



# Julia Brettschneider

#### **Data Science and Covid-19**

I Hawkes process modelling of the pandemic

2 Simulations about Covid management schemes in schools

3 Microscopic imaging of blood samples in (long) Covid

#### Applied statistician/data scientists

Collaborators: engineers, life scientists, clinicians...

Domains: genomics, microscopy, detectors, cancer, screening, finance, OR...

Methodological topics: data quality, spatial statistics, decision theory,

concepts of probability and risk

## **Short biography**

- Reader (since 2021), Associate Professor (2010-2021), Assistant Professor (2007-2010),
   Dept of Statistics, University of Warwick, UK
- Turing fellow since 2017
- Assistant Professor, Dept of Math/Stats & Dept of Community Health/Epidemiology & Cancer Research Institute, Queen's University, CN
- Visiting Assistant Professor and Research Statistician, Dept of Statistics at University of California at Berkeley, USA
- Postdoctoral fellow in Computational Biology at Eurandom, NL
- PhD (2001) in Mathematics, thesis supervisor Prof H Föllmer, Humboldt Uni Berlin, D
- Masters in Mathematics (with Computer Sciences and Psychology), thesis supervisor Prof H Föllmer, University Bonn, D

4th year integrated Master's projects by Marianna Mafleftherou and by Adam Davison Students of MORSE (Mathematics+Operational Research+Statistics+Economics), Department of Statistics, University of Warwick

Supervision Dr Julia Brettschneider

# Hawkes Process I

#### **Definition: Point Process**

Point processes are a class of random process whose <u>realisations</u> are a set of points on some given space.

<u>i.e.</u> A sequence of random variables  $t = \{t_1, t_2, \ldots, t_d\}$  taking values in a subset of  $\mathbb{R}^d$ .

#### **Definition: Temporal Point Process**

Temporal Point process is a point process over time: It describes the occurrence of random events over time.

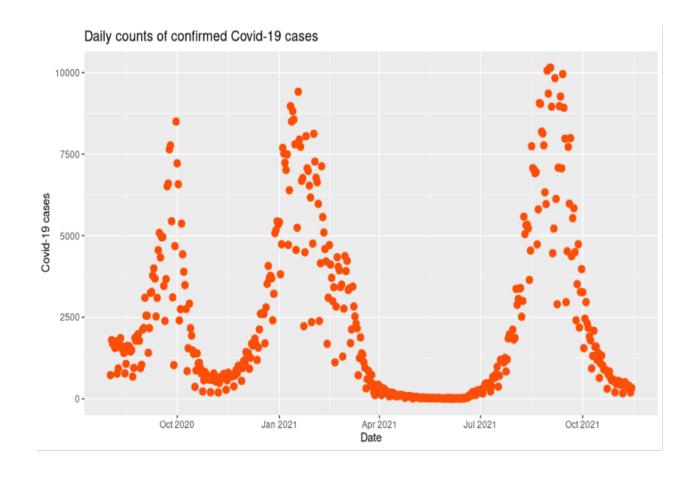
<u>i.e.</u> a sequence of events  $t = \{t_1, t_2, ..., t_d\}$  s.t.  $0 \le t_1 < t_2 < ... < t_d$ 

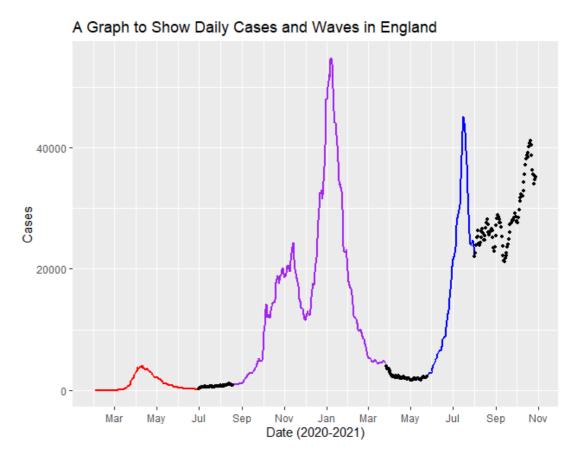
#### 1. Data from Israel

Vaccine for data deal with Pfizer/BioNTech (Marianna Mavroleftherou's project)

#### 2. Data from England

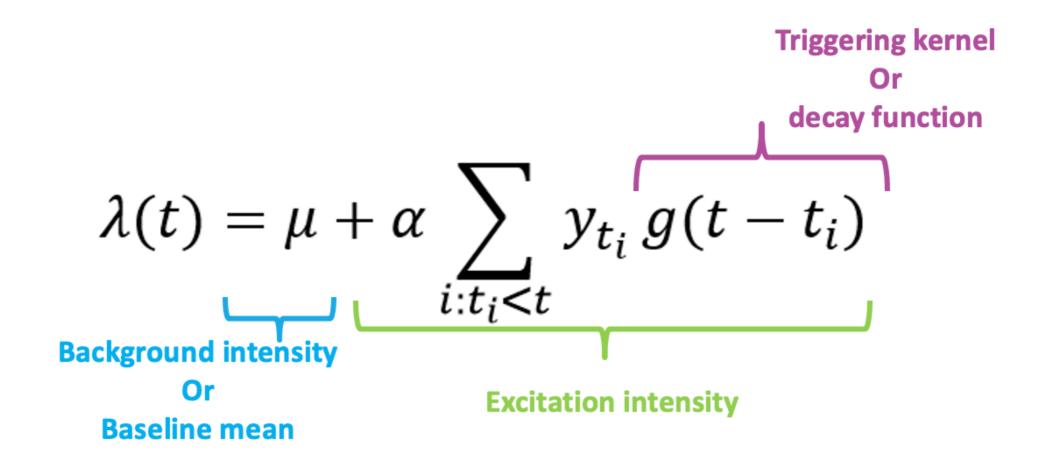
ONS/Oxford survey (Adam Davison's project)





# Hawkes Process

Self-exciting temporal point process described by the conditional intensity function:



# Model Setup

Number of daily cases (or deaths) [e.g. Rousseau et al 2020]

 $\succ$  It is a natural response to assume that Y(t) follows Poisson( $\lambda(t)$ )

Since Poisson distribution is governed by one parameter  $\lambda$ , which is the expected number of times an event occurs in an interval of time or space.

Hence, we set:

$$P(Y(t) = y \mid \lambda(t)) = \frac{\lambda(t)^{y} e^{\lambda(t)}}{y!}$$

> Further to this:

we choose the triggering kernel g() to be the geometric excitation kernel:

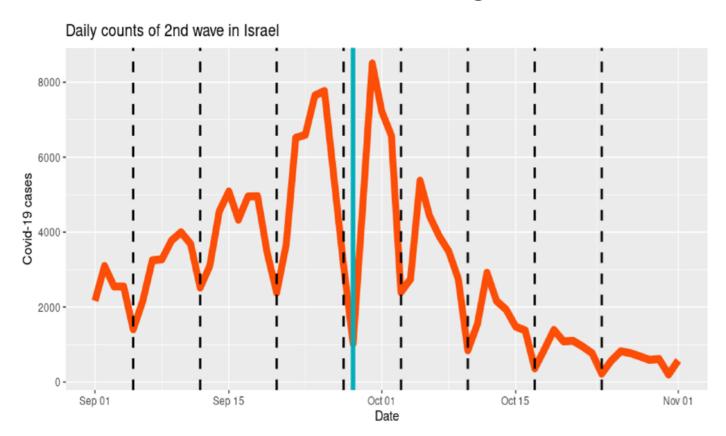
$$g(t - t_i | \beta) = \beta (1 - \beta)^{t - t_i - 1}$$

Since it can be shown to be the generalization of the exponential distribution in discrete time.

## Model fitting in practice:

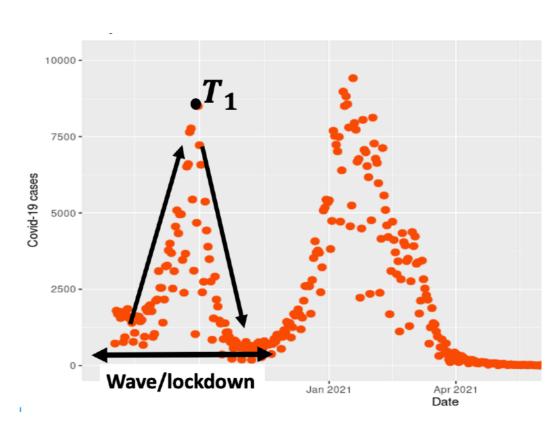
#### 1. Data preprocessing

Small counts, smoothing



#### 2. Waves

Piecewise fitting, piques

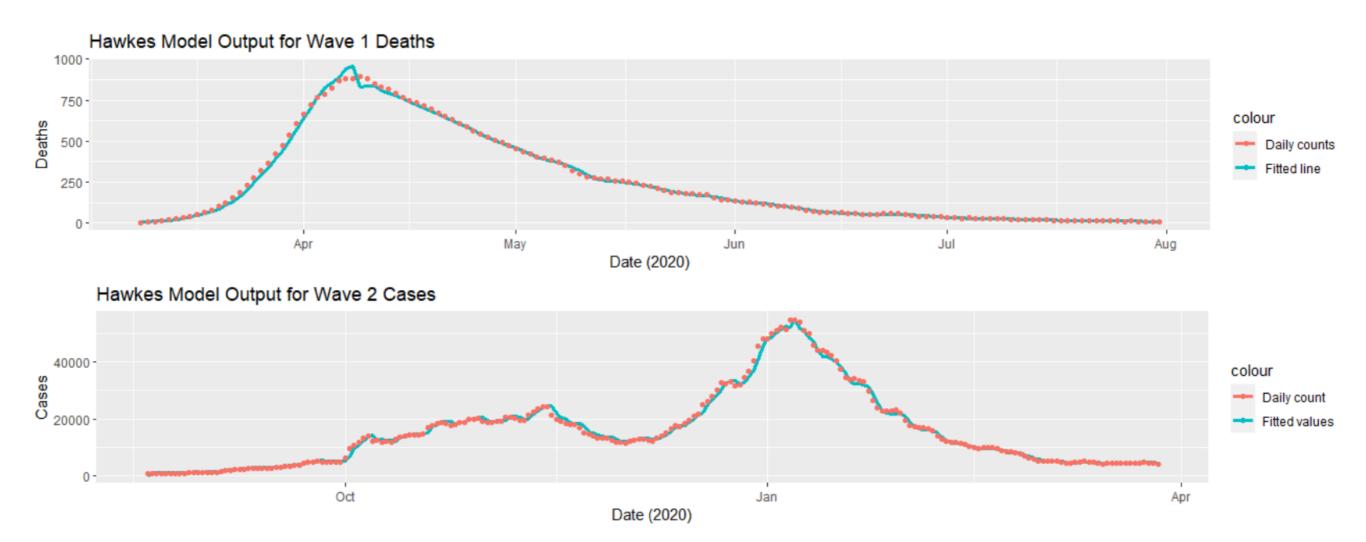


#### 3. Likelihood function

#### 4. Inference

- ML with Nelder-Mead
- Bayesian posterior MCMC

#### **English data:**

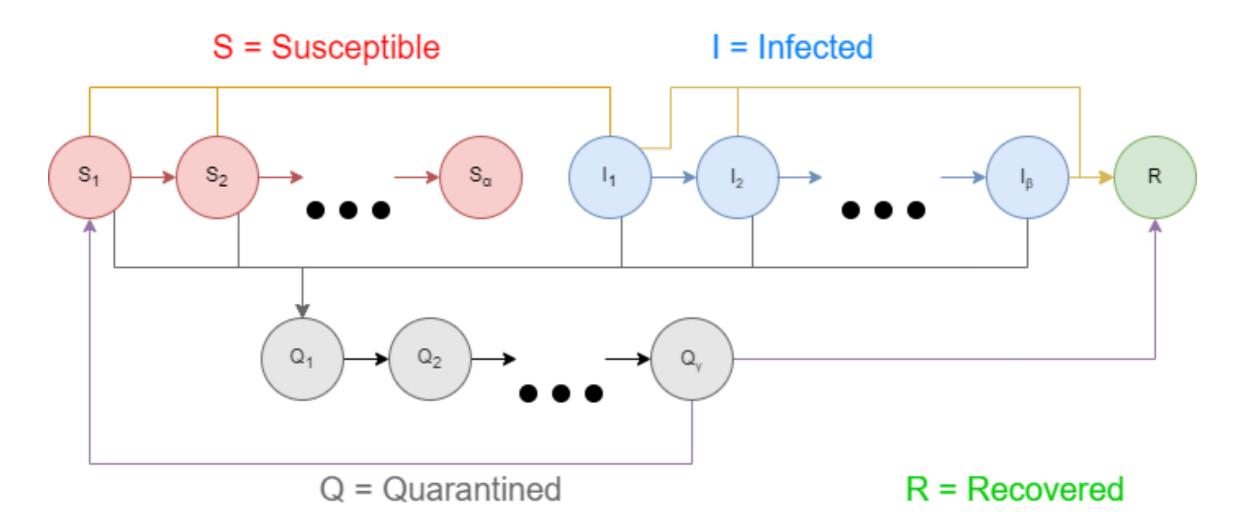


#### **Further and future work:**

- Models including age
- Including vaccination rates
- Testing coverage/reliability
- Behavioural indicators (e.g. google searches or mobility)
- Lockdown effects
- Events (e.g. football, holidays) and interaction with other factors
- Mixture population
- Regional models

3rd year project by Jonathan Cordell
Data Science student, Department of Statistics, University of Warwick
Supervision Dr Julia Brettschneider

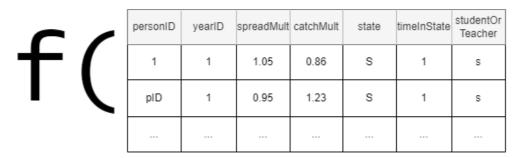
#### State Flow



#### **Data Structure**

			р	ersonI	)	yearID	sp	oreadMu	ılt c	atchMu	lt	state	tin	neInSta	ate		dentOr acher
		pers	onID	ye	arlD	sprea	adMult	catcl	hMult	st	tate	timeIr	State		dentC ache		s
personID		yea	arlD	spreadMult		catc	chMult s		ate	timel	nState	stude Tea	entOr cher	s	$\neg$	s	
personID		yea	rID	spreadMult		catch	Mult	state		timeIn	timeInState studen			s		$\dashv$	
1 1			1.0	05 0.86		6	s		4	ı	s				$\dashv$	S	
2	!	1		0.9	95	1.2	23	s		4	ı	s			S	4	
3	,	1		1.4	12	0.9	16	1		1						_	t
	'	'		1.4	+2	0.8	,0	'		<u>'</u>		s			t		s
	-		-		-						-			t	s	T	
3	1	1		0.8	37	0.9	9	S		4	ı	t		5		十	
32	2	2	2	0.9	94	1.0	)5	ı		2	2	s			$\vdash$		
															J		Time
																/	•

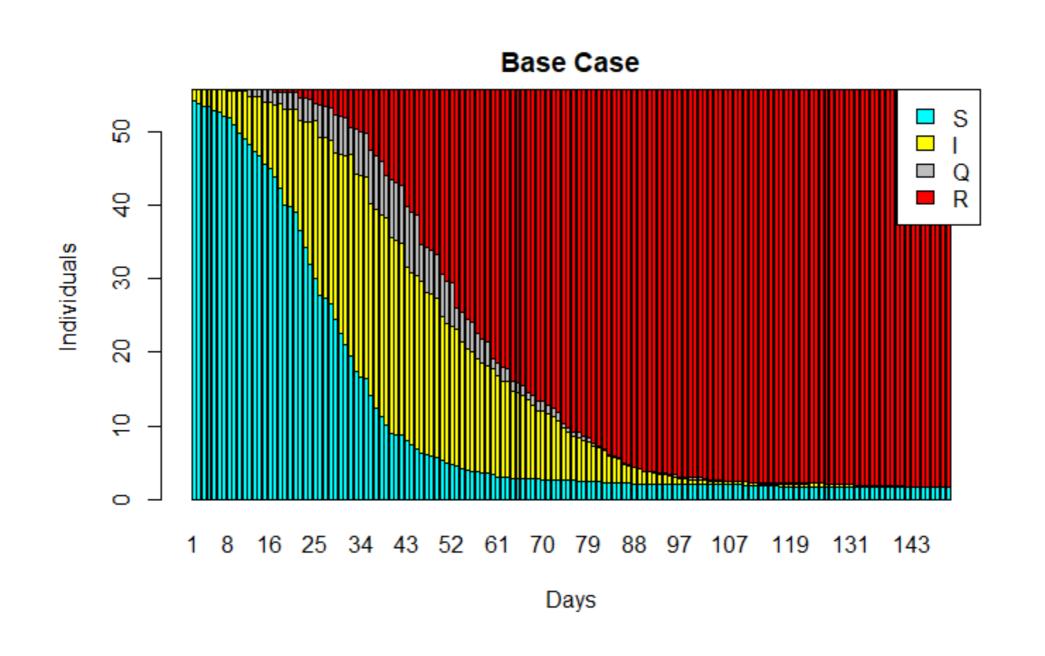
#### 4.3.2 Next state



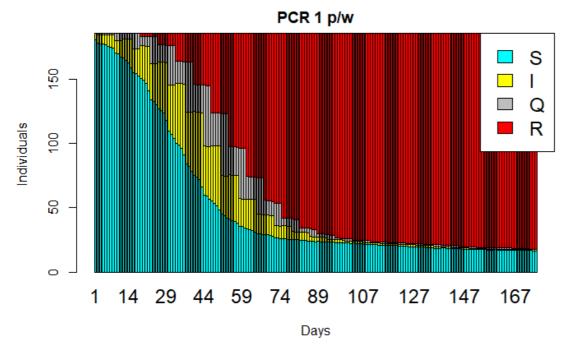


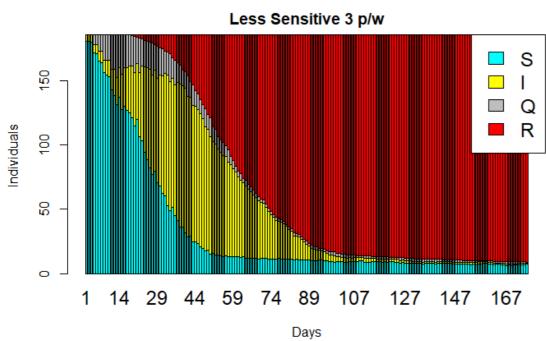


personID	yearID	spreadMult	catchMult	state	timeInState	studentOr Teacher
pID	1	0.95	1.23	s	2	s



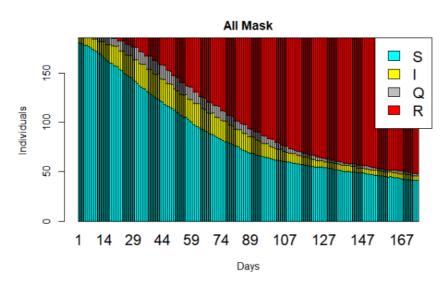
#### Scenario 1: Testing

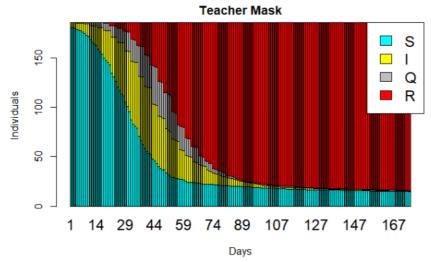


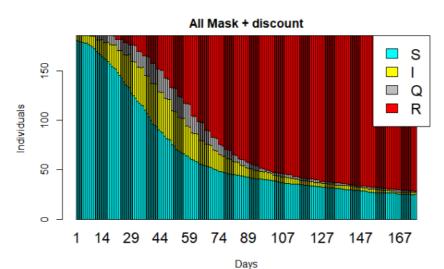


name	PCR 1 p/w	Less Sensitive 3 p/w
totalQ	1633.8	1206.3
avgQ	8.78	6.50
finalI	169.2	177.8
infectionEnd	119	NA
overThreshold	16.2	2.9
meanVar	2.0255380	0.9610914
classMax	8.5	5.6
percVaccInfected	0.723913	0.826087
percUnVaccInfeced	0.9142857	0.9742857
totalTests	1756.3	4604.1









name	Teacher Mask	All Mask	All Mask + discount
totalQ	1301.7	1145.1	1287.6
avgQ	7.01	6.16	6.91
finalI	171.2	143.4	160.4
infectionEnd	120.9	NA	NA
overThreshold	13.6	0.0	1.2
meanVar	1.3405309	0.6720547	0.9838840
classMax	5.8	4.3	5.3
percVaccInfected	0.7434783	0.4847826	0.6260870
percUnVaccInfeced	0.9414286	0.6628571	0.8250000
totalTests	3114.1	5074.2	4037.7

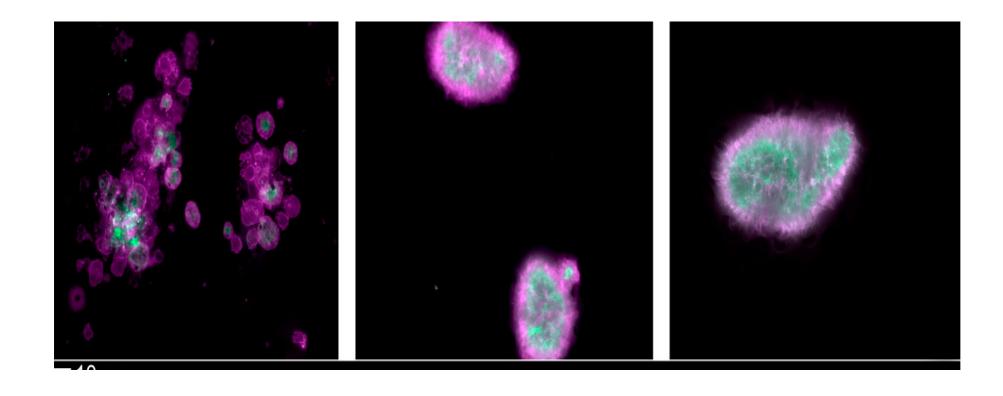
#### **Further and future work:**

- Vaccinations
- Fitting/comparing with real data
- Case study based on data from a secondary school

4th year integrated Master's projects by Marilena Diamantidou and Grace Barnes Students of MORSE (Mathematics+Operational Research+Statistics+Economics), Department of Statistics, University of Warwick

Supervision Dr Julia Brettschneider

Data from experimental work by Pretorius et al., 2021



#### **Challenges:**

- Diagnostic criteria
- Treatment
- Progression
- Timing of intervention
- Automation of diagnosis

#### **Challenges:**

- Diagnostic criteria
- Treatment
- Progression
- Timing of intervention
- Automation of diagnosis

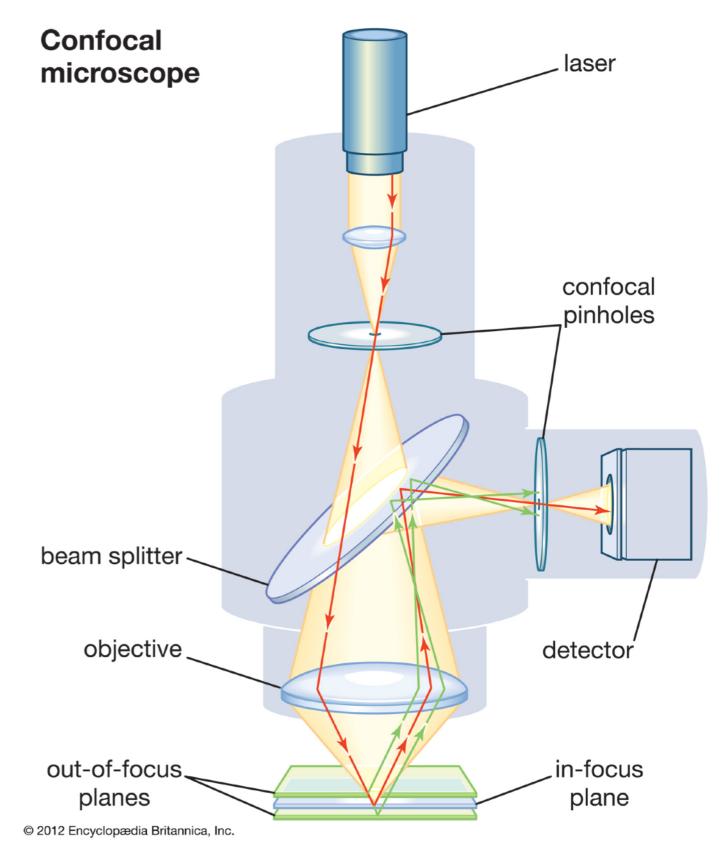
# Confocal microscope

#### Wide-field microscopy:

- All of specimen excited at the same time
- Large unfocused background

#### **Confocal microscope:**

- Field of view limited by geometric optics
- Pinhole in front of the detector to eliminate out-of-focus signal
- Long exposure required
- Scanning arrangement to build up image of larger region
- Better resolution



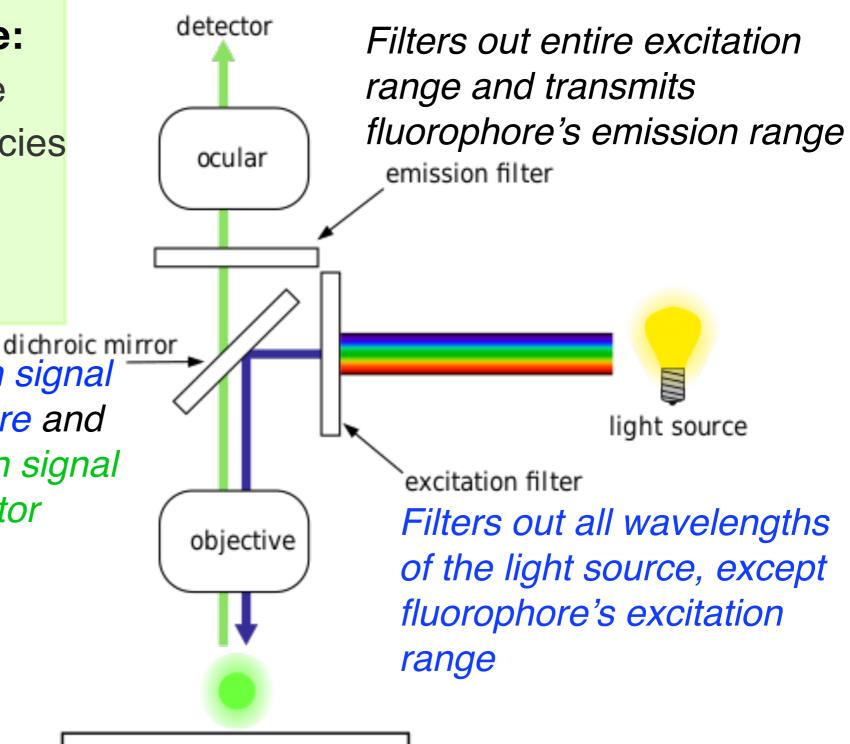
https://www.britannica.com/technology/microscope/Confocal-microscopes

# Fluorescent microscope

#### Fluorescent microscope:

- high intensity light source
- excites a fluorescent species in a sample
- Sample emits different wavelength

Reflects excitation signal towards fluorophore and transmits emission signal towards the detector



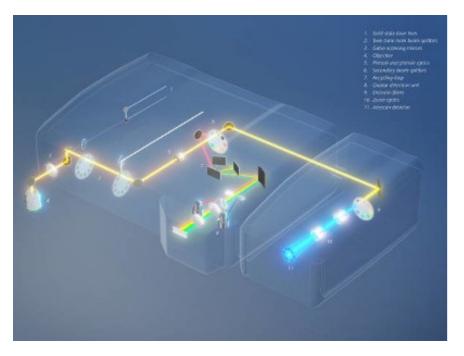
Labelled with fluorescent protein (e.g. GFP)

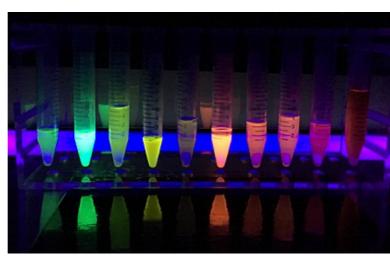
https://www.wikiwand.com/en/ Fluorescence\_microscope

# Confocal fluorescent laser microscope

#### Fluorescent confocal microscope:

- Combination of two ideas in microscopy technology
- High resolution images
- Life cells
- 2D or 3D through scanning schemes
- Multi-channel through use of range of fluorescent proteins



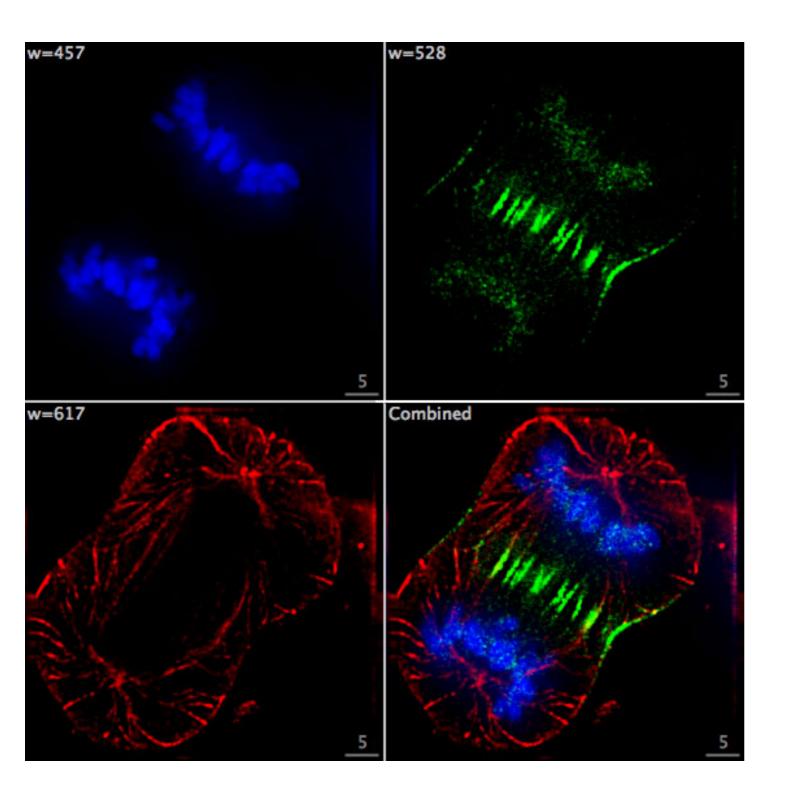




https://www.biocompare.com/25608-Microscopes-and-Cell-Imaging-Systems/14617250-ZEISS-LSM-980-Confocal-Laser-Scanning-Microscope/?pda=25608|14617250\_0\_1|2254289,2254327|1|&dfp=true

https://en.wikipedia.org/wiki/Green\_fluorescent\_protein#/media/File:Fluorescence\_from\_Fluorescent\_Proteins.jpg

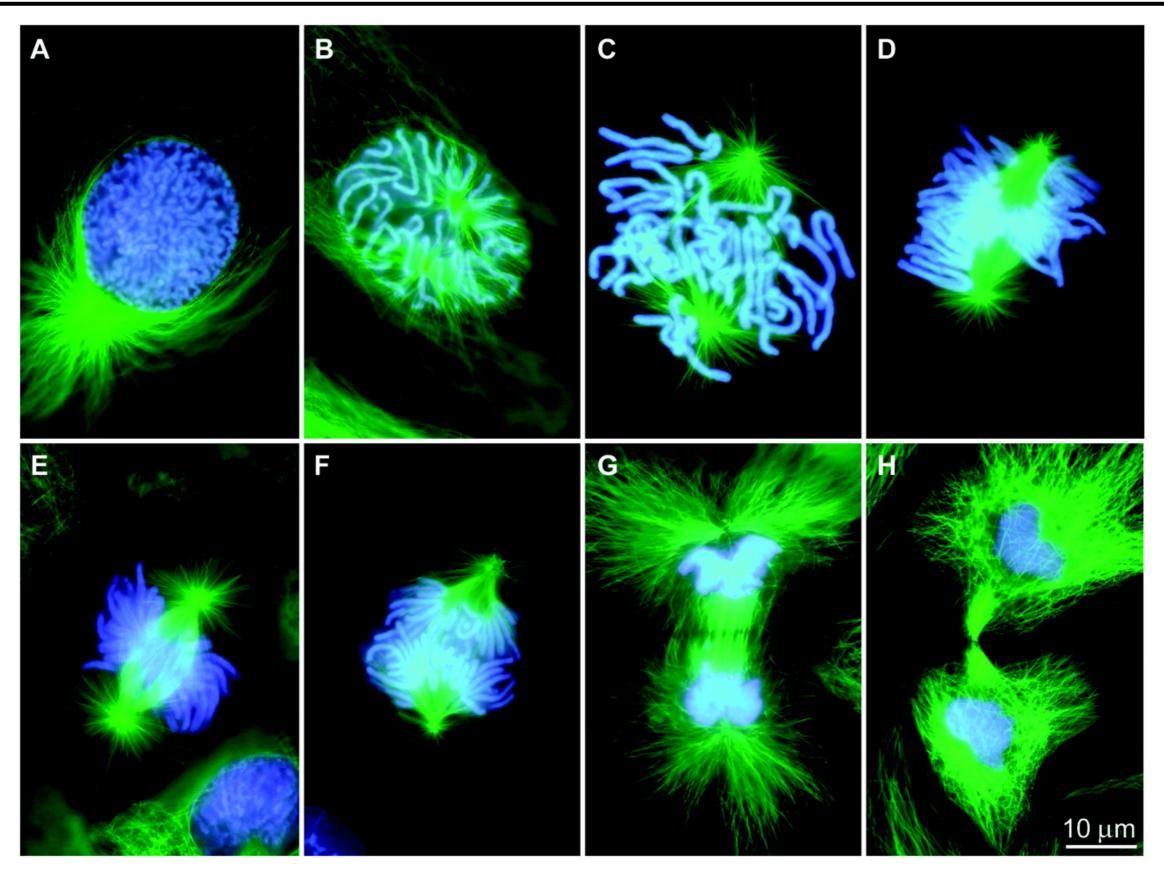
# Example: 3 components in dividing human cancer cells



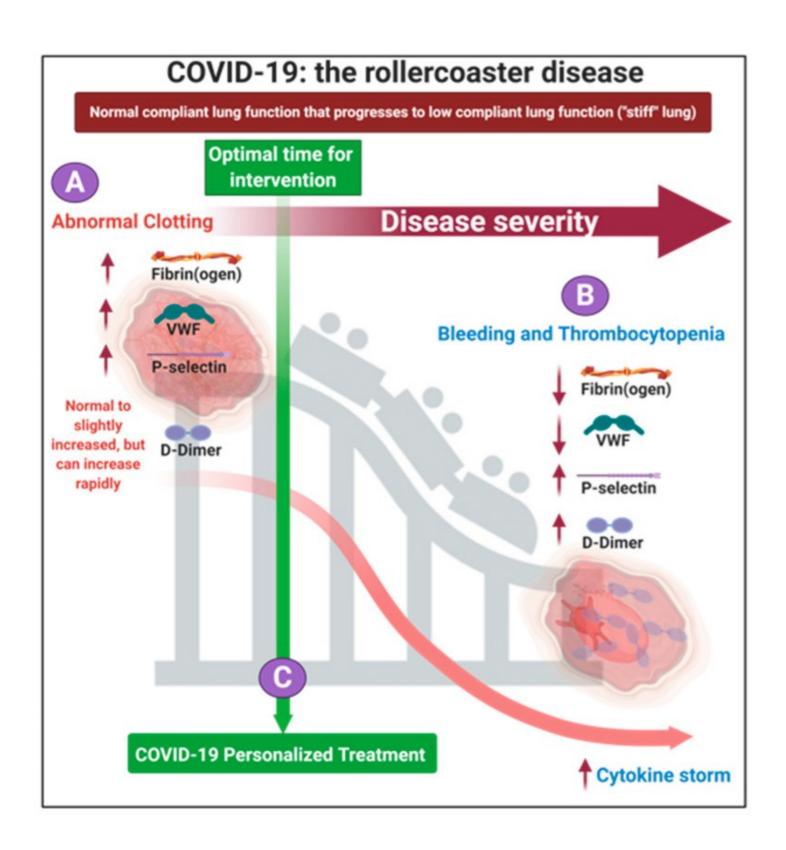
# Scanning scheme for fluorescent imaging:

- Blue: Chromosomes (DNA)
- Green: INCENP (protein)
- Red: microtubules
- Fluorophores imaged separately using different excitation and emission filters
- Images captured sequentially
- Overlaid

# Microtubules formation during mitosis



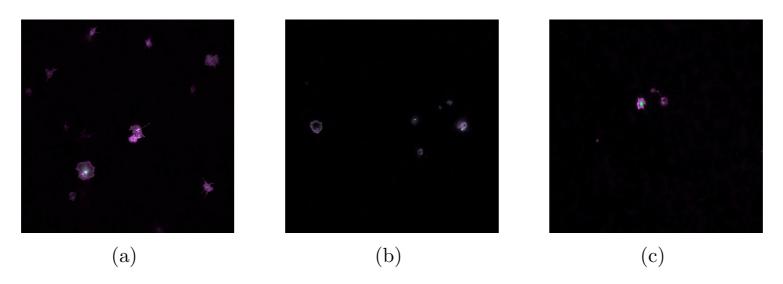
https://science.sciencemag.org/content/300/5616/91/tab-figures-data



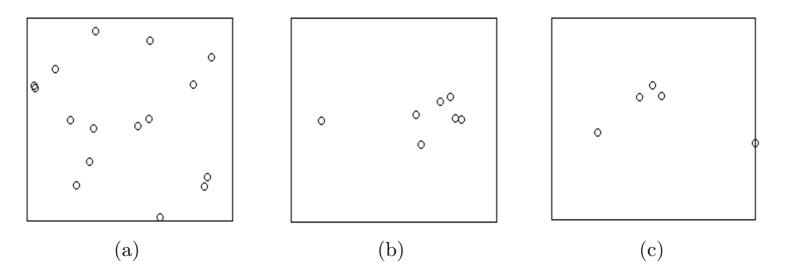
#### **Challenges:**

- Diagnostic criteria
- Treatment
- Progression
- Timing of intervention
- Automation of diagnosis

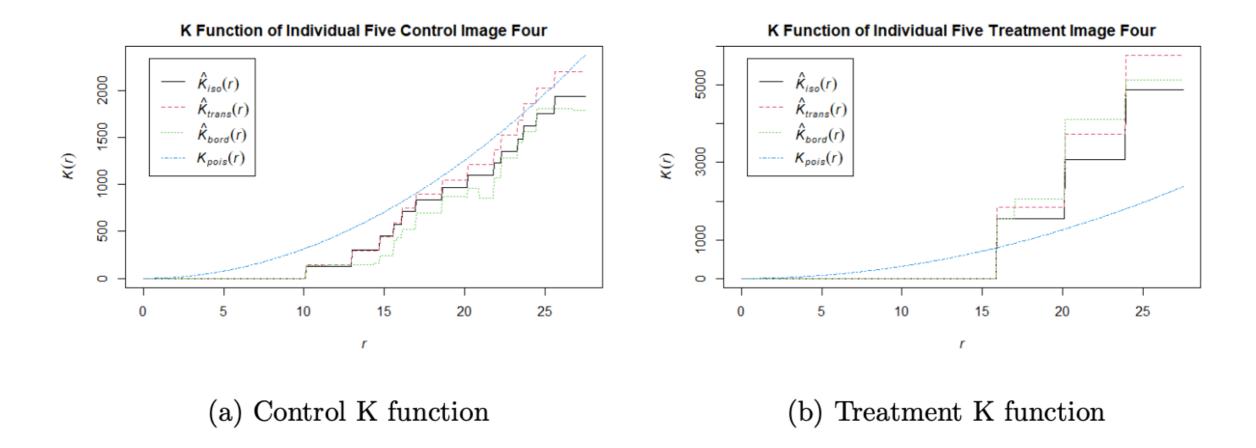
#### Spatial point processe models for platelets in Covid blood samples



Original microscopy images of (a) Covid-19 case subject 7, image 4, (b) Control subject 2, image 4, and (c) Control subject 2, image 7.



Spatial point patterns of (a) Covid-19 case subject 7, image 4, (b) Control subject 2, image 4, and (c) Control subject 2, image 7.



Controls showing patterns corresponding to being completely spatially at random

#### Morphological measures

#### **Circularity:**

ratio of the surface area of an object to the square of its perimeter (Cox [1927], Leach [2013]). Mathematically,

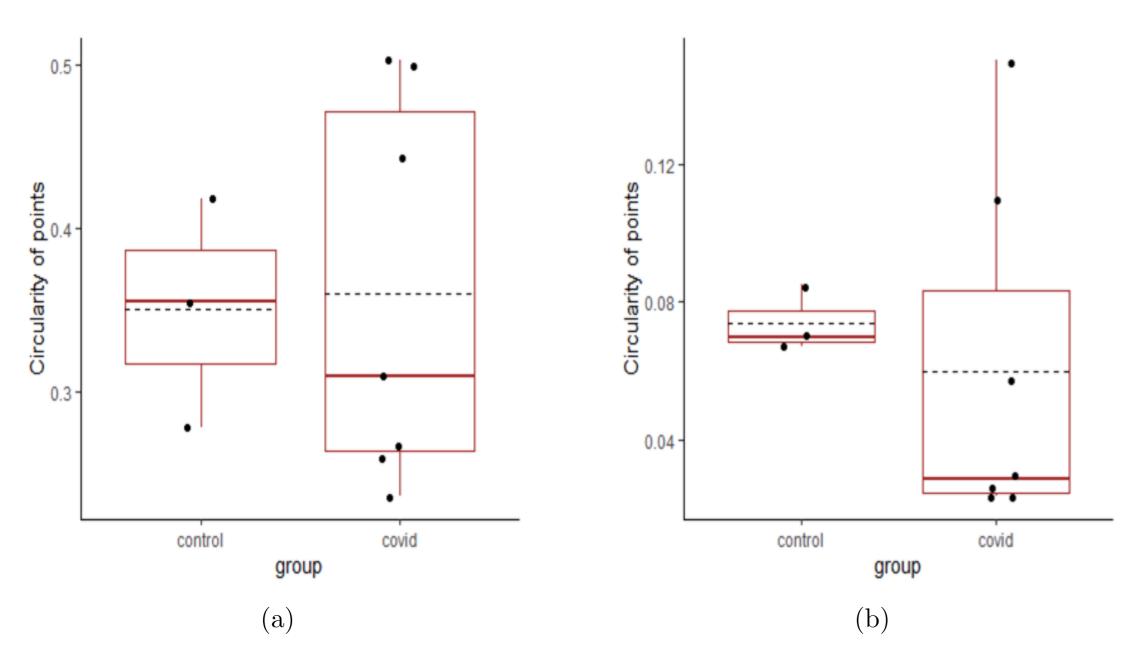
$$M_{Ff} = \frac{4\pi A}{p^2}$$

A: surface area, and P: perimeter. Circularity is

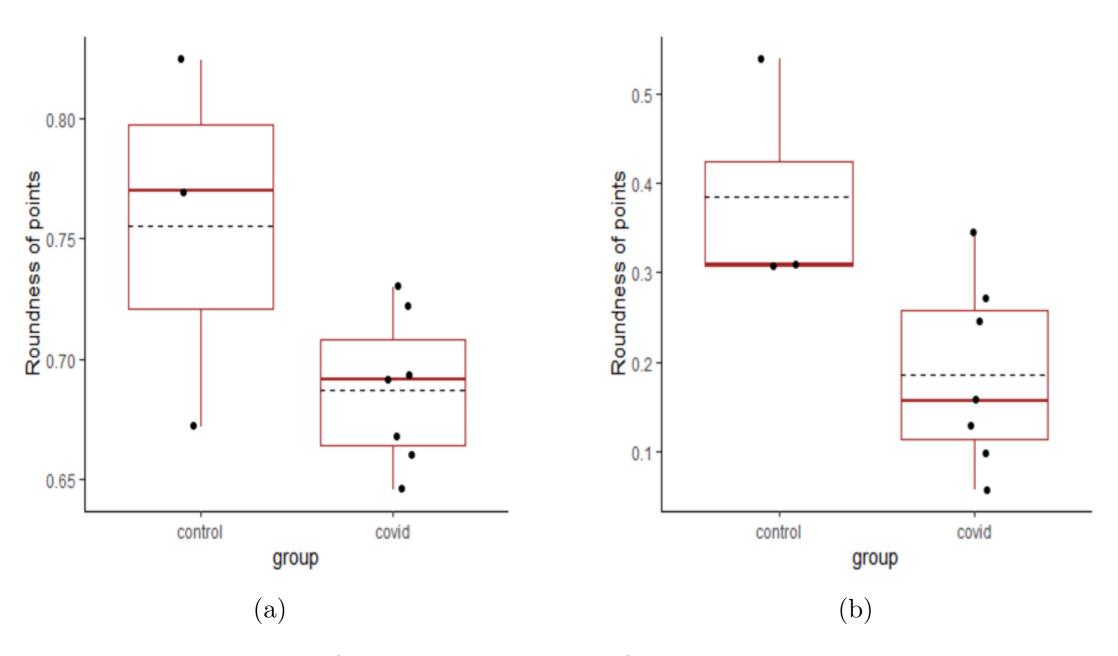
#### **Roundness:**

$$M_{RN} = \frac{4A}{\pi D_{\text{max}}^2},$$

 $D_{\max}$ : maximum diameter, A: surface area and where the diameters are calculated using euclidean distances. Roundness is essentially a ratio



Boxplots of the circularity index, for observations divided into controls and treatments. Figure (a) uses as scores the average values of circularity indexes, and Figure (b) uses as scores the overall minimum circularity. Medians are indicated by solid horizontal lines and means by dashed horizontal lines.



Boxplots of the roundness index, for observations divided into controls and treatments. Figure (a) uses as scores the average values of roundness indexes, and Figure (b) uses as scores the overall minimum roundness. Medians are indicated by solid horizontal lines and means by dashed horizontal lines.