Suppressing Covid-19: Public Health Policy and Effective Mass-Testing Rates

Division F Conference
Department of Engineering, U of Cambridge

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Outline

- △ **Covid-19 tests**
  - ▷ Antibody tests
  - ▷ PCR tests
  - ▷ Antigen tests
    - ⇝ Rapid, cheap, at-home tests
- △ **Epidemiological models**
  - ▷ SIR models on random population networks
    - ▶ Erdős-Rényi graphs
    - ▶ Random graphs with given degree distribution
  - ▷ SIR epidemics with mass testing
- △ **Necessary testing rates for suppression**
  - ▷ **Rigorous results for a broad class of models**
  - ▷ Explicit numerical examples

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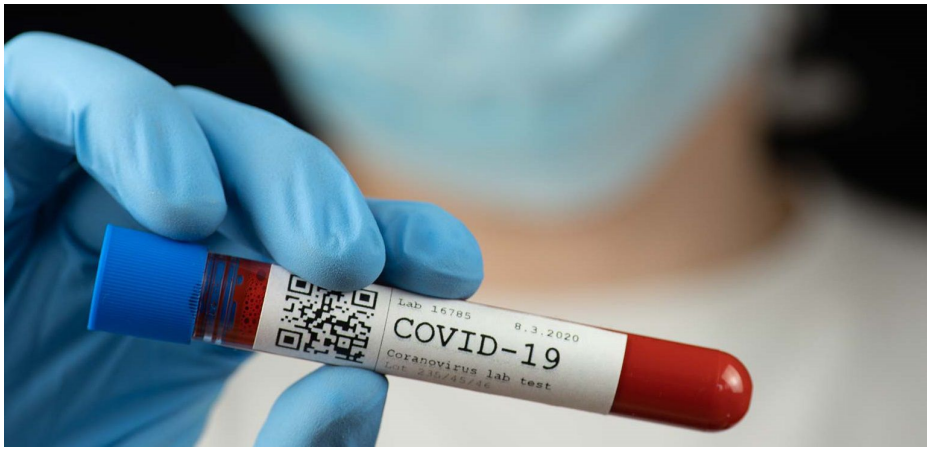

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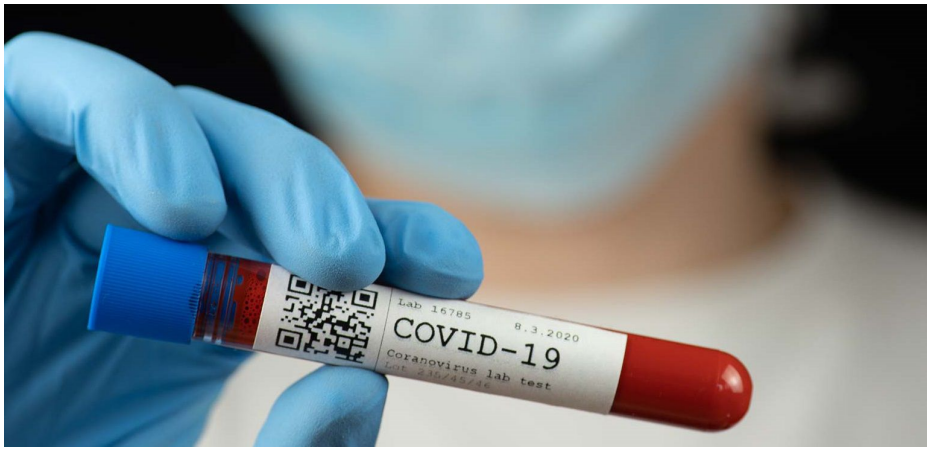

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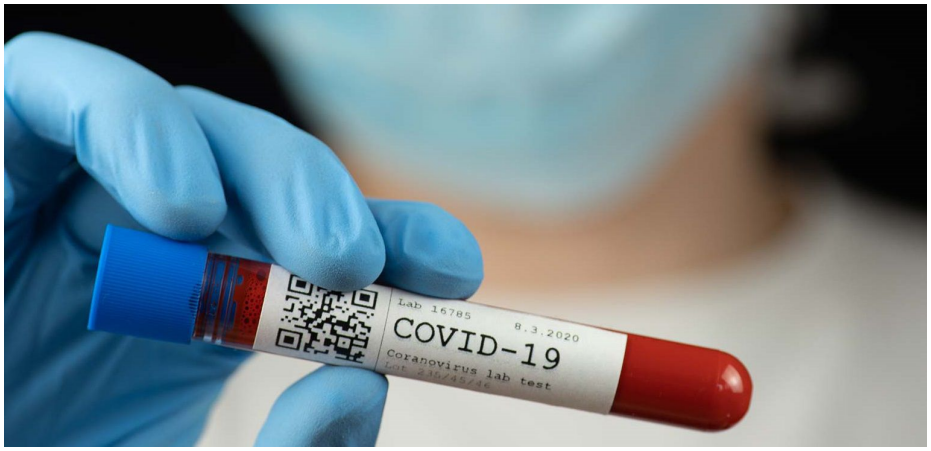

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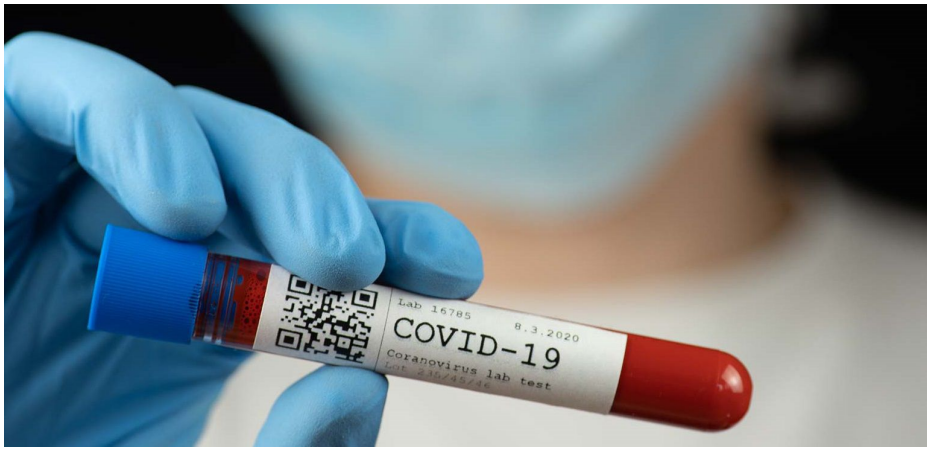

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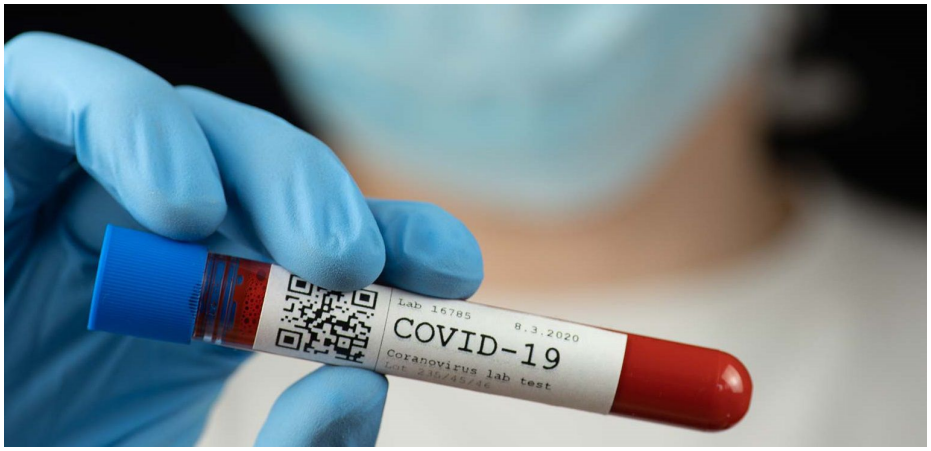

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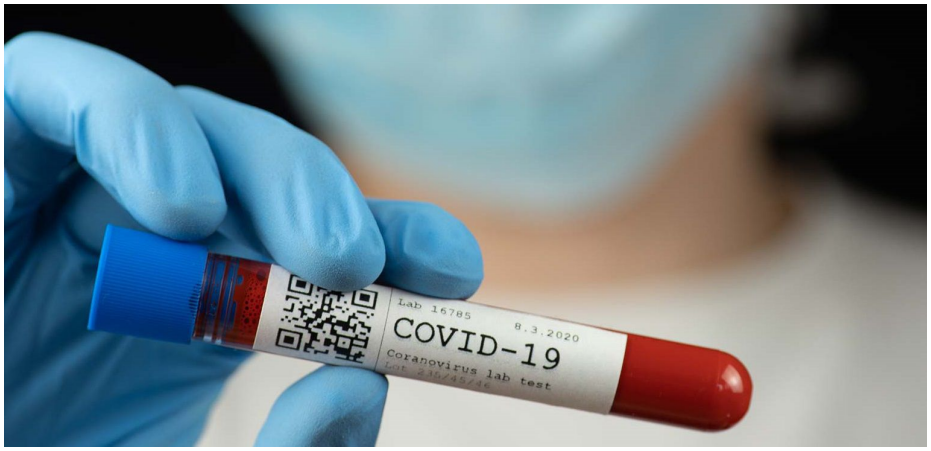

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Currently: ≈ 200 Covid-19 FDA-approved tests in the US (+many more in development) using different technologies . . .

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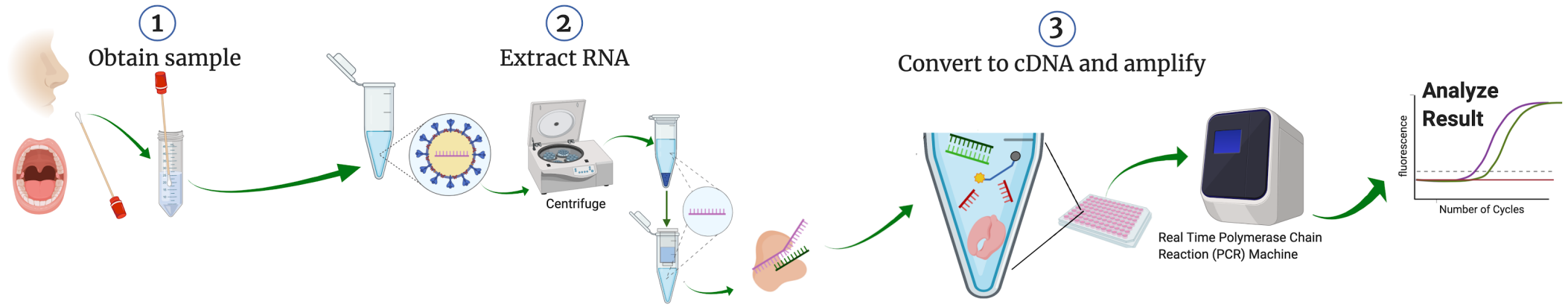
- ▷ Important and possibly becoming much more common soon

PCR tests [reverse-transcription polymerase chain reaction tests]



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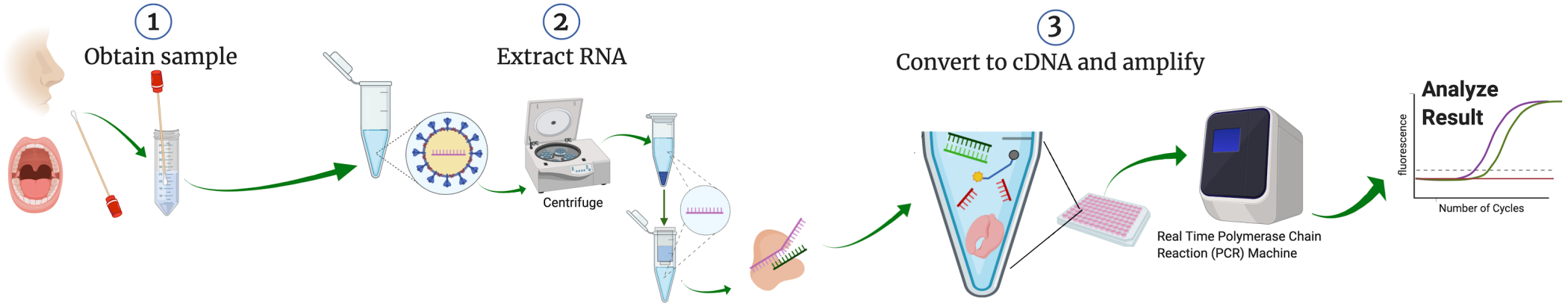

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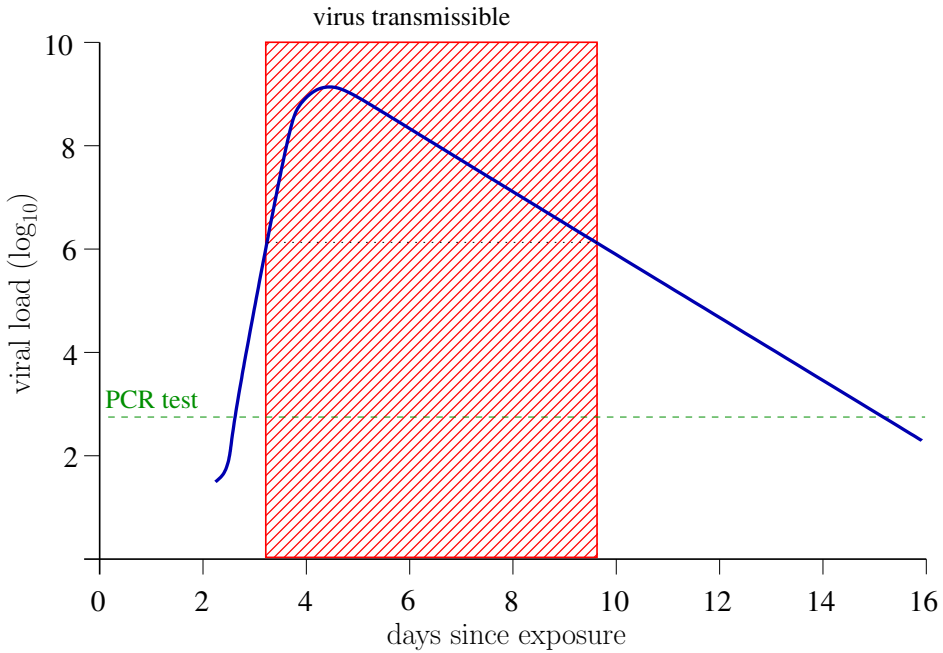

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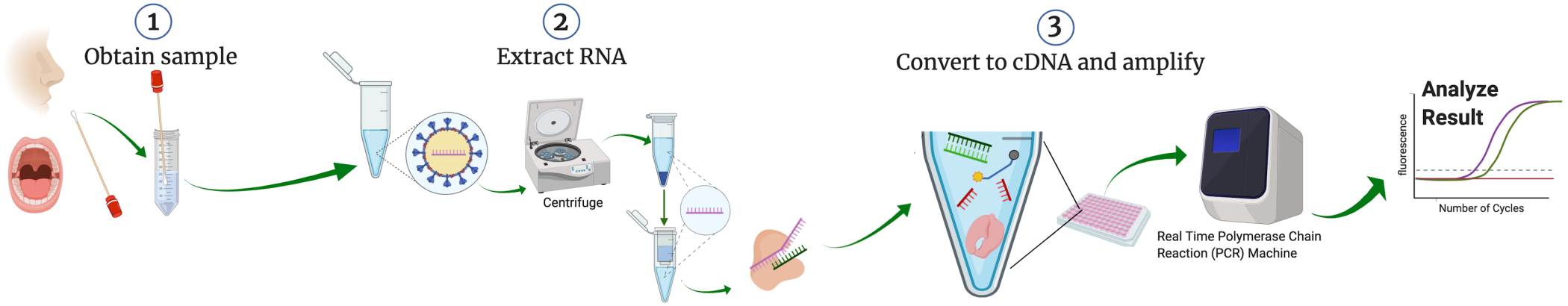

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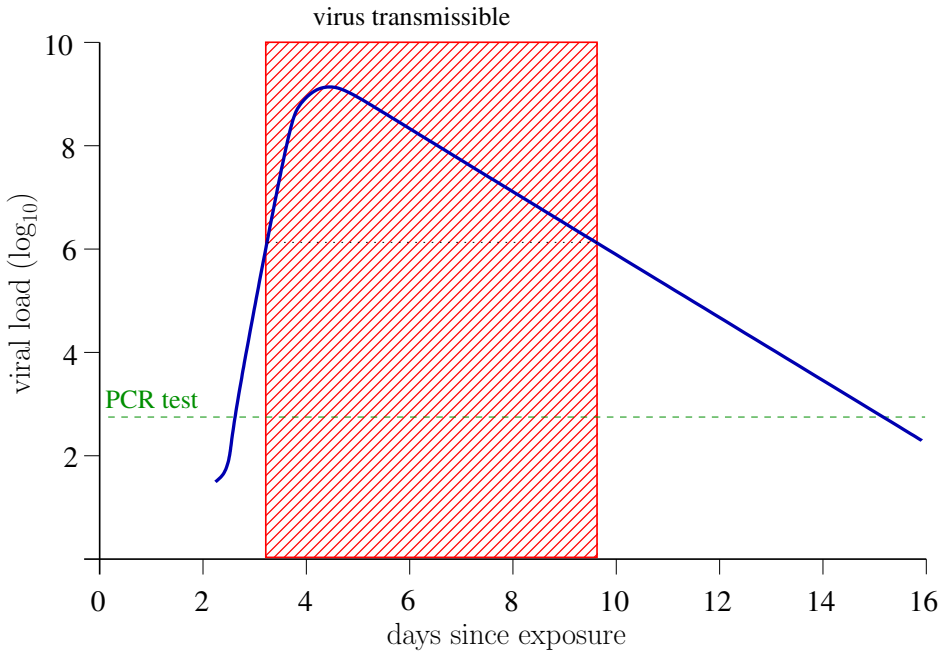

- ▷ Indeed, **the** FDA test standard
- ▷ **But**: Not designed for an out-of-control pandemic

PCR tests

Problems

- ▷ Very **slow** turnaround times (3-14 days in most places in the US)

  $\rightsquigarrow$ they miss the most infectious period

- ▷ **Not enough** of them: Bottlenecks:
  Chemical reagents, lab supplies, PCR machines

- ▷ **Expensive** [$35-200], very tightly regulated, require specialized personnel and equipment [$\Rightarrow$ social inequality issues]

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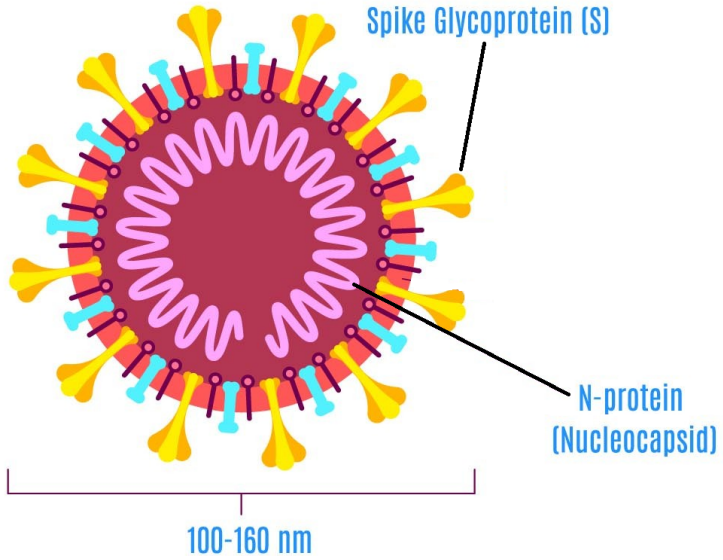
Partial fixes

- ▷ Pooling or "**group testing**": Still expensive and not fast enough
- ▷ Saliva-based tests with Ginkgo Bioworks's **Illumina sequencing machines** instead of PCR. Factor of 6 faster, still slow:
  Samples must be shipped centralized locations
- ▷ Saliva-based modified-PCR laboratory tests: UIUC's **I-COVID**, Yale's **SalivaDirect**. Results in 2-6 hours, cost $10-20.
  UIUC story highlights the need for even more, cheaper tests

Antigen tests: I lab-based

They do not identify virus RNA
but an **antigen**, typically a protein



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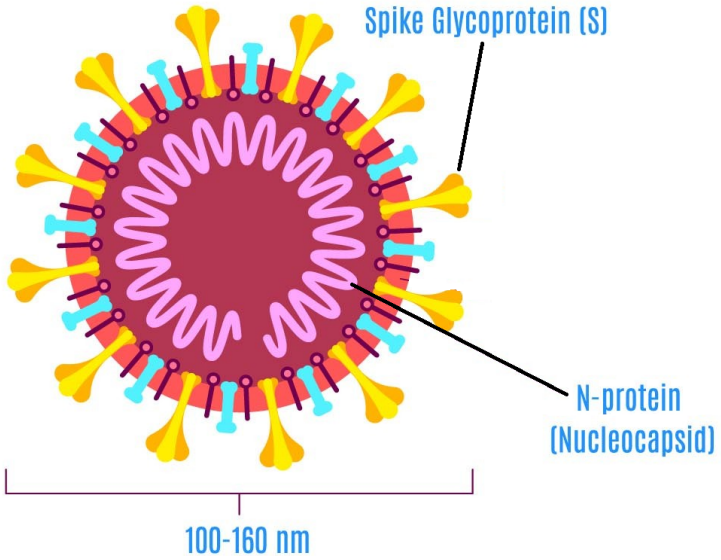

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- E.g., tests made by *Quidel* and *Becton-Dickinson* (US)
  detect the **nucleocapsid** (N) protein in nasal/throat swab samples

  Tests cost is $\approx$ half of PCR, give results in 15 mins

  Can be administered at a point-of-care location

  Will be making 14 million tests/month by end of September

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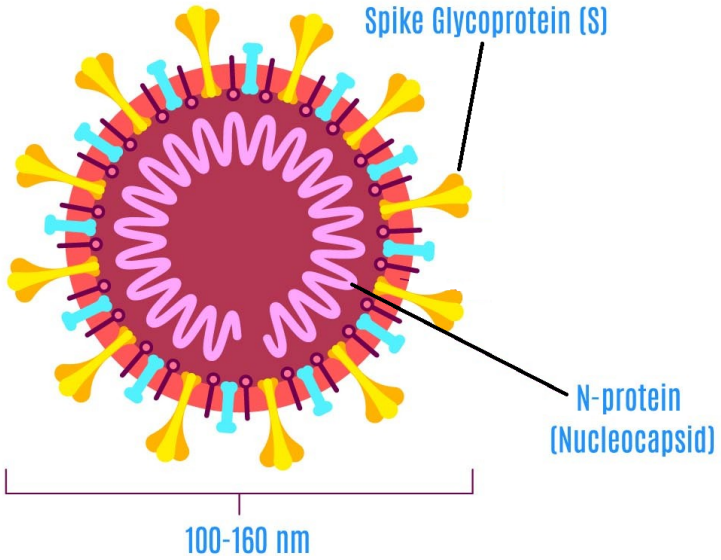

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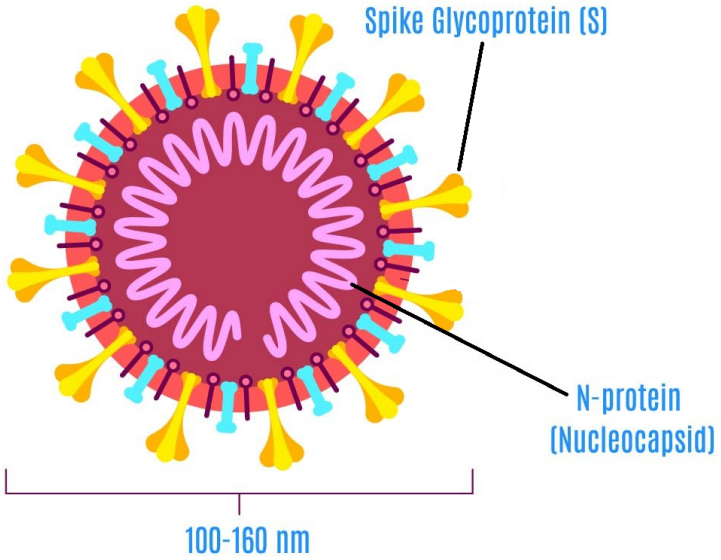
Drawbacks

- ▷ They only work with a proprietary reader
  but companies cannot produce it at same scale
- ▷ Since nucleocapsid is *inside* the virus
  they need reagents to break down its outer membrane

Antigen tests: II rapid tests



Made by US-based companies including e25 Bio, Sona Nanotech, Iceni Diagnostics, OraSure

Characteristics

Cheap: $1-2

Results in 15 minutes

Home tests, no equipment: Saliva + saline solution + small cup

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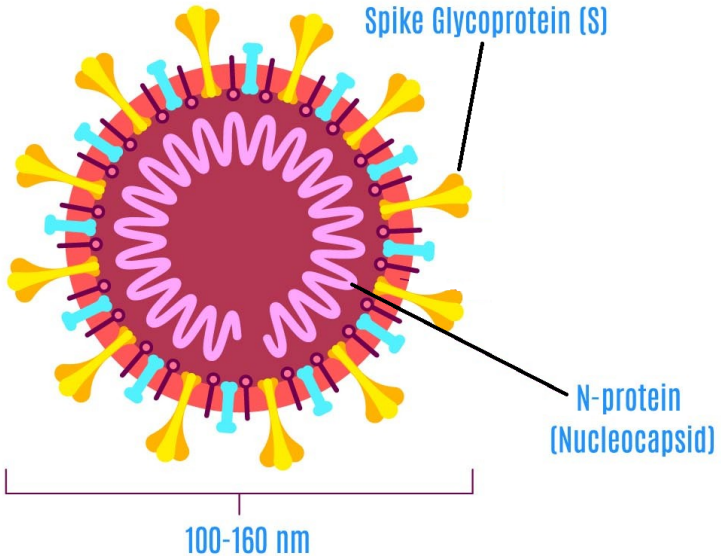

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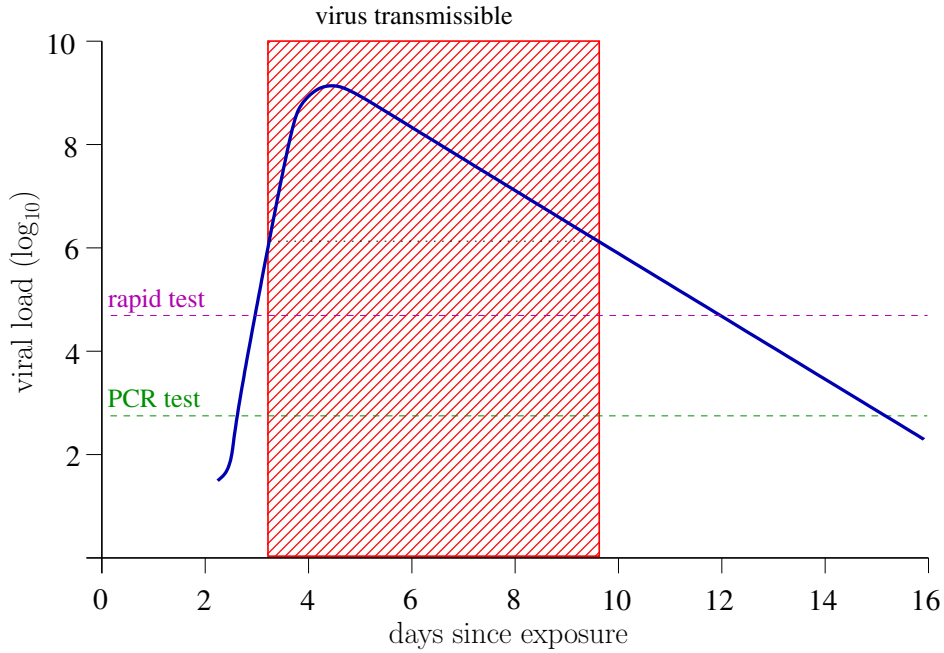

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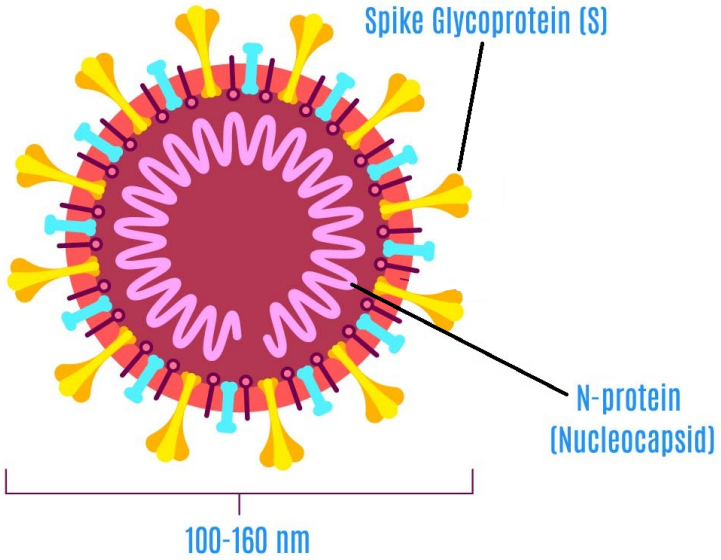

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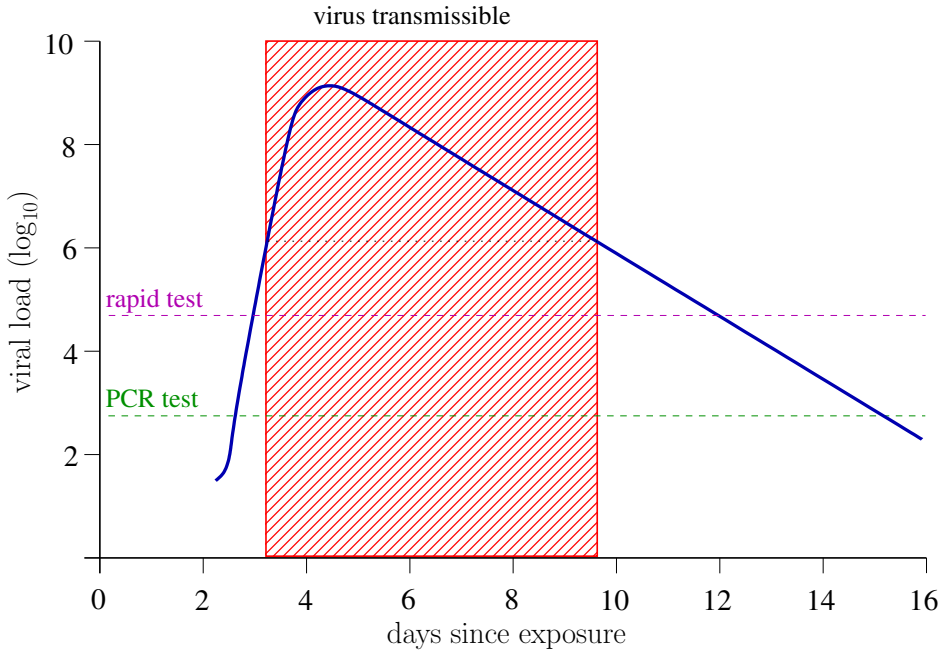
e25 Bio test

Paper strip no larger than 1x5 in

Looks for the **spike** (S) protein
on the *outside* of the virus

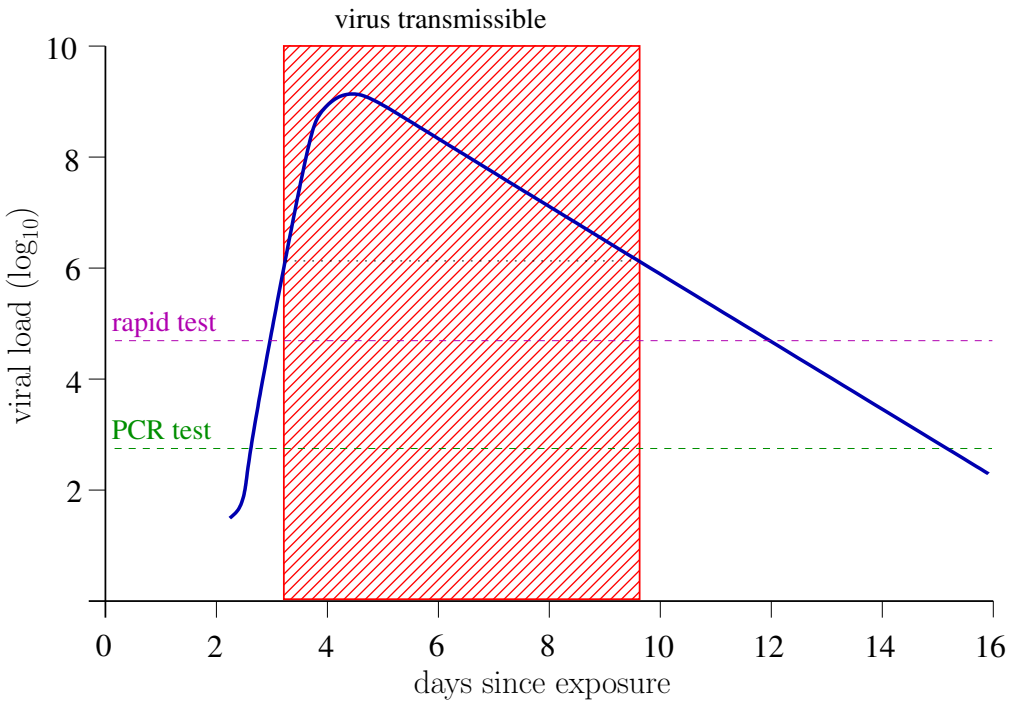
Sensitivity: 60-80%



PCR vs rapid tests

For ≈24 hours in the beginning the tests give different results, rapid tests give false negatives

BUT: For a long time in the end PCR detects mostly dead virus



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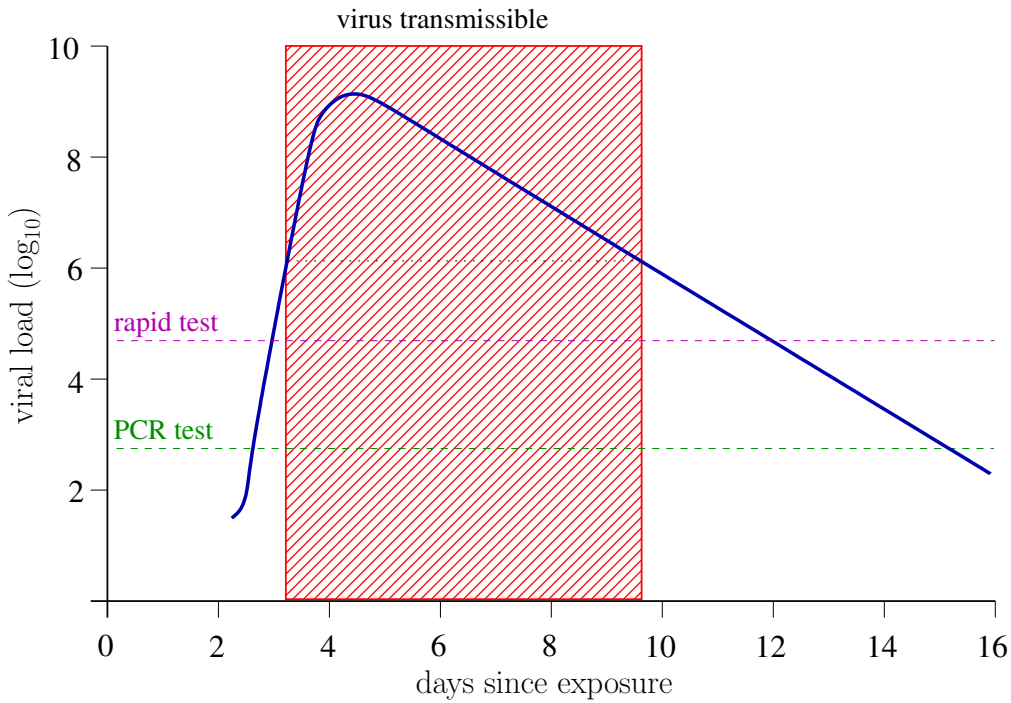

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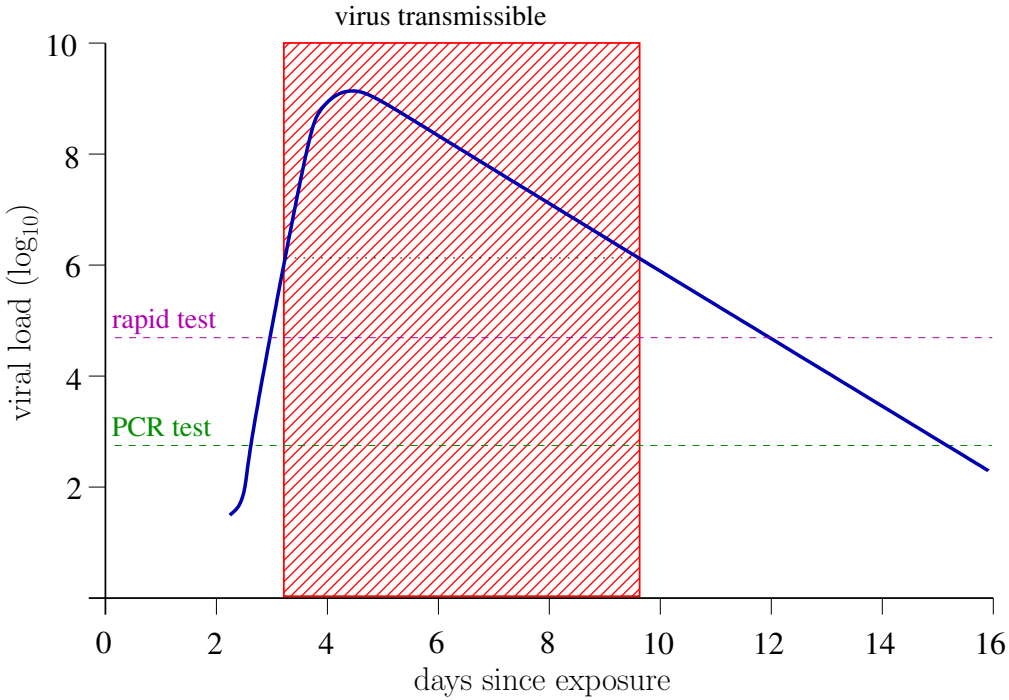

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- FDA will not change its regulations to approve antigen tests but could re-frame them as *transmission-detecting tests* or *surveillance tools*
- The FDA recently stated they would consider less sensitive tests as part of a high-frequency testing plan

Population-scale daily testing

△ Growing movement advocating 10s-100s of millions of rapid tests/day

Idea: **Test every individual before every major social contact**:
Work, school, cinema, shopping, etc

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$\rightsquigarrow$ **How much testing is needed for this to work?**

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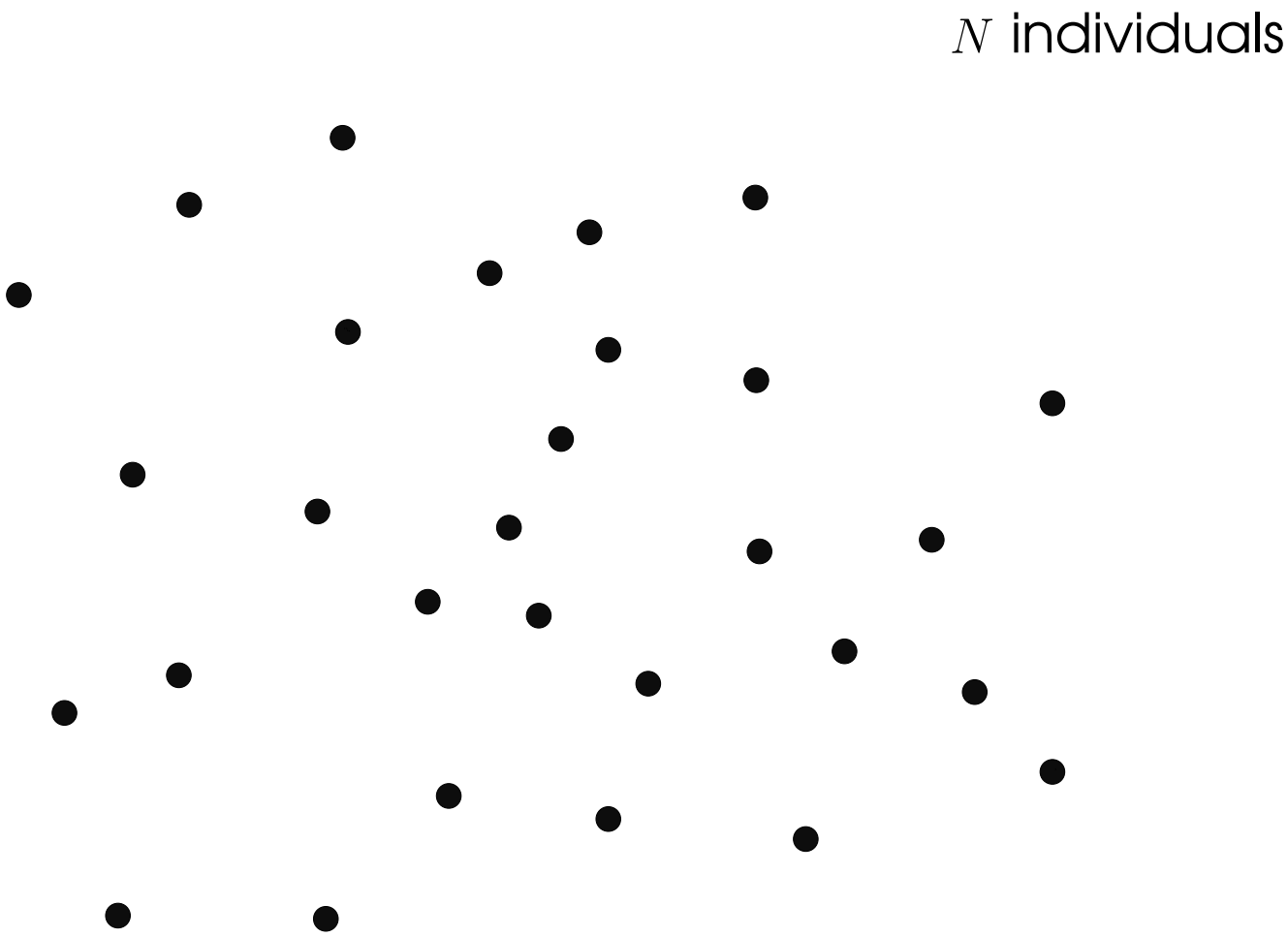

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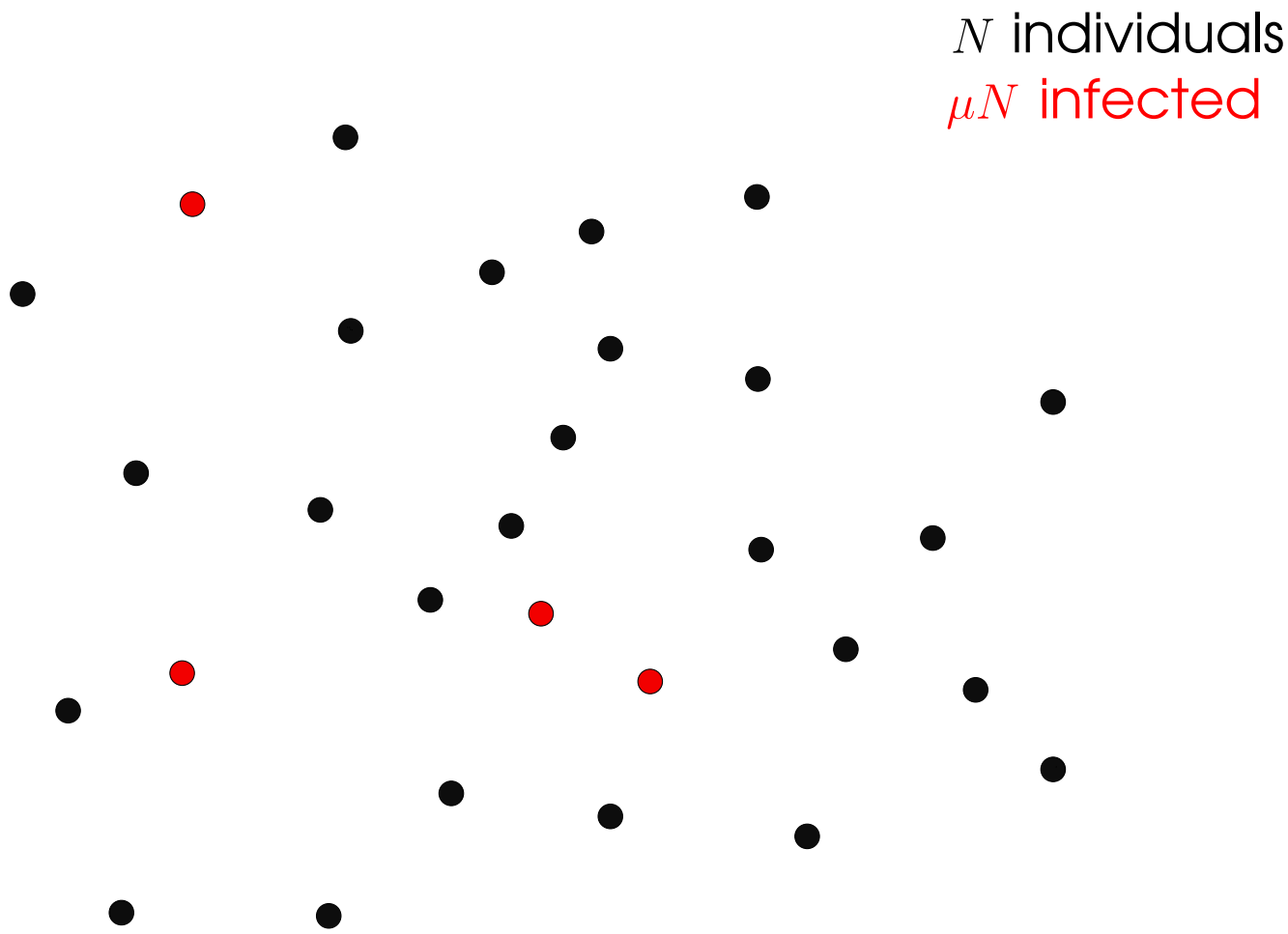

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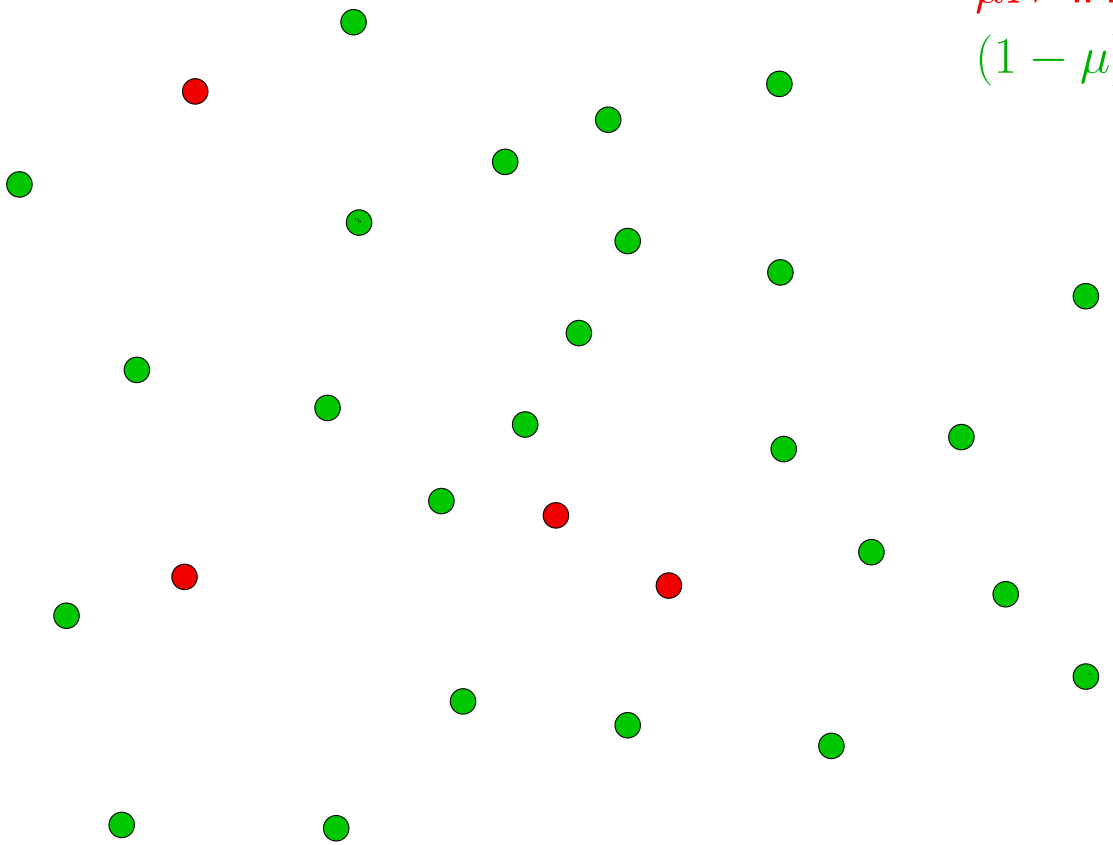

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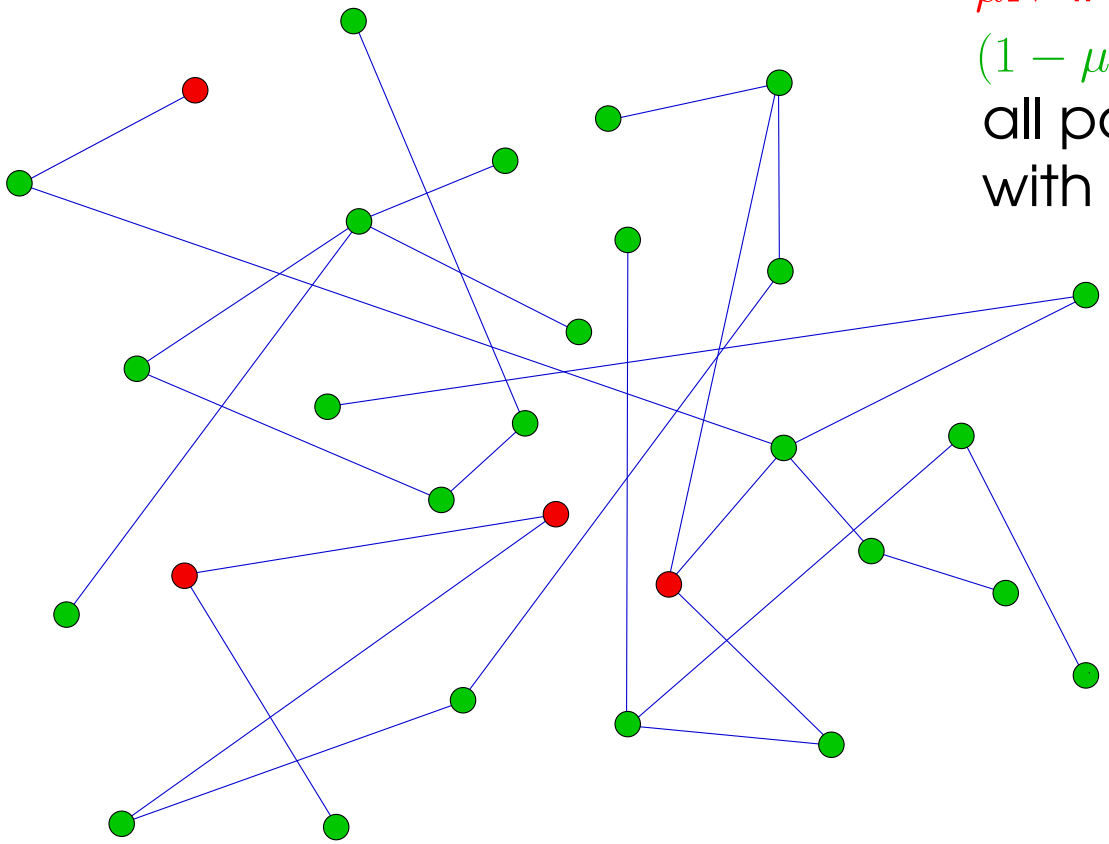

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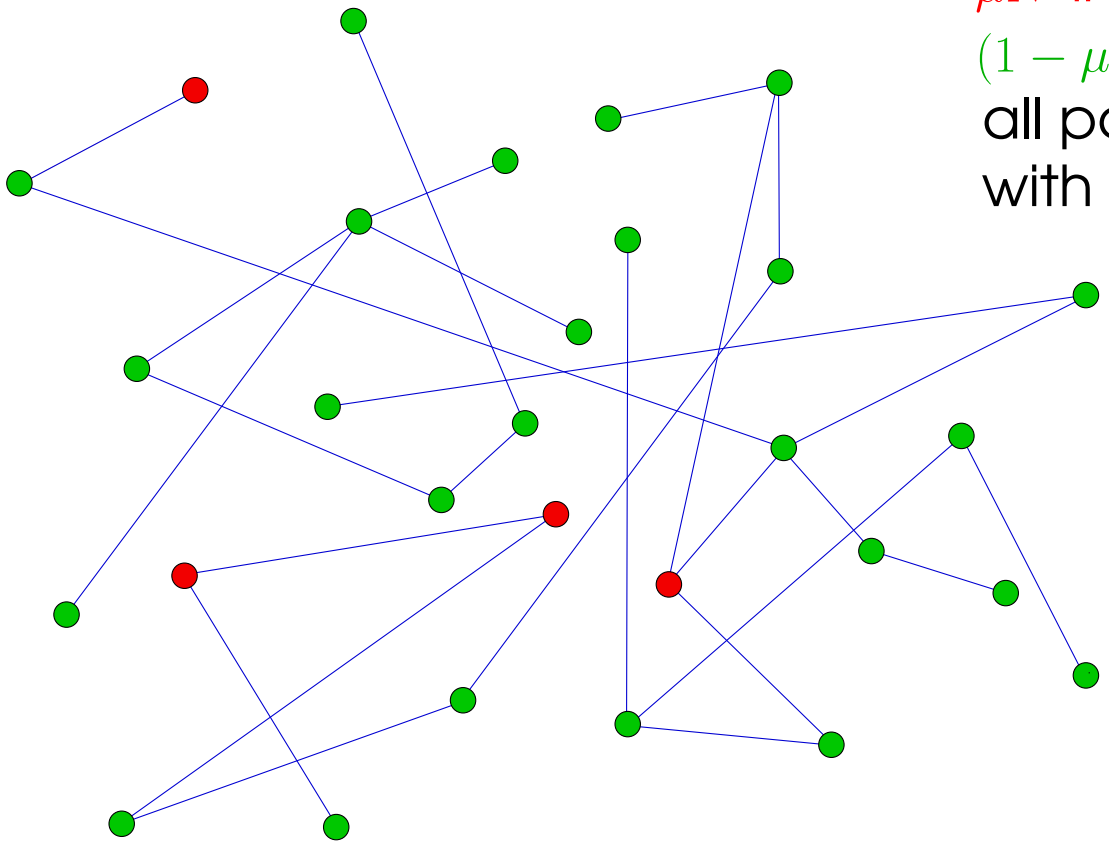

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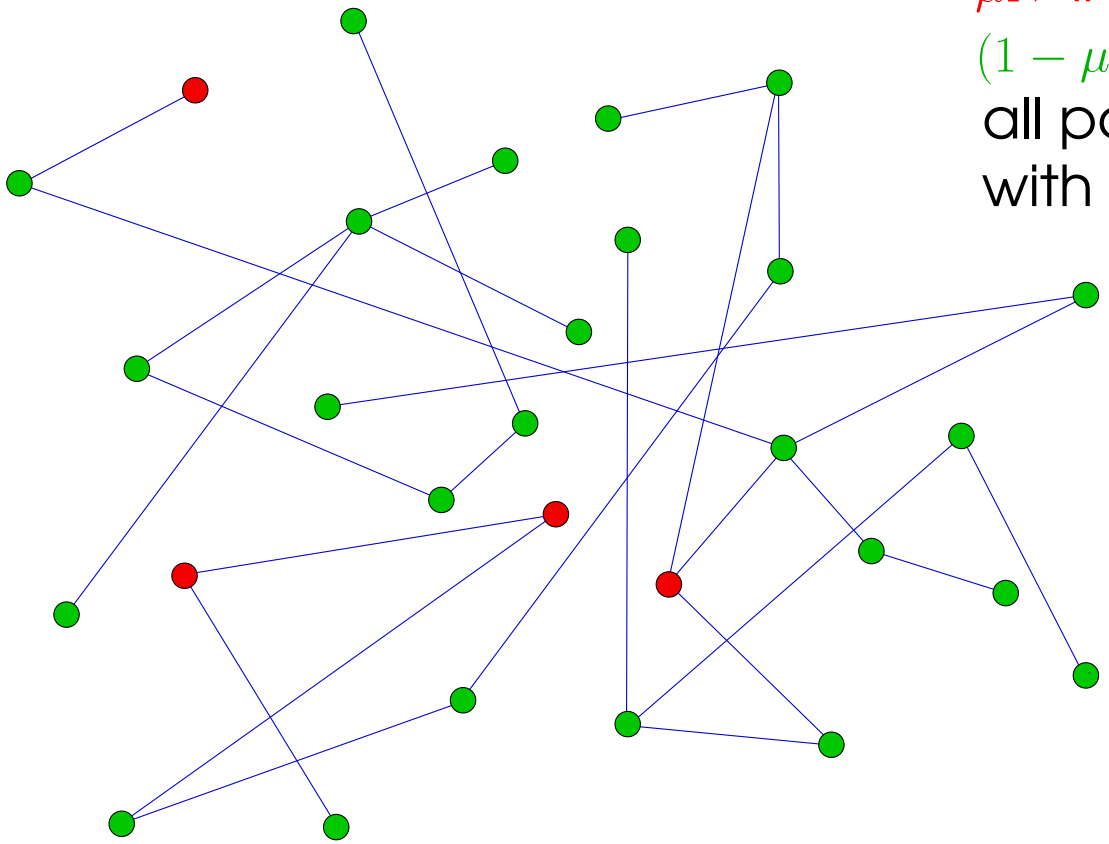

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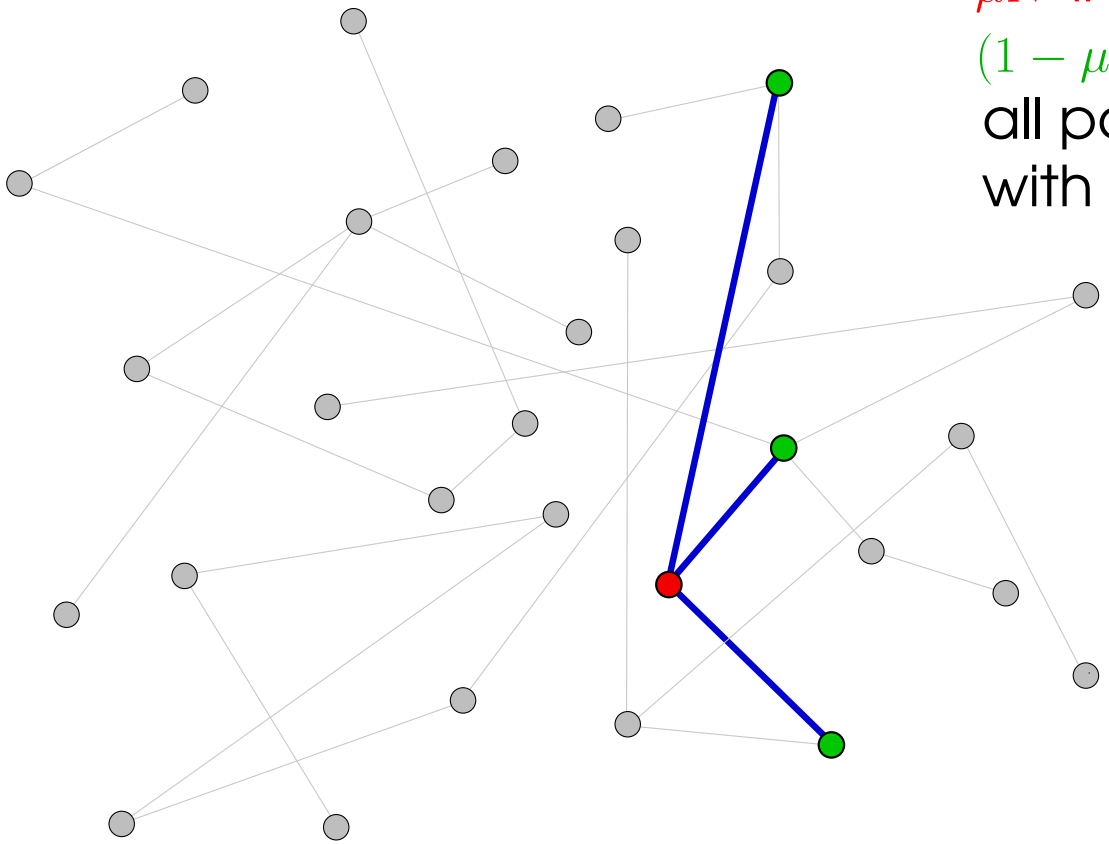

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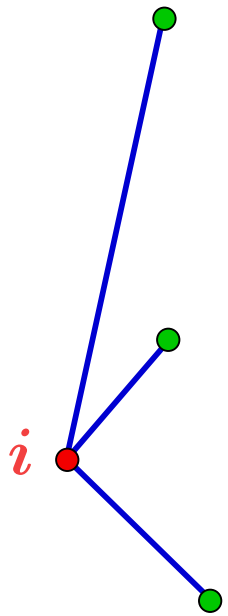
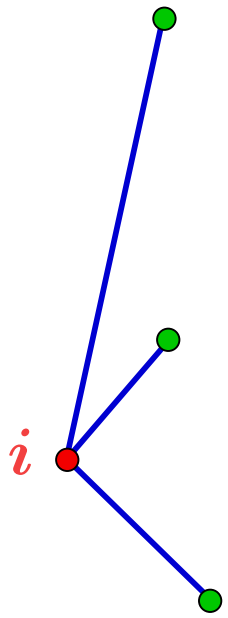
SIR epidemic + random testing



Infections

- Each infected individual becomes **recovered** at the end of their infection period

SIR epidemic + random testing



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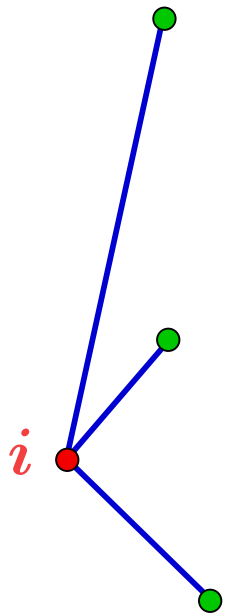

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A parallel random testing process

- ▷ At the event times of a Poisson process with rate θN an individual is selected uniformly and tested, so that on average a **proportion θ of the population is tested daily**

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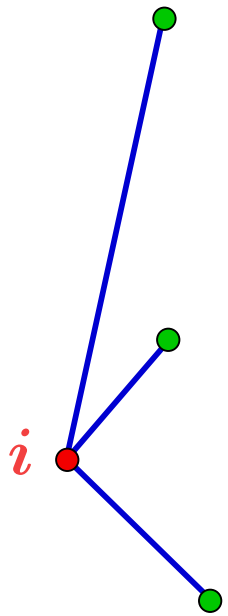

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A parallel random testing process

- ▷ At the event times of a Poisson process with rate θN an individual is selected uniformly and tested, so that on average a **proportion θ of the population is tested daily**
- ▷ If found **+ve**, individual is quarantined until she becomes **recovered**

SIR epidemic + random testing: Process evolution

Testing parameters

Sensitivity: $1 - \delta$, with $\delta =$ probability of false negative

Specificity: assume no false positives

Compliance: $q =$ probability of quarantine compliance

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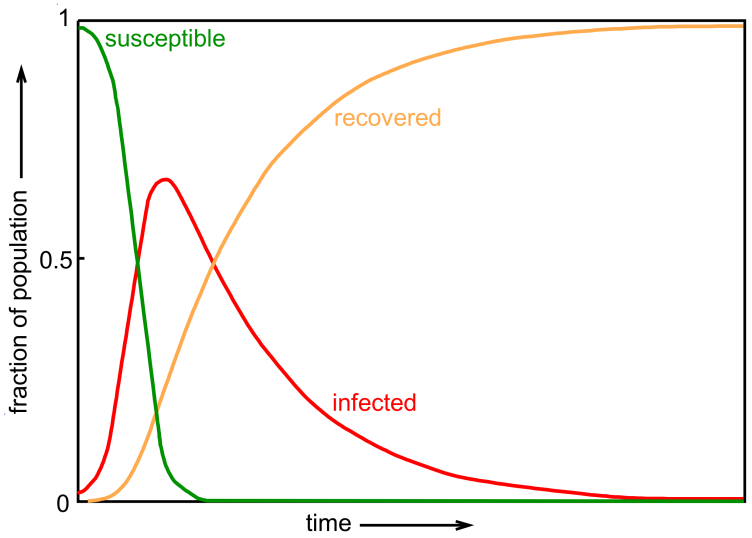
- ▷ All random variables are independent
- ▷ This produces a large, continuous-time Markov process $\{S_t, I_t, R_t\}$
- ▷ Typical SIR behaviour for large N



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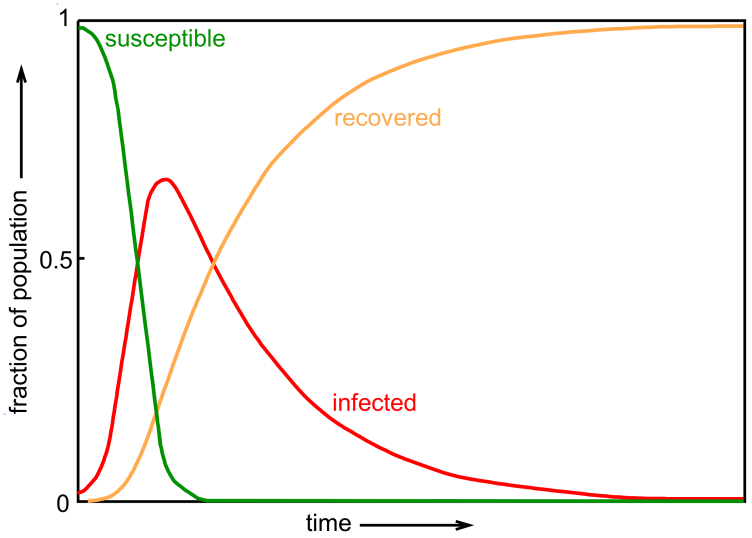
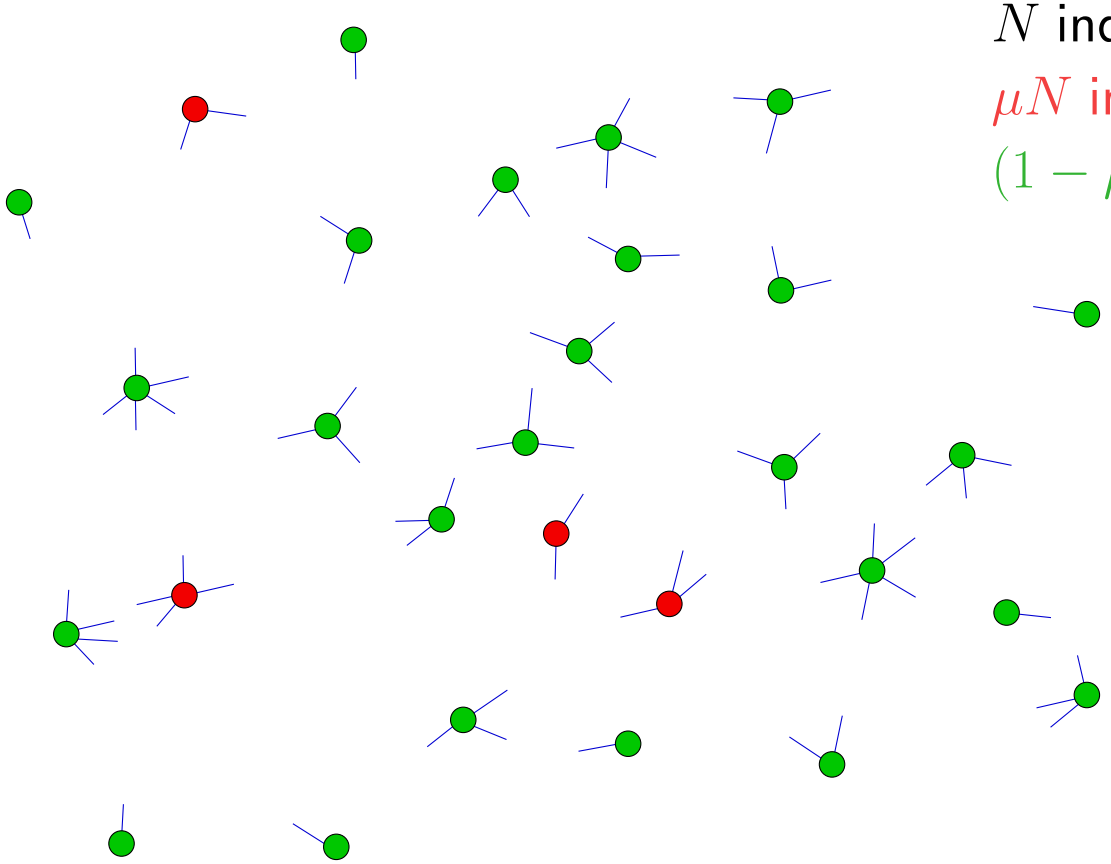


Assumptions

⇝ Model contains several unrealistic assumptions:
Poisson degree distr, no false positives, no geographical structure, no disease-specific characteristics, completely random testing

⇝ But these mostly only make our results more conservative

SIR epidemic on the configuration model



N individuals

μN infected

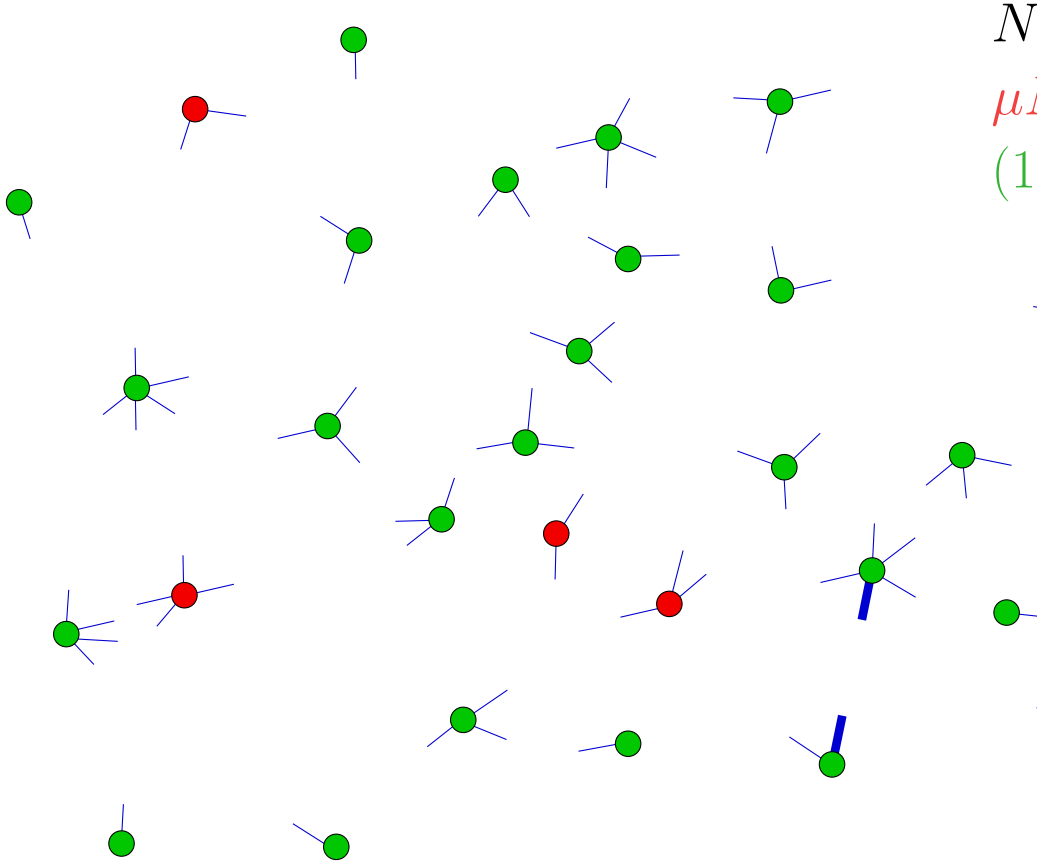
$(1 - \mu N)$ susceptible

arbitrary degree sequence d_i

give each node i degree d_i

draw d_i half-edges at each i

SIR epidemic on the configuration model



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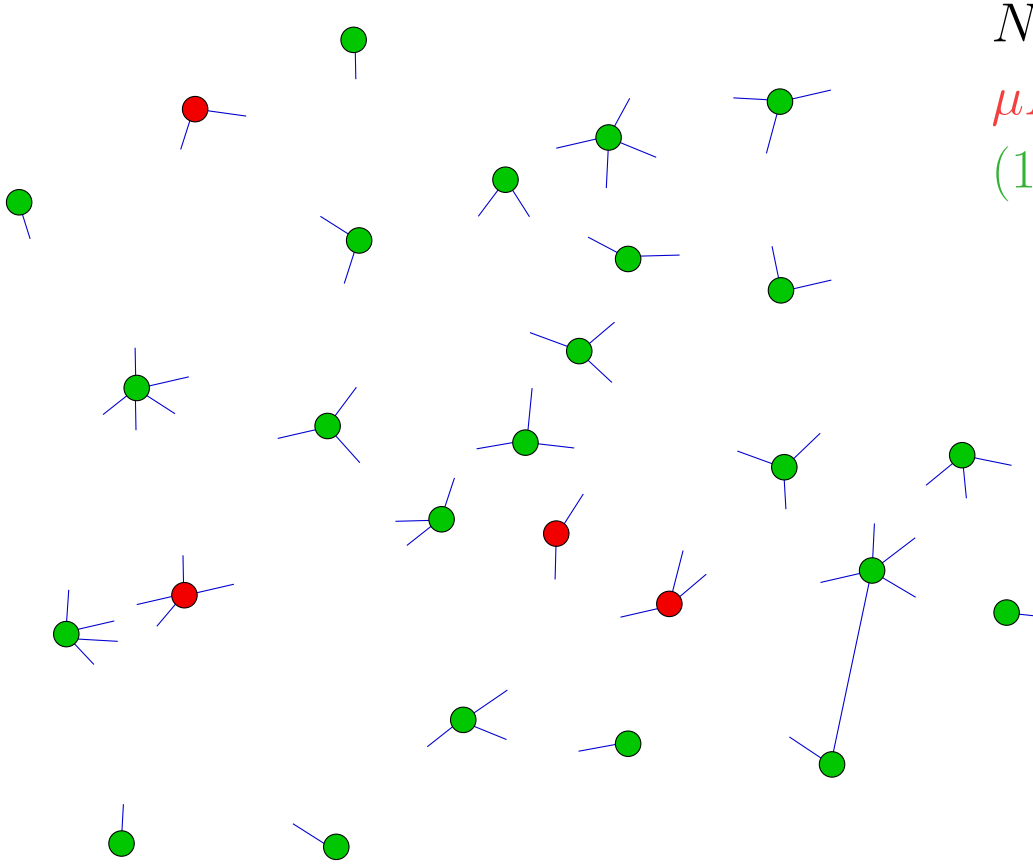

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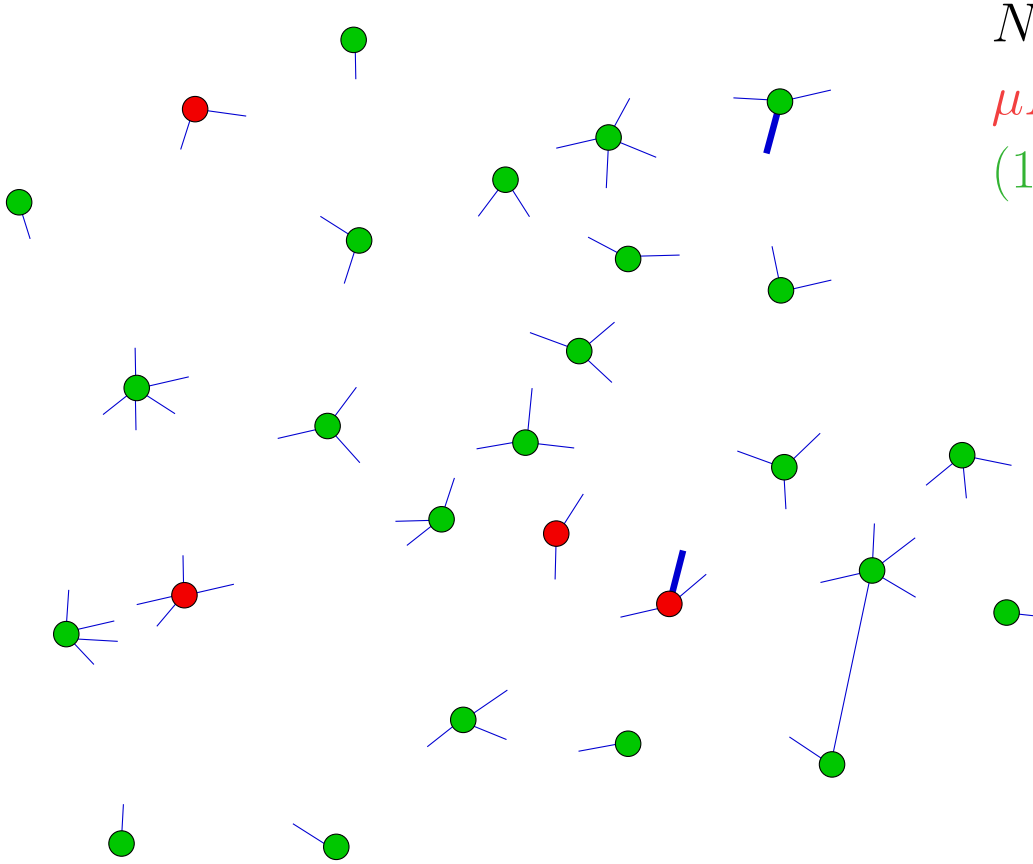

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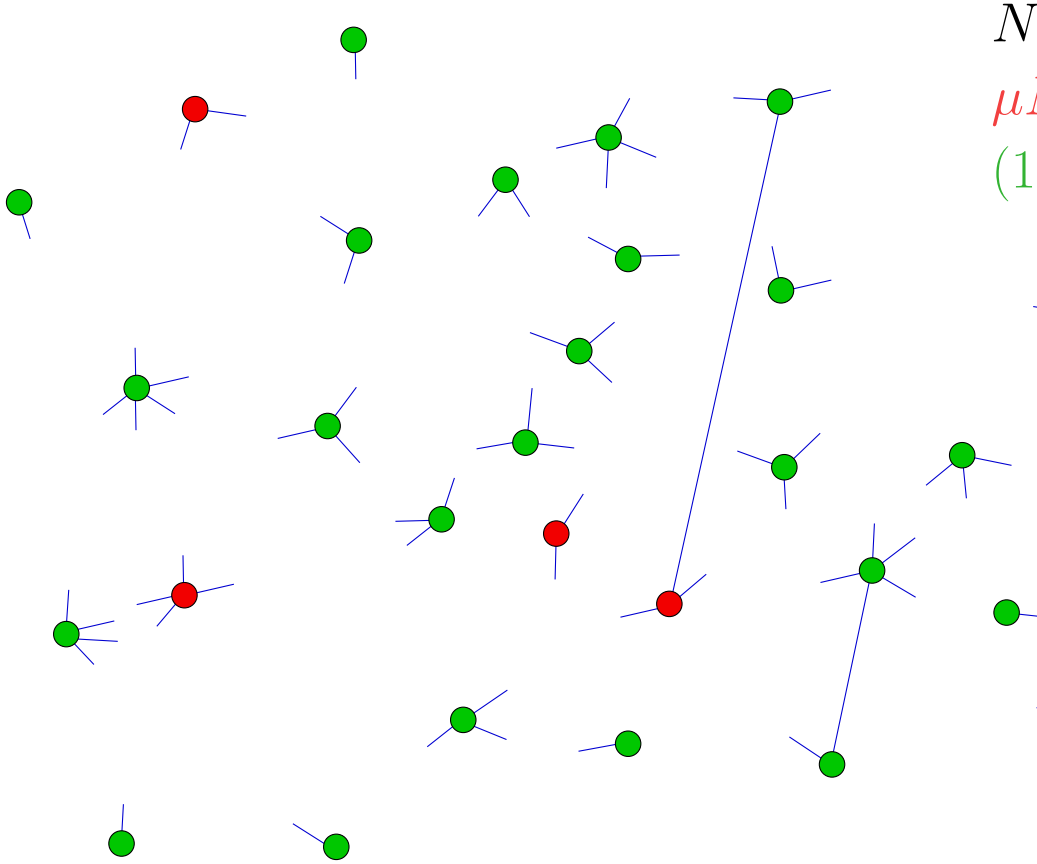

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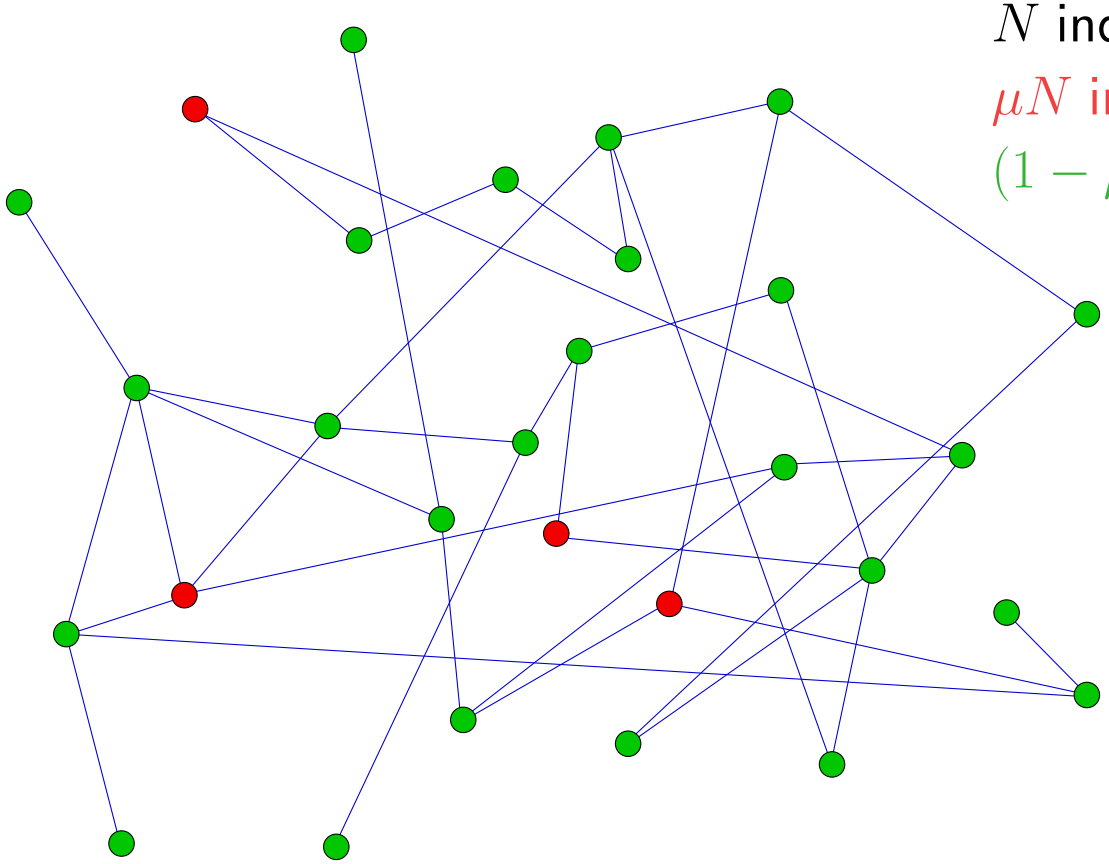

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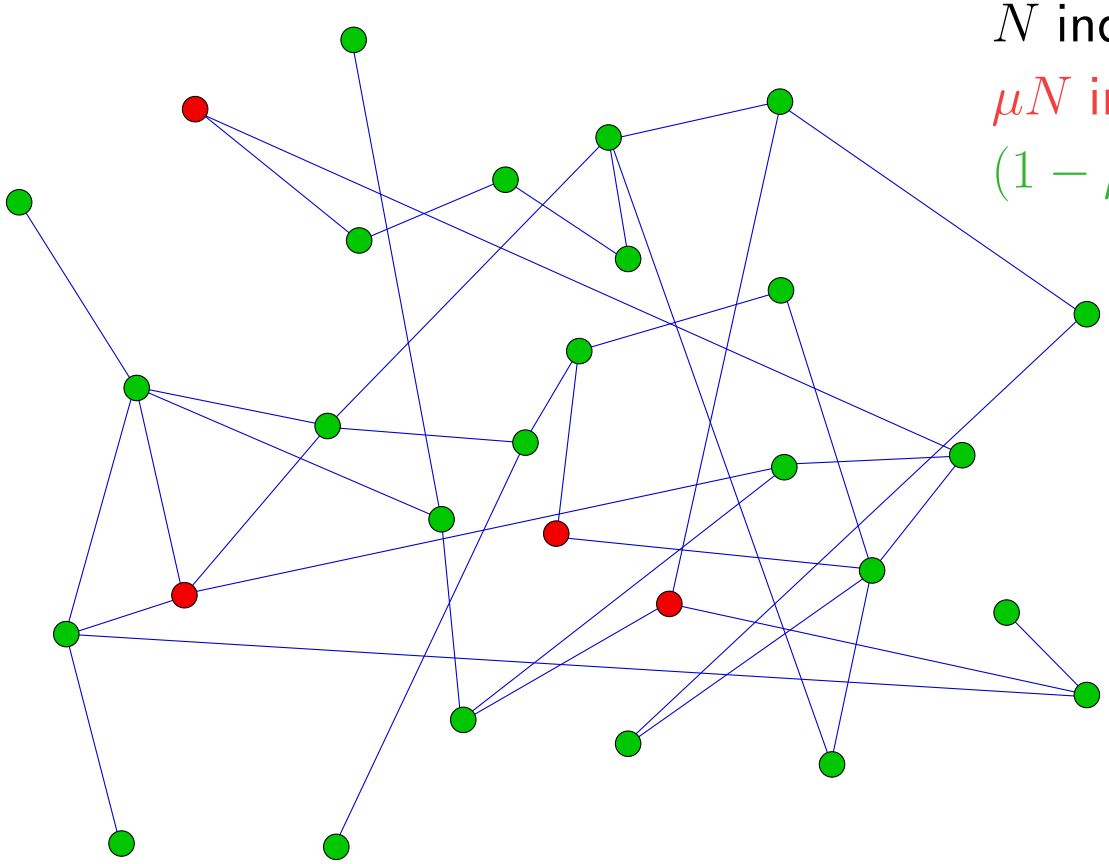

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▷ Possible problem: There may be self-loops or multiple edges

▷ Easy fix: Re-do the pairing until there are no self-loops or multiple edges

▷ Result: Graph uniformly chosen among those with degree sequence $\{d_i\}$

SIR epidemic + testing on the configuration model

Assumptions

- Degree sequence $\{d_i\}$ can be chosen arbitrarily. But:
- $\{d_i\}$ usually chosen according to a given degree distr $\{p_k\}$
- Proportion of individuals with degree k is $\approx p_k$

  $\rightsquigarrow$ This holds separately for both infected and susceptible nodes

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- ▷ Exactly the same as before (once graph is fixed)
- ▷ Again, typical SIR behaviour for large N

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$\rightsquigarrow$ **How does the testing rate affect the evolution of the epidemic?**

Outline

- △ **Covid-19 tests**
  - ▷ Antibody tests
  - ▷ PCR tests
  - ▷ Antigen tests
    - ⇝ Rapid, cheap, at-home tests
- △ **Epidemiological models**
  - ▷ SIR models on random population networks
    - ▶ Erdős-Rényi graphs
    - ▶ Random graphs with given degree distribution
  - ▷ SIR epidemics with mass testing
- △ **Necessary testing rates for suppression**
  - ▷ **Rigorous results for a broad class of models**
  - ▷ Explicit numerical examples

Basic reproduction number R_0 for the E-R model

For the SIR epidemic on the Erdős-Rényi graph

Theorem

As $N \to \infty$:

i. no testing [e.g. Andersson (1999), Neal (2003)]

$$R_0 = \frac{\alpha\beta}{\beta + \gamma}$$

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Proof.

Adding testing to the model is exactly equivalent to shortening the mean infection duration:

$\gamma \mapsto \gamma + \theta(1-\delta)q$

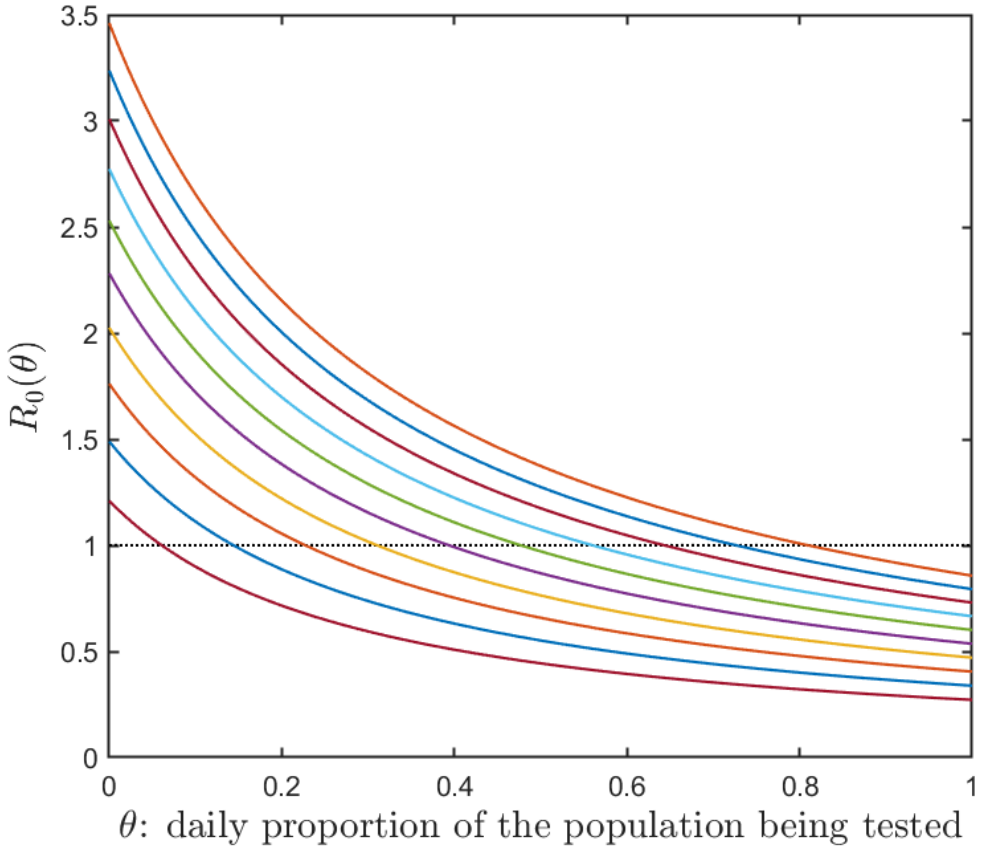
□

R_0 for the E-R model: Examples

1-in-10000 initially infected
20 acquaintances/individual on average
average infectious period 7 days
contact rate β varies

$\Rightarrow \mathbf{1.2 \leq R_0 \leq 3.5}$

quarantine compliance 75%
test sensitivity 70%
testing rate θ



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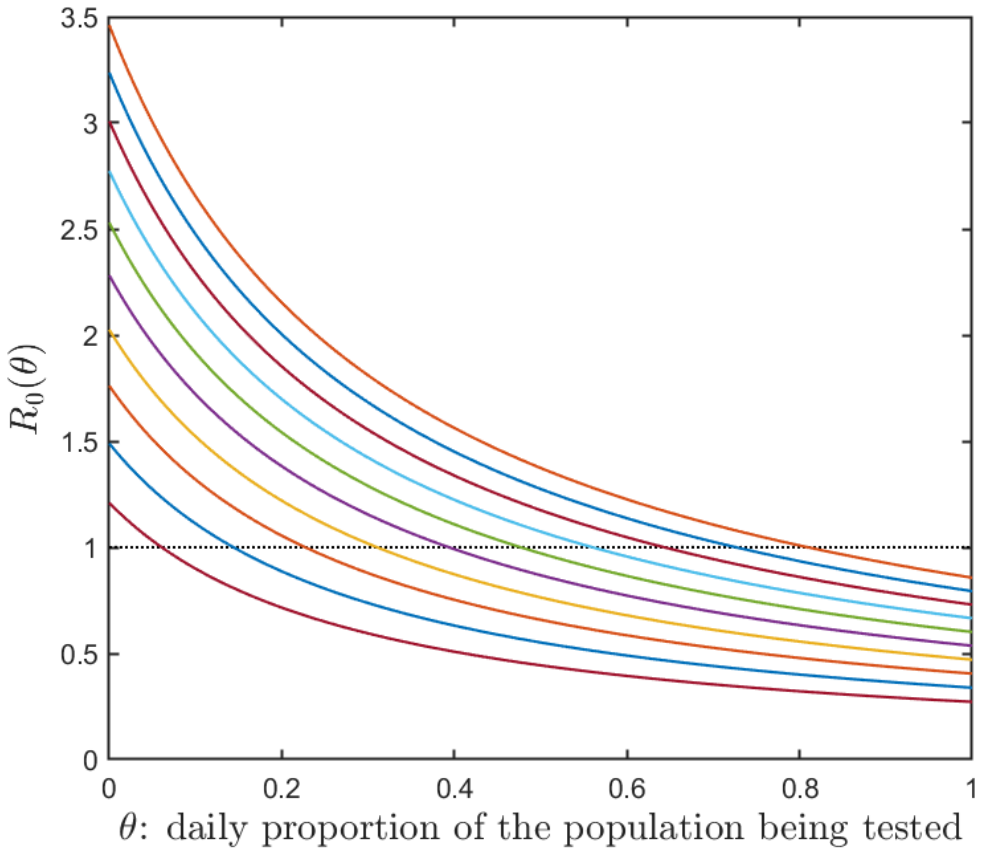
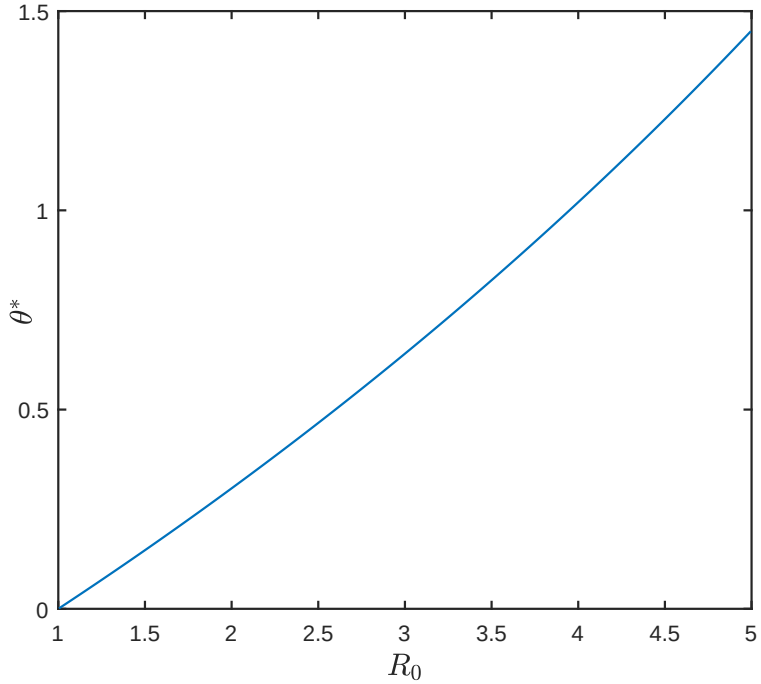


Corollary

Testing rate required for $R_0(\theta) < 1$:

$$\boldsymbol{\theta > \theta^* = \frac{\alpha\beta - \beta - \gamma}{q(1-\delta)}}$$



Epidemic size for the E-R model

For the SIR epidemic on the Erdős-Rényi graph, write

$$T_N = \text{ total size of the epidemic}$$

and let

$$\begin{aligned} \tau(r,\mu) &= \min\{t > 0 \ : \ e^{-rt} = 1 + \mu - t\} \\ s(r,\mu) &= 1 - e^{-r\tau(r,\mu)} \end{aligned}$$

Theorem

As $N \to \infty$:

i. no testing [e.g. Neal (2003)] $\qquad \dfrac{T_N}{N} \to s = s(R_0, \mu)$

ii. random testing

$$\frac{T_N}{N} \to s(\theta) = s\Big(R_0(\theta), \mu\Big)$$

Proof.

Same as before $\square$

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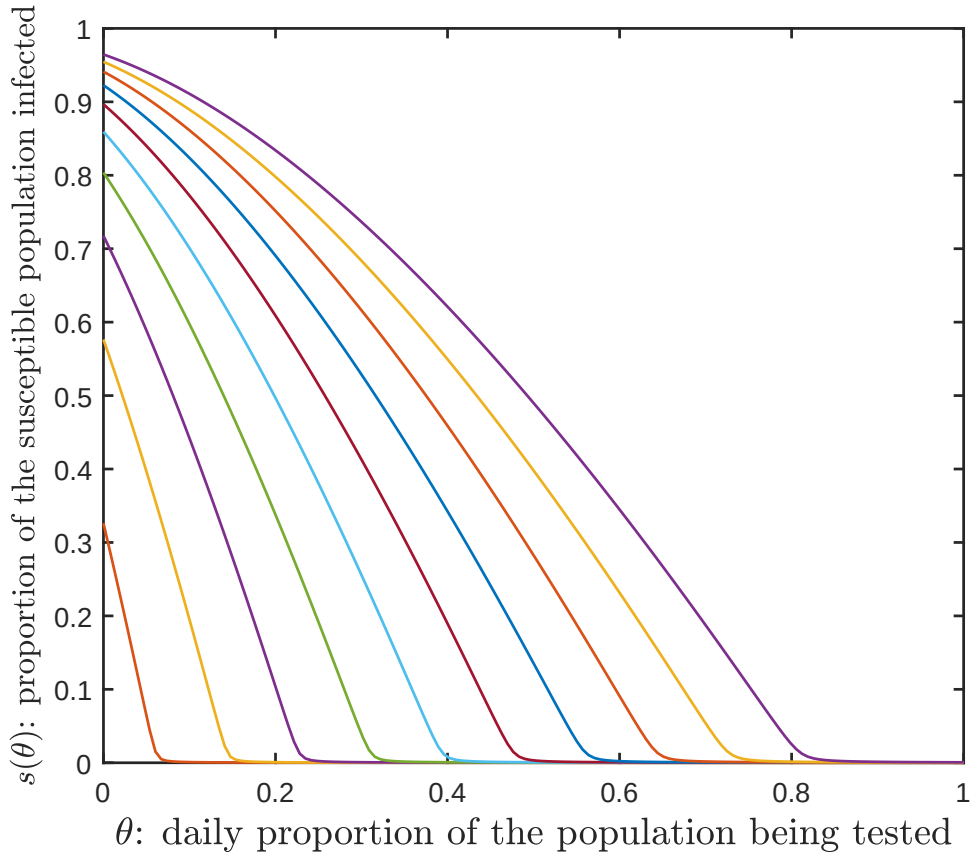

Small epidemics with the E-R model

For the SIR epidemic on the Erdős-Rényi graph suppose that instead of μN initially infected individuals we only have m of them

Let $$f(p,\gamma) = \gamma \int_0^\infty \exp\Big\{ -\gamma z - \alpha(1-p)(1-e^{-\beta z}) \Big\} dz$$

We say there is a **small epidemic** if $T_N = O(1)$ as $N \to \infty$

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i. no testing [Martin-Löf (1986)]

Suppose $R_0 > 1$

Let $\boldsymbol{p}$ be the smallest root of $f(p,\gamma) = p$ in $[0,1]$

$\Rightarrow$ With prob $\boldsymbol{p}^m$ there is only a **small epidemic**

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Same idea as before $\square$

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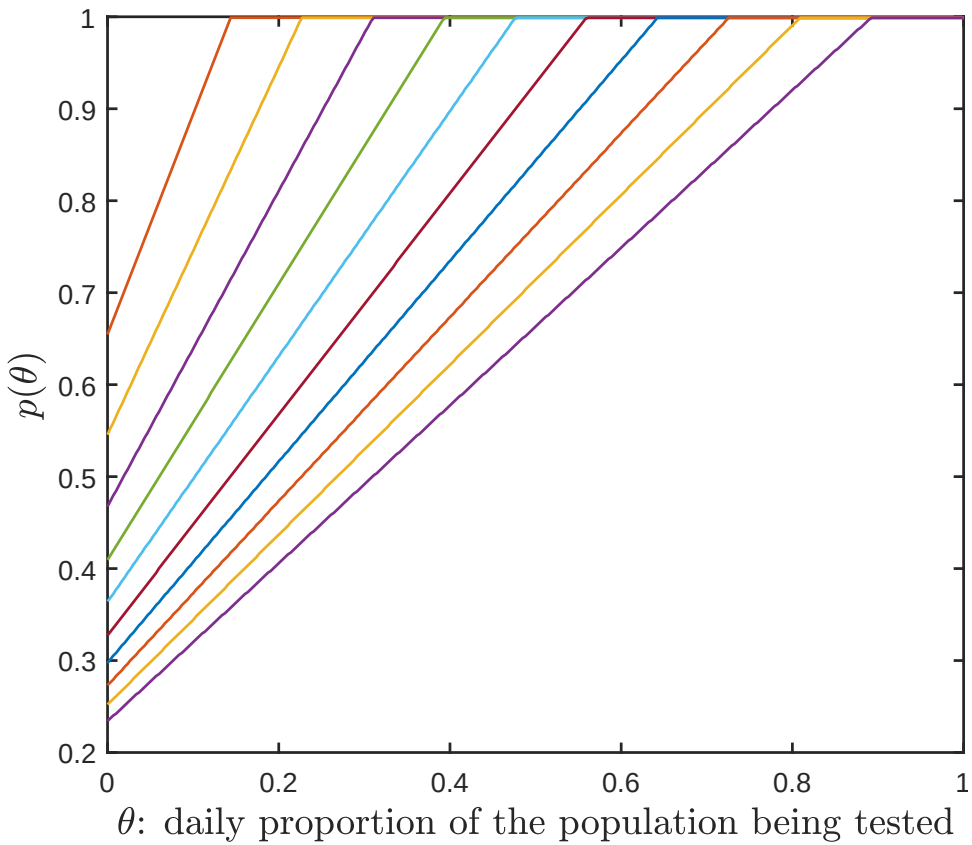

Basic reproduction number R_0 for the configuration model

For the SIR epidemic on the configuration model with degree distr $\{p_k\}$ let

$$\lambda = \sum_{k=0}^{\infty} k p_k \qquad\qquad v^2 = \sum_{k=0}^{\infty} k(k-1) p_k$$

Theorem

As $N \to \infty$ (under mild conditions):

i. no testing [e.g. Janson-Luczak-Windridge (2014)]

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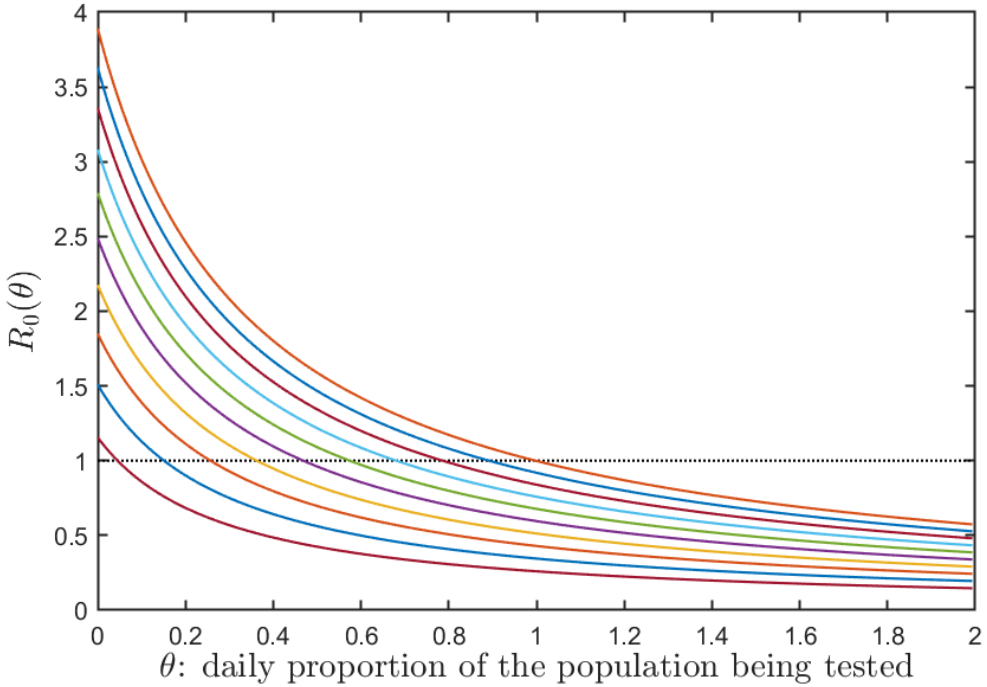

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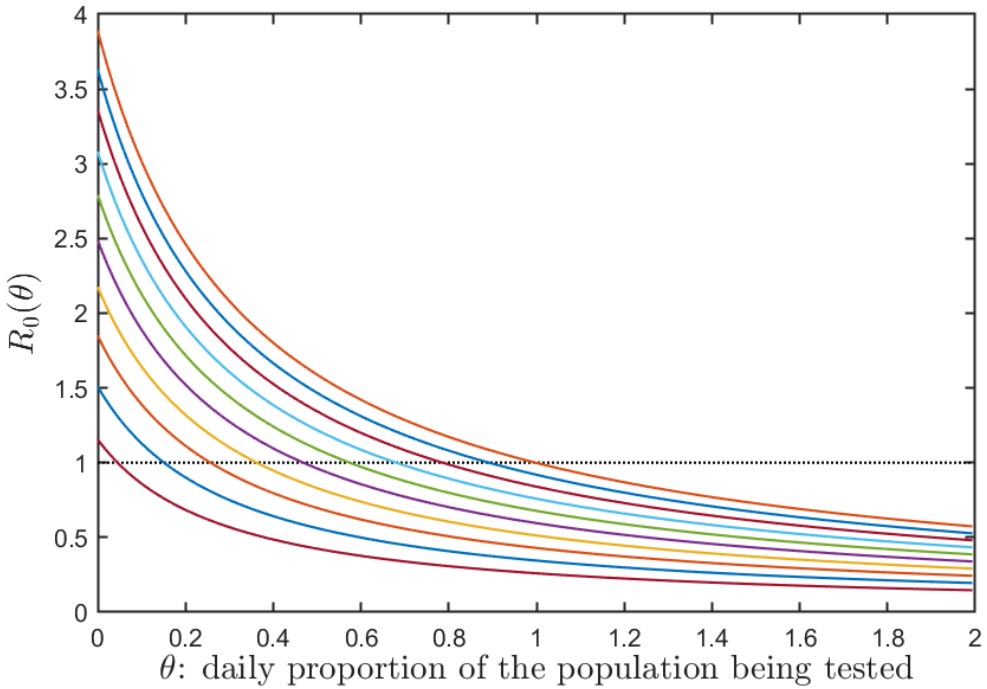

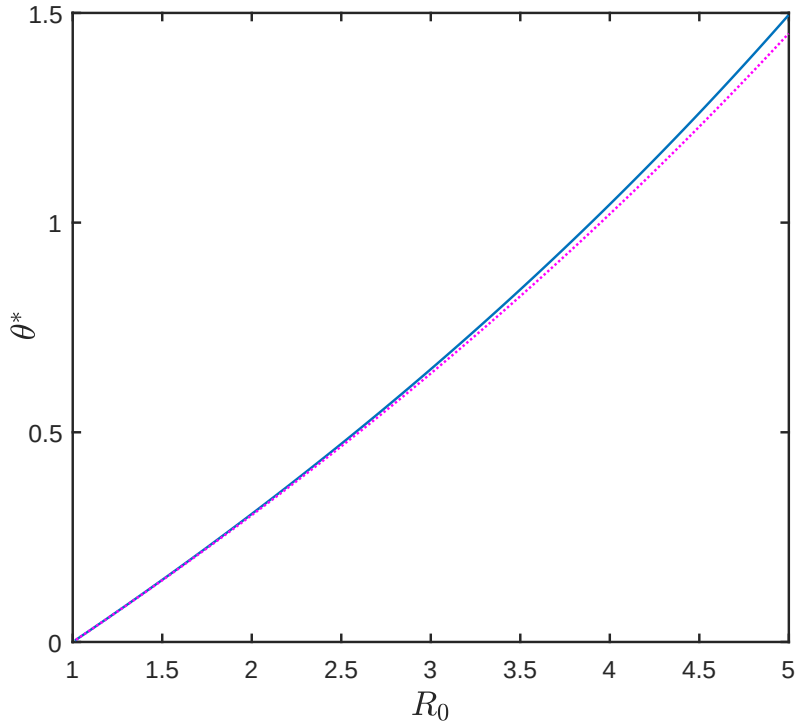

Concluding remarks

$\rightsquigarrow$ **A Covid-19 pubic policy proposal**

- $\triangleright$ Rapid, cheap, at-home, saliva-based, paper tests
- $\triangleright$ Daily population-scale testing

$\rightsquigarrow$ **Epidemiological models suggest**

- $\triangleright$ Random testing is effective
  - ▶ Reduces R_0
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- $\triangleright$ Random testing is effective
  - ▶ Reduces R_0
  - ▶ Decreases epidemic size
  - ▶ Its benefits are additive to other measures
- $\triangleright$ Approximately daily testing *may* in fact be sufficient to suppress the pandemic

$\rightsquigarrow$ **Precise mathematical results offer**

- $\triangleright$ Strong, quantitative evidence of effectiveness
- $\triangleright$ Useful, conservative rules of thumb

In recent news

△ The rapid testing proposal is gaining traction

Aug 27: First FDA-approved rapid test: Abbott's $5, 15-minute test
White House announced $750 million deal with Abbott

Sept 1: New rapid test by Roche-SD Biosensor partnership
will be made available in Europe and the UK

Sept 9: UK PM announced "Operation Moonshot", likely cost £100bn
aiming for 10 million daily tests by spring

△ Around the world

Italy. Approved 3-minute saliva test the "Daily Tampon"

France. New "antigénique rapide" test used by authorities

Senegal. UK-Senegal partnership developed $\approx$ $1 home antigen test

India. Authorities switching over to a rapid antigen test

References https://www.dpmms.cam.ac.uk/~ik355/PAPERS/Covid_talk_bib.pdf

Slides https://www.dpmms.cam.ac.uk/~ik355/PAPERS/Covid_talk_slides.pdf

Our paper https://www.dpmms.cam.ac.uk/~ik355/pubs.html

Technical assumptions for the configuration model

Assume initially N_I infected individuals s.t. $N_{I,k}$ have degree k
and $N_S = N - N_I$ susceptible individuals s.t. $N_{S,k}$ have degree k

Assume $N_I/N \to \mu$ and $N_S/N \to (1-\mu)$ for $\mu \in (0,1)$, that $\lambda \in (0,\infty)$
and that for all k

$$\frac{N_{S,k}}{N_S} \to p_k, \qquad \frac{N_{I,k}}{N_I} \to p_k$$

$$\sum_{k=0}^{\infty} k\frac{N_{S,k}}{N_S} \to \sum_{k=0}^{\infty} kp_k = \lambda, \qquad \sum_{k=0}^{\infty} k\frac{N_{I,k}}{N_I} \to \sum_{k=0}^{\infty} kp_k = \lambda.$$

Two last technical assumptions are required
For $N_k =$ total no of individuals with degree k:

$$\max\{k\ ;\ N_{I,k} > 0\} = o(N) \qquad \text{and} \qquad \sum_{k=0}^{\infty} k^2 N_k = O(N)$$