of HIV]. … strategies that … address age-disparate sexual partnering is crucial to … ending AIDS as a public health threat.[1]

Partner age disparity did not predict HIV acquisition in a rural community in KwaZulu-Natal [addressing] age-disparate sexual relationships may not be a cost-effective … in this setting.[2]

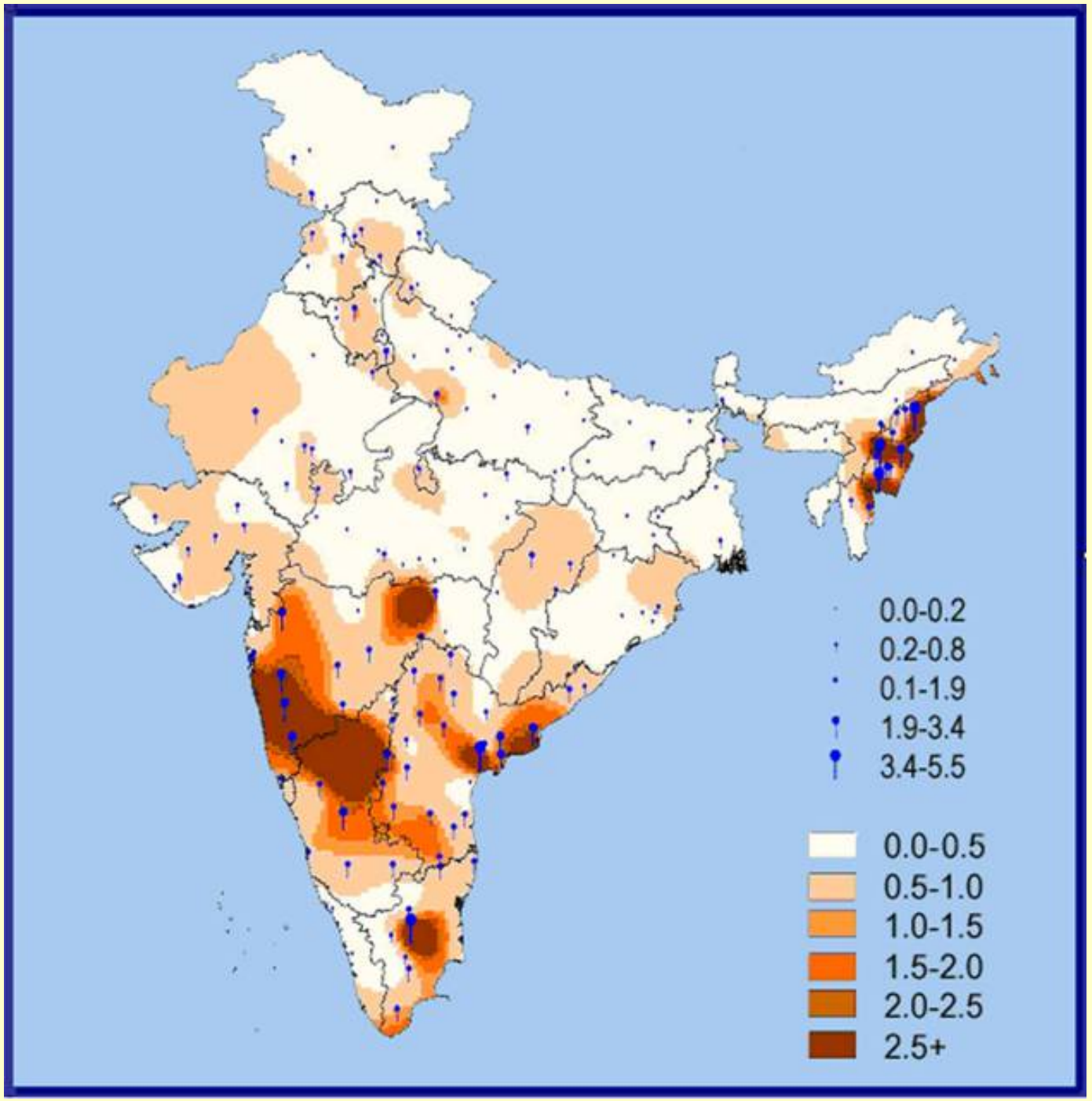
1. Oliveira *Lancet* and Gouws *Lancet* In press 2016; 2. Harling *JAIDS* 2014;

Life cycle approach to AIDS



UNAIDS 2016; Oliveira *Lancet* 2016.

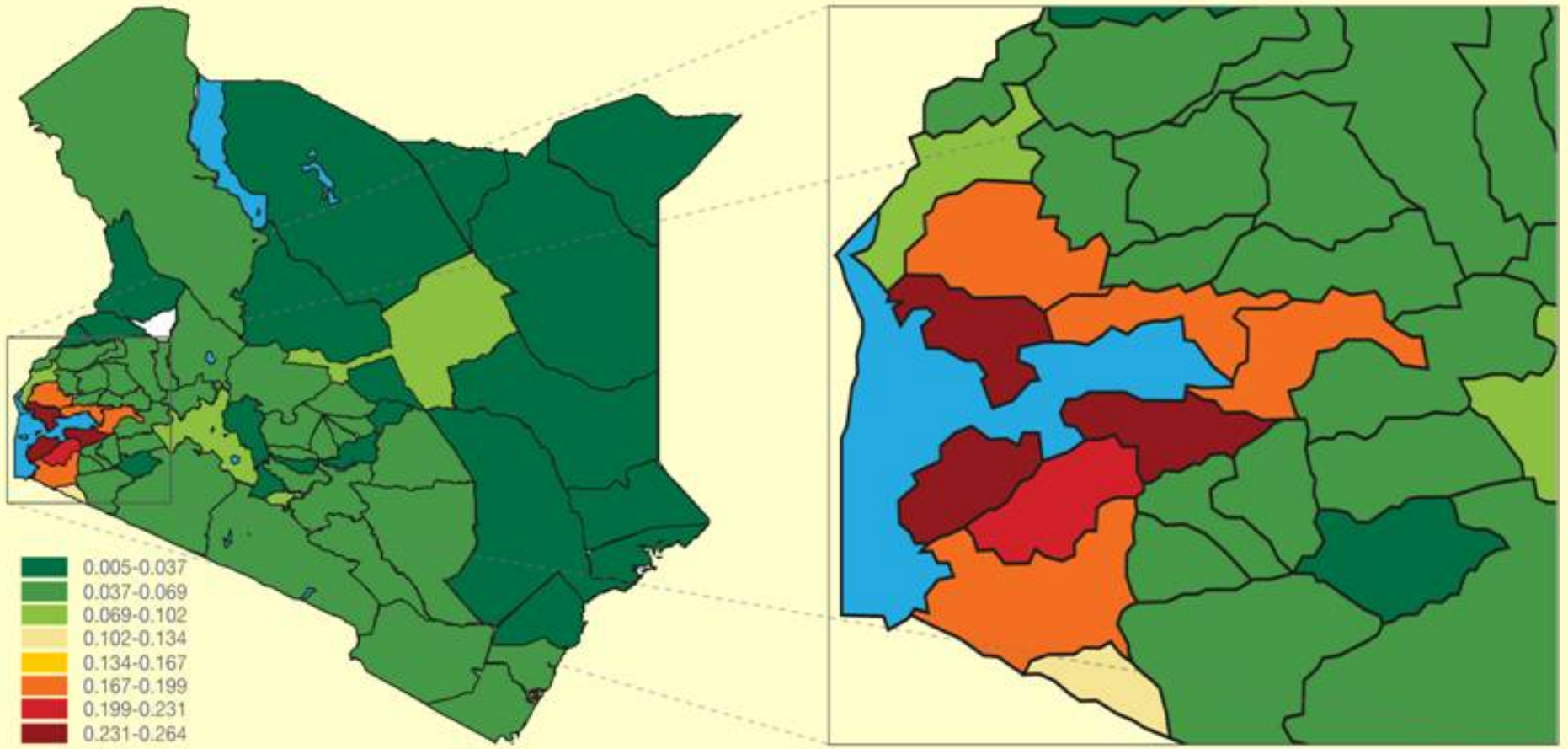
HIV in India



Concentrated in the far east: Manipur and Nagaland;
and in the south: Maharashtra, Karnataka, Andhra Pradesh, and Tamil Nadu, but not Kerala

Williams *PNAS* (2005) 102: 9619-24.

HIV in Kenya



Concentrated in eight districts of Nyanza province bordering Lake Victoria but not Busia (light green, extreme west).

WHO. A Brief History of Tuberculosis Control in Kenya. Geneva: World Health Organization, 2009.

Where does this leave us?

- No shortage of questions
- Not many answers
- Intuitively it has to be about networks
- The data are hard to collect
- The models can take forever to run

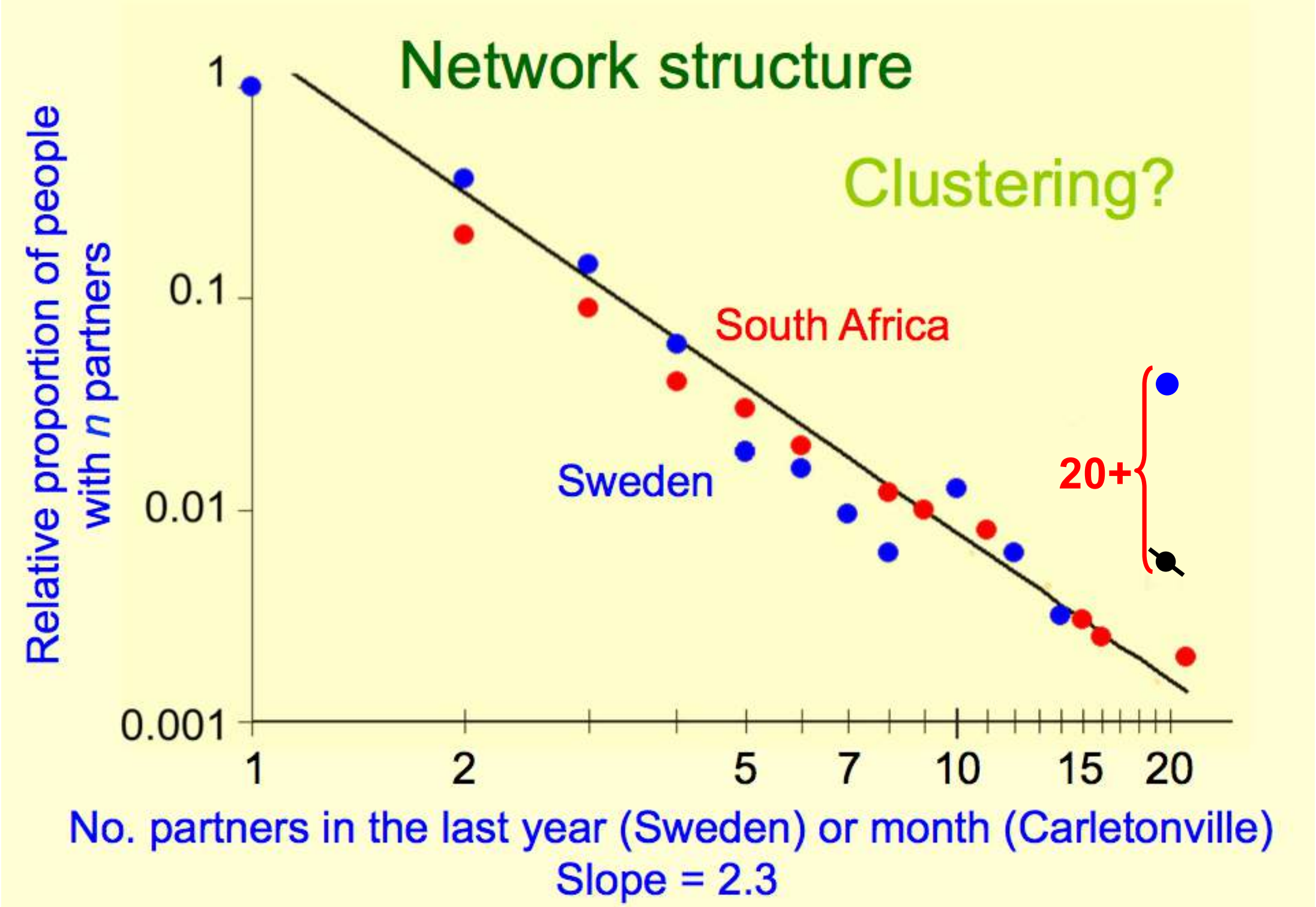
Perhaps some of the questions might point the way to some of the answers

Advice to young epidemiologists

Never make a calculation until you know the answer. Make an estimate before every calculation, try a simple biological argument (R_0, generation time, selection, survival, control). Guess the answer to every puzzle.

Courage: no one else needs to know what the guess is. Therefore, make it quickly, by instinct. A right guess reinforces this instinct. A wrong guess brings the refreshment of surprise. In either case, life as an epidemiologist, however long, is more fun.

Plagiarised from E.F. Taylor and J.A. Wheeler *Space-time Physics* 1963

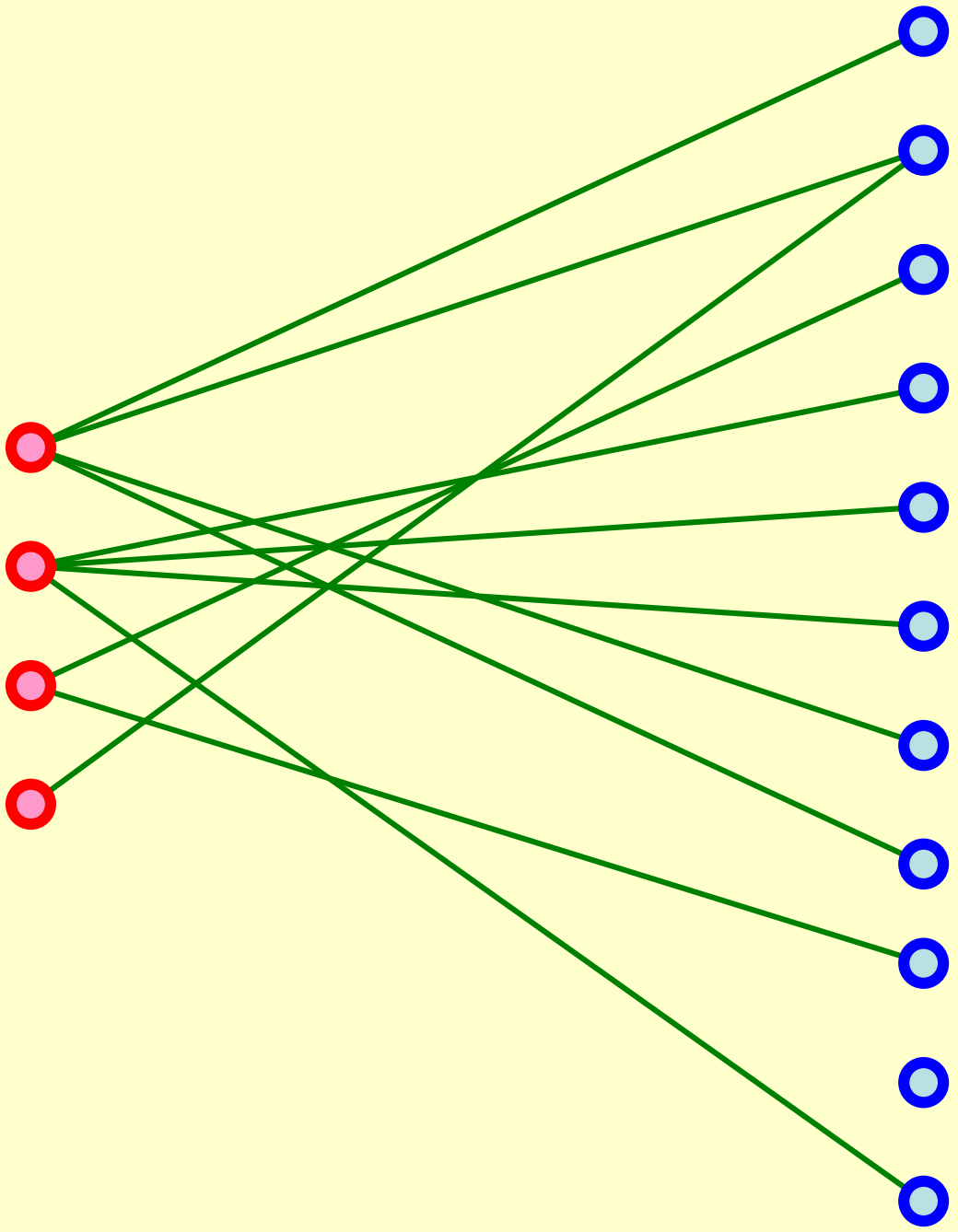


Liljeros et al. Nature 2001; Williams et al. Natural History of HIV/AIDS in Carletonville (CSIR)

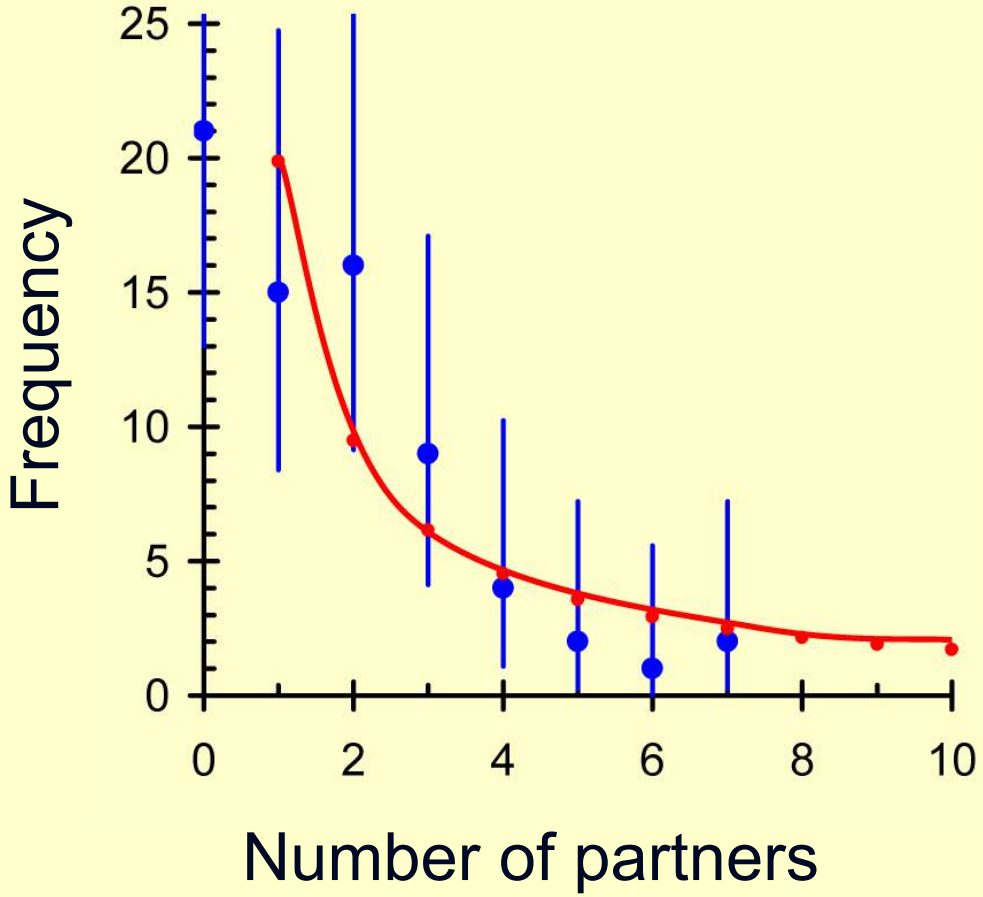
Why are social networks scale free?

Sandy Rutherford

If we start with a set of nodes with any degree distribution on the left and then connect it randomly to a set of nodes on the right the nodes on the right will have a Poisson degree distribution.

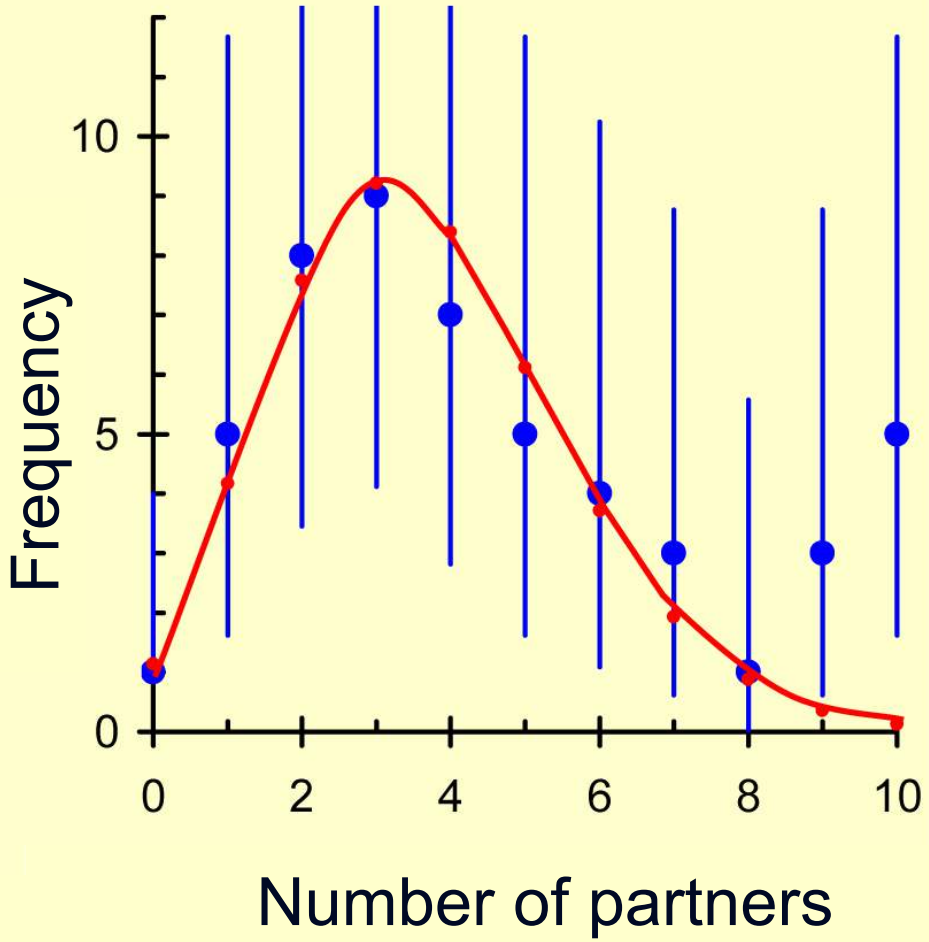


Sex workers and mine workers in Carletonville



Mine workers

Poisson



Sex workers

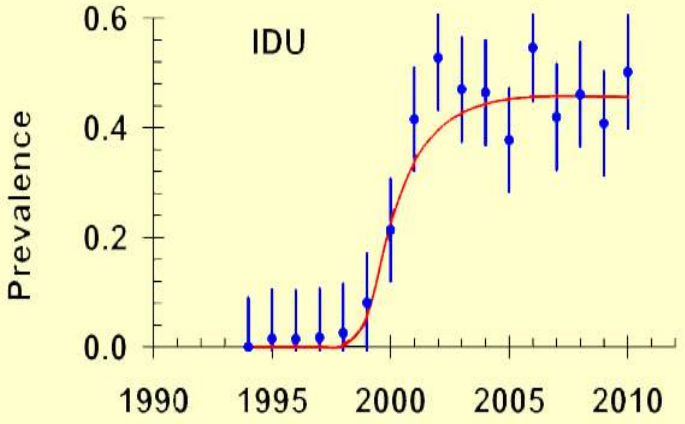
Scale free

Understanding and managing concentrated epidemics

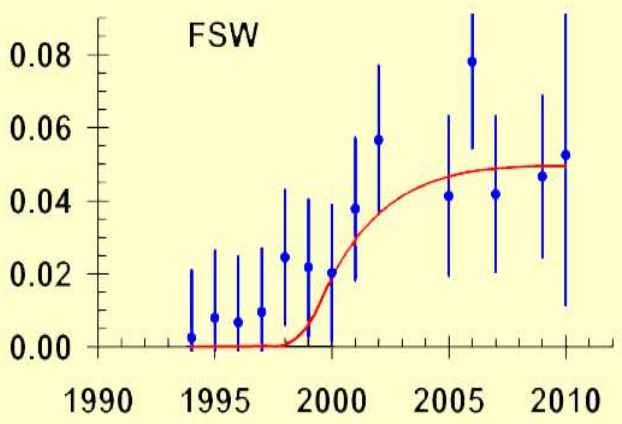
Can Tho Province, Vietnam

Concentrated HIV epidemics: Can Tho, Vietnam

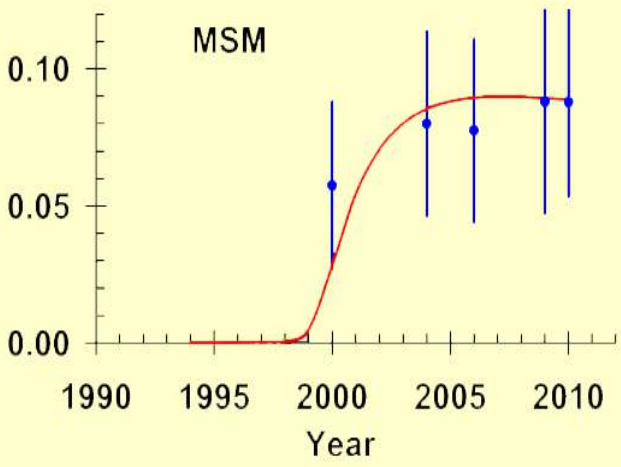
No.	%	Pos.
3157	46	1446

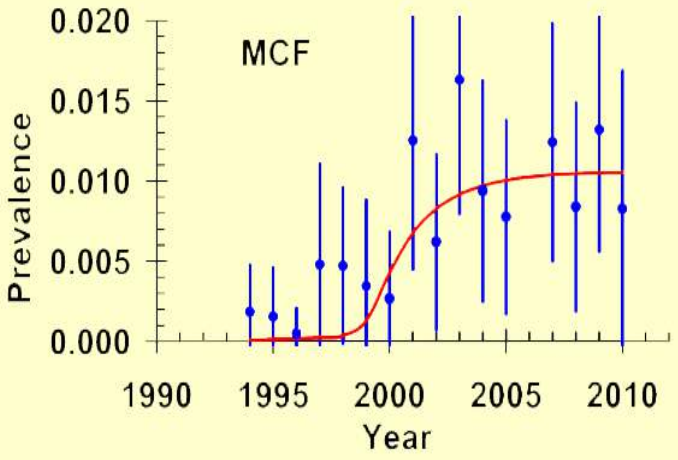


No.	%	Pos.
2034	5.4	109

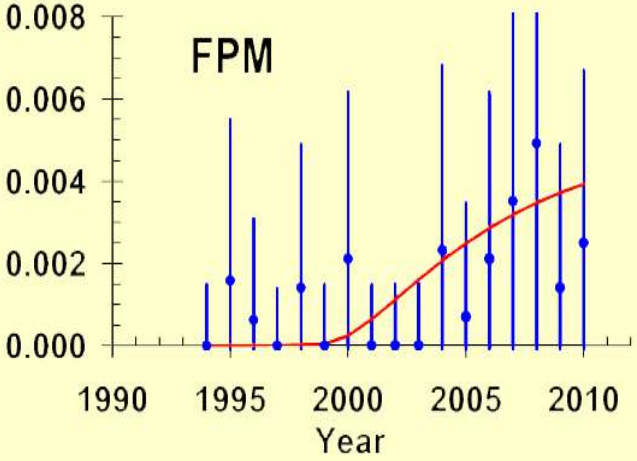


No.	%	Pos
1492	8.8	131





No.	%	Pos.
62k	1.0	615

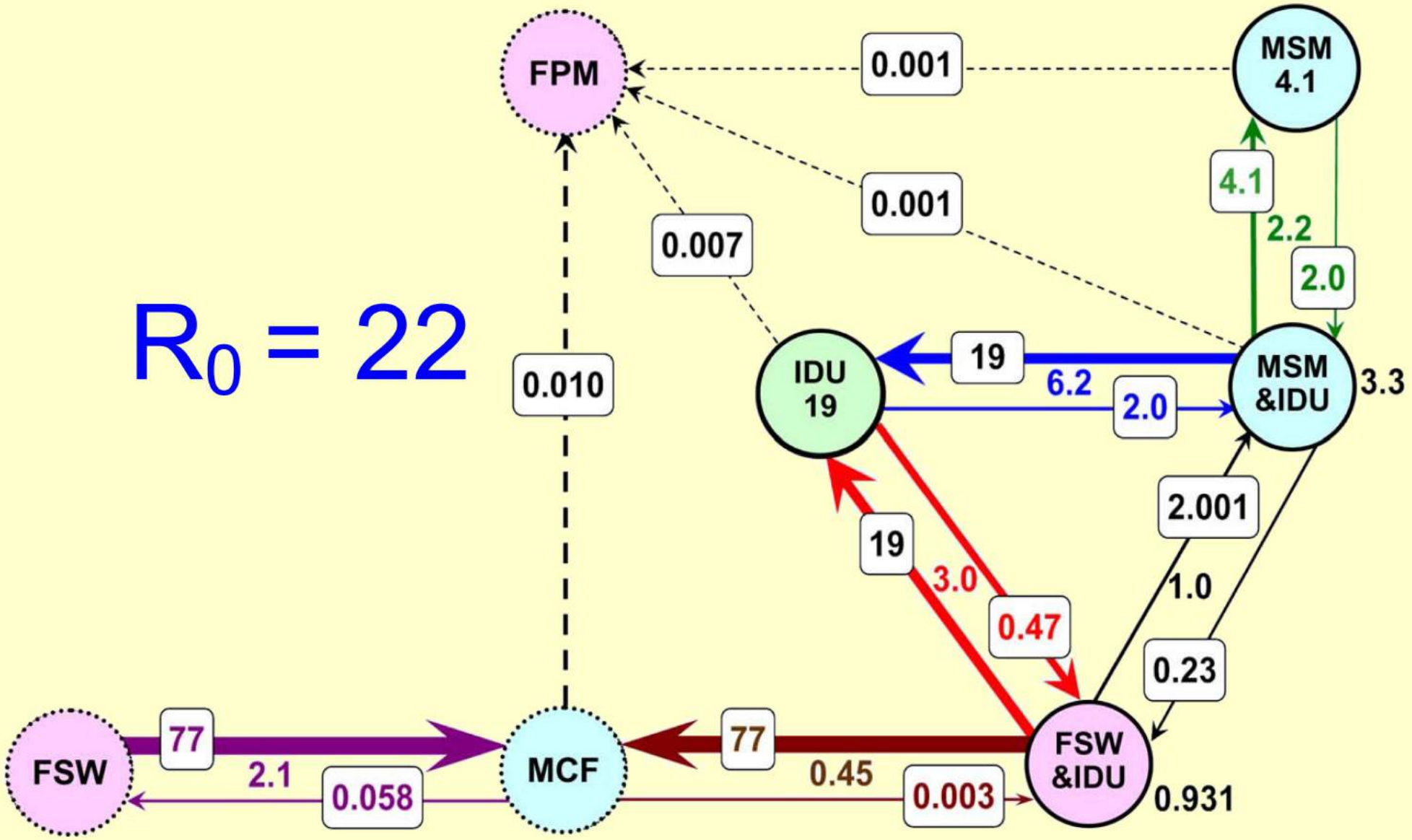


No.	%	Pos.
454k	0.4	1776

IDU: intravenous drug users
FSW: female sex workers
MSM: men who have sex with men
MCF: male clients of female sex workers
LRW: low risk women

Prevalence varies Group size varies Groups overlap

Transmission in Can Tho, Vietnam



FPM: Female partners of male clients MSM: Men who have sex with men

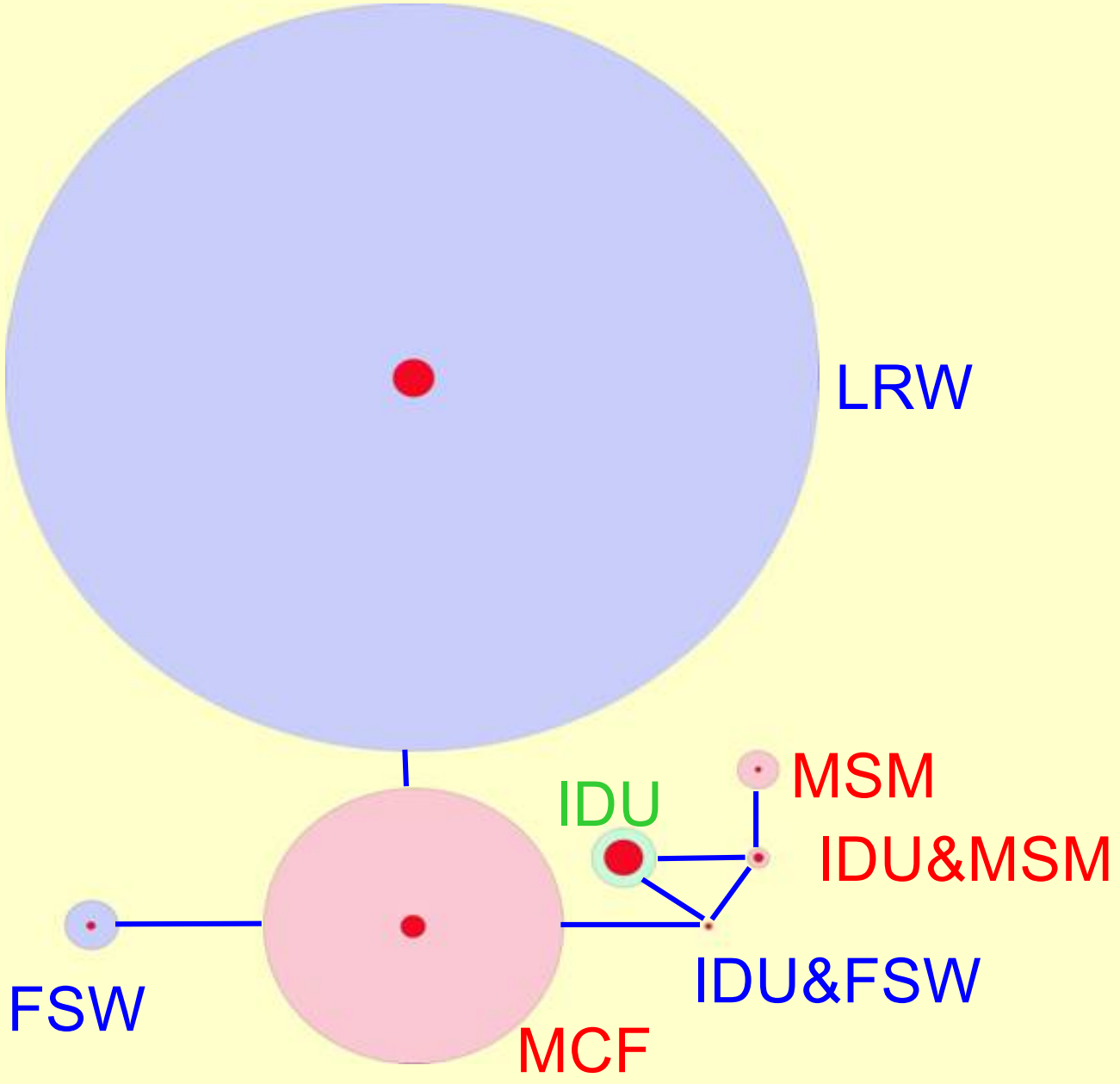
IDU: Intravenous drug users

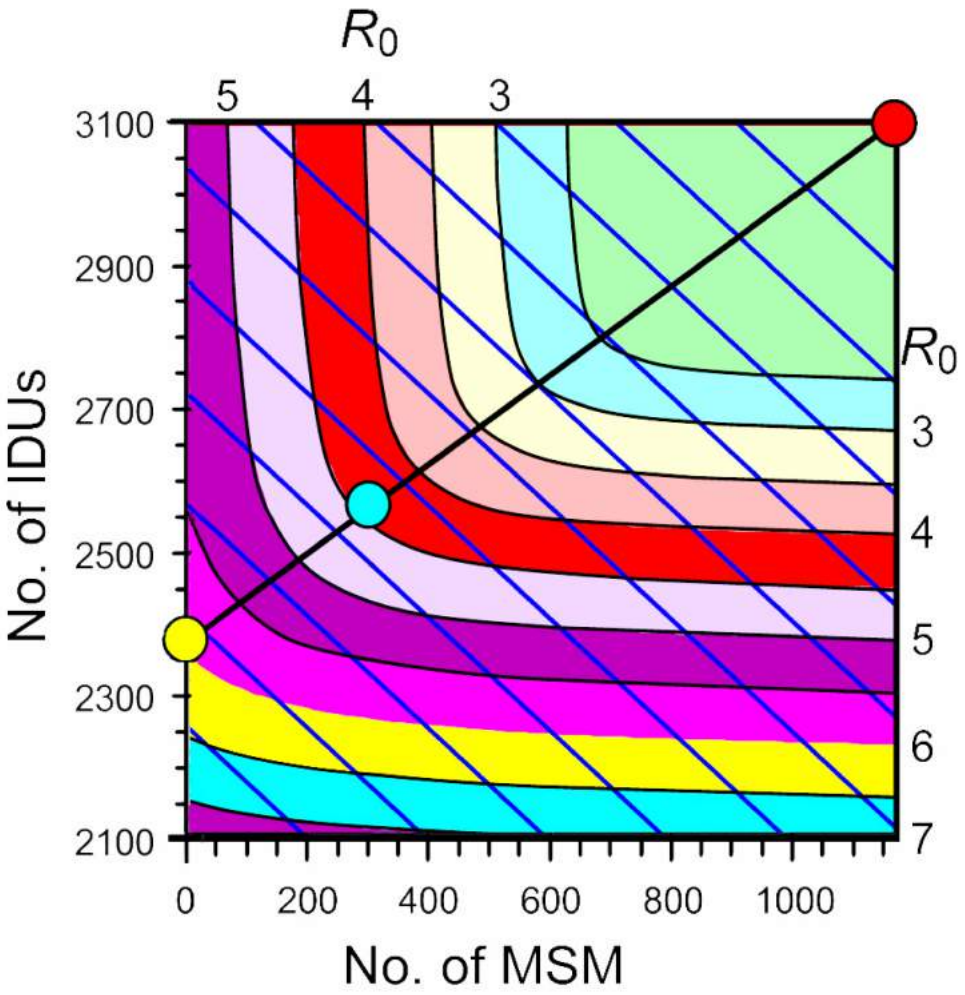
FSW: Female sex workers MCF: Male clients of female sex workers

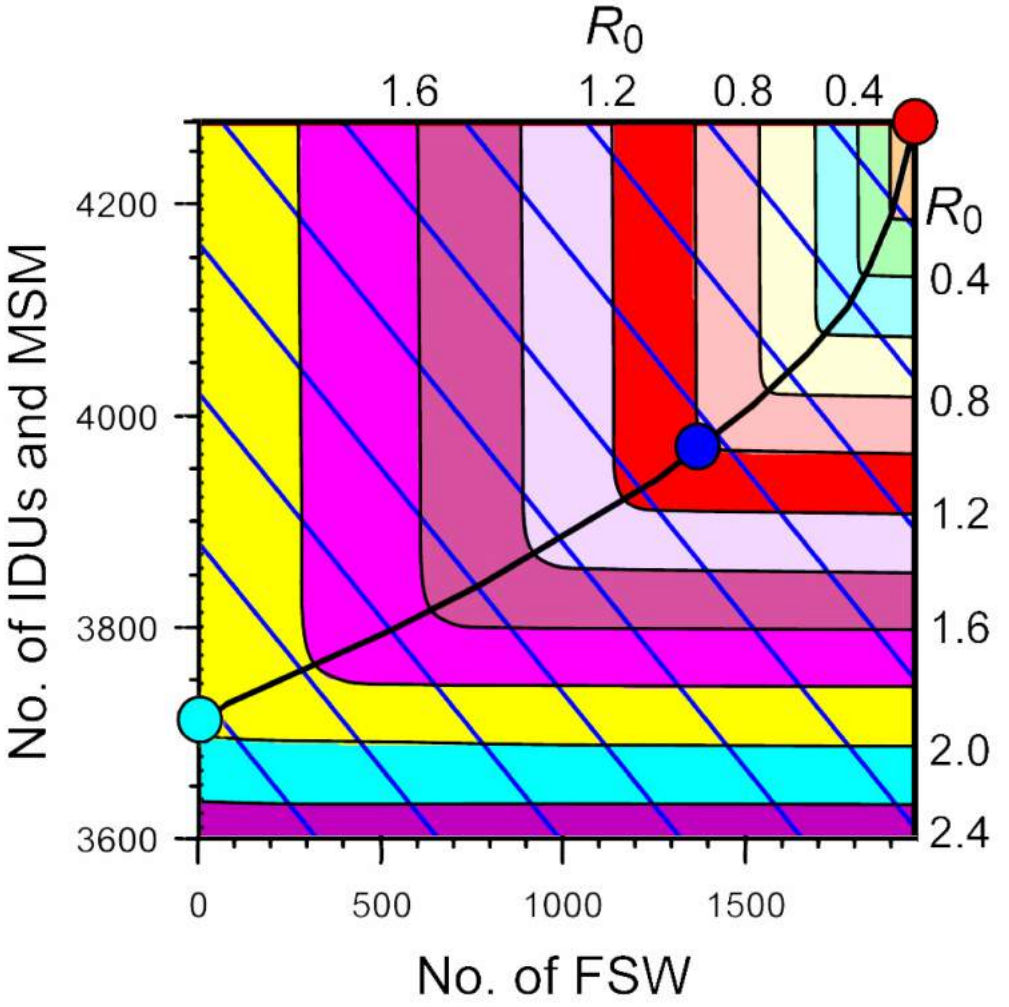
Transmission network: Can Tho, Vietnam

Big circle
Group size

Small circle
No. infected




R_0
5
4
3
3100
2900
2700
2500
2300
2100
No. of IDUs
R_0
3
4
5
6
7
0
200
400
600
800
1000
No. of MSM


R_0
1.6
1.2
0.8
0.4
4200
4000
3800
3600
No. of IDUs and MSM
R_0
0.4
0.8
1.2
1.6
2.0
2.4
0
500
1000
1500
No. of FSW