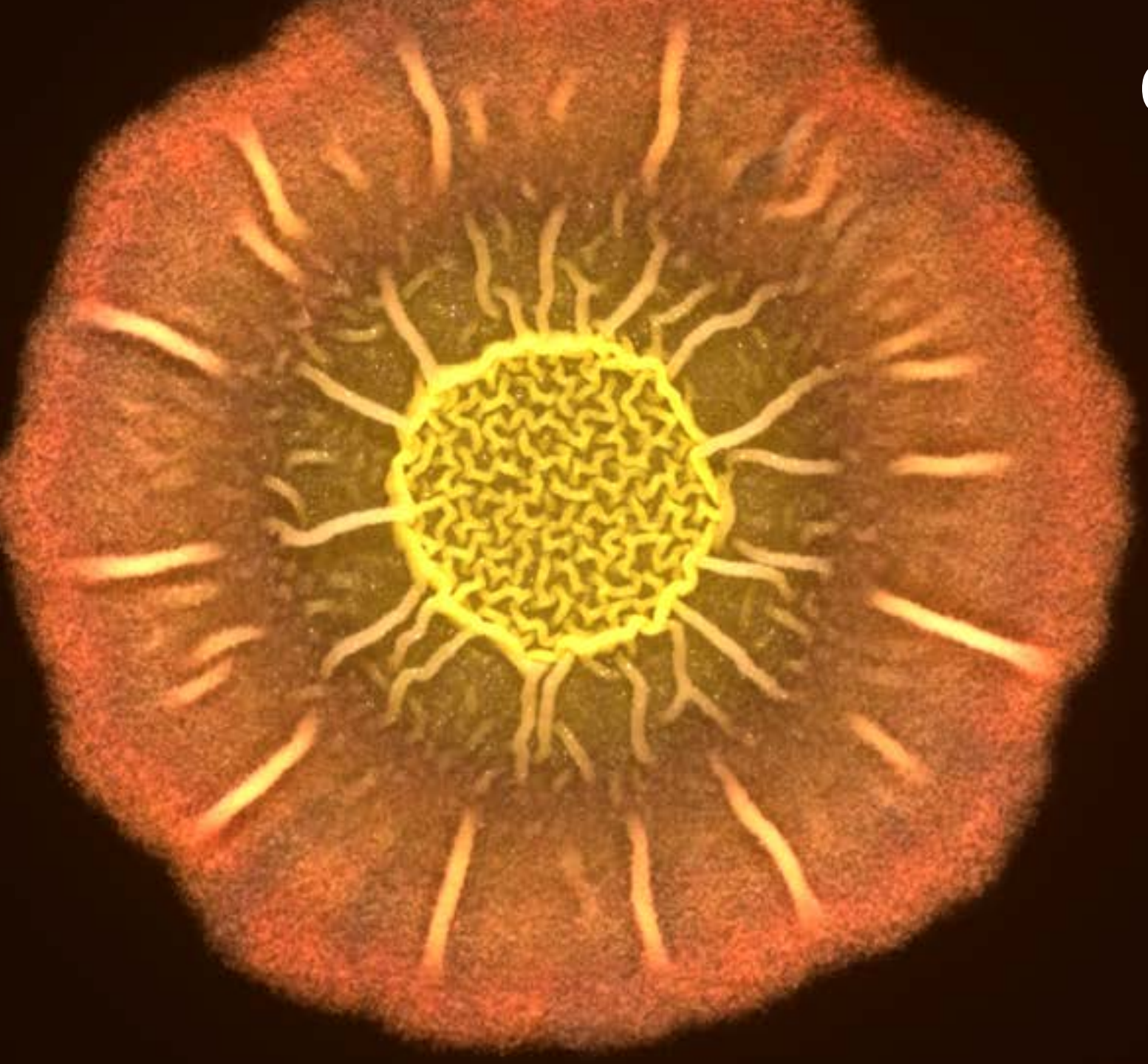


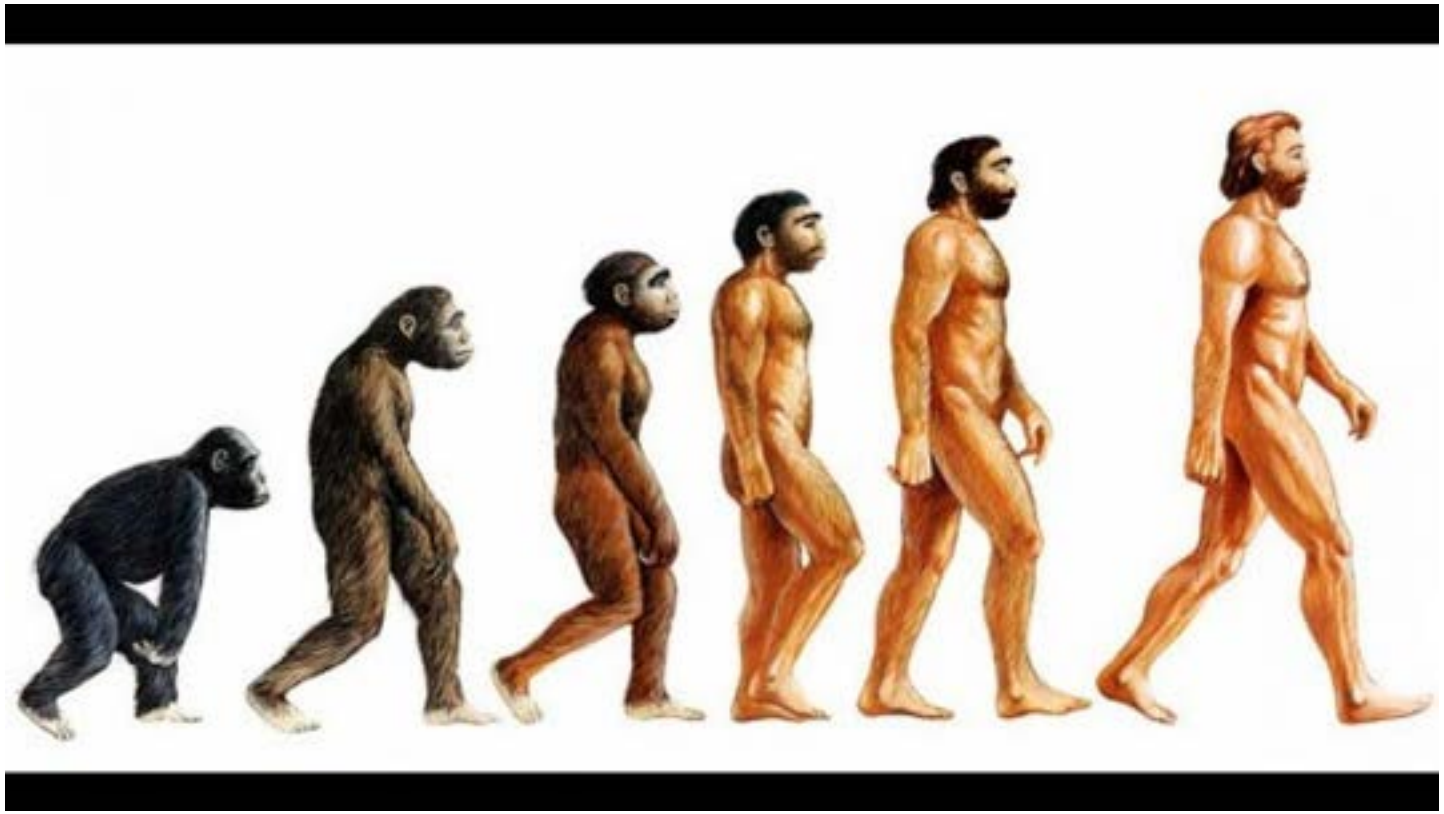
Quando il bene di uno e' piu' importante del bene di molti: *cosa ci insegnano le comunita' batteriche*

Diana Fusco
Cavendish Laboratory
University of Cambridge

Club Donegani 21/2/24

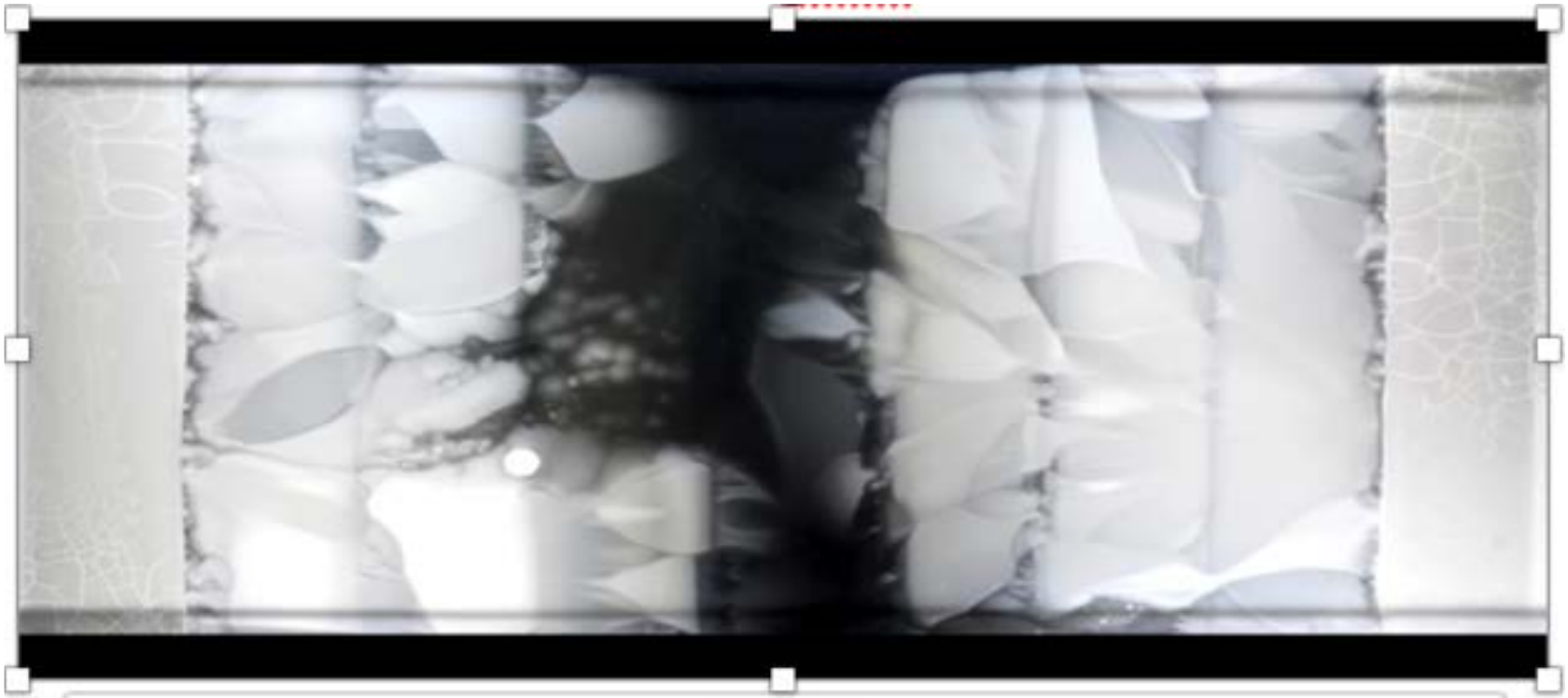
L’evoluzione e’ un processo lento? Dipende…

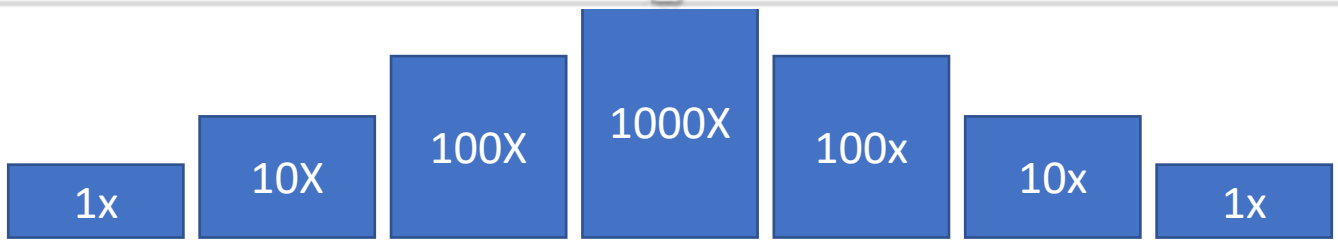
Milioni di anni



L’evoluzione e’ un processo lento? Dipende…

10 giorni



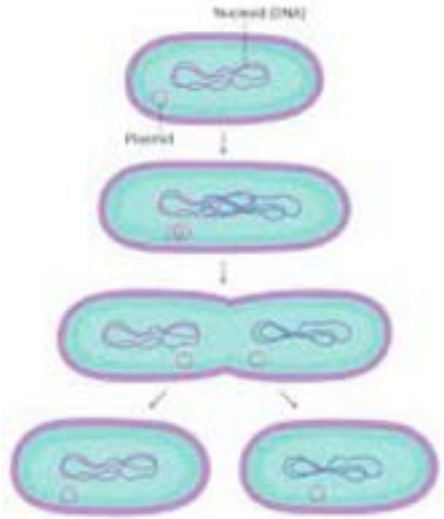


Baym et al. *Science,* 2016

Concentrazione di antibiotici

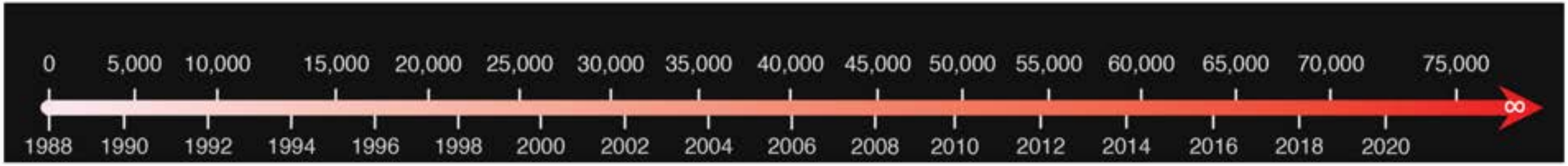
Cosa determina l'orologio evolutivo?

- Il tempo generazionale Ogni 20 minuti



Da 1 a un miliardo in 10 ore

Equivalente a 2 milioni di anni umani



Richard Lenski, Michigan State,https://the-ltee.org/about/

L’evoluzione puo’ essere osservata una volta, poi un’altra, poi un’altra… in modo da capirne le regole!

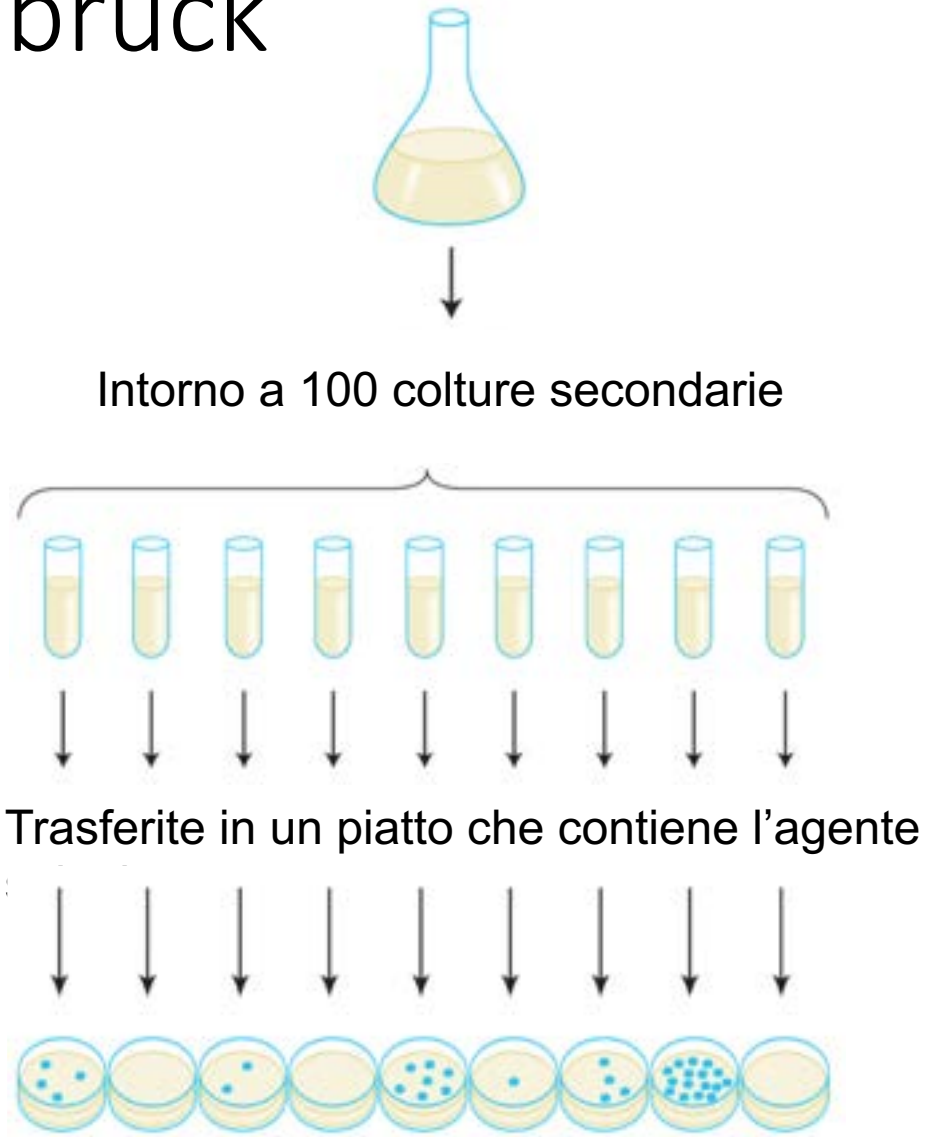
1943 – L'esperimento di Luria e Delbrück

Le mutazioni che danno resistenza sono?

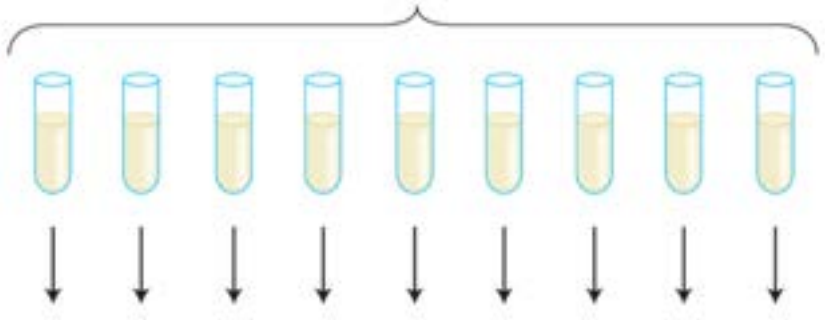
- Indotte:
  Occorrono **come risultato** di uno stress
- Spontanee:
  Occurrono **a caso e inevitabilmente** e sono selezionate dallo stress

Luria, Salvador E., and Max Delbrück. *Genetics* 28.6 (1943): 491.

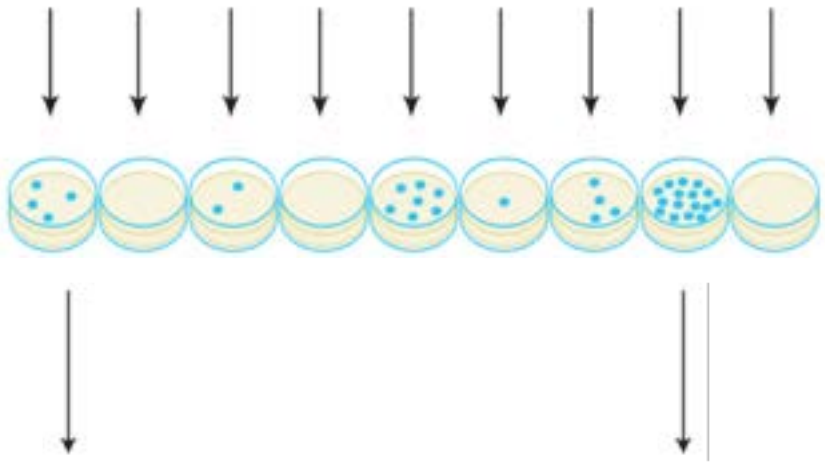
L’esperimento di Luria e Delbrück



Cosa predicono le due ipotesi?

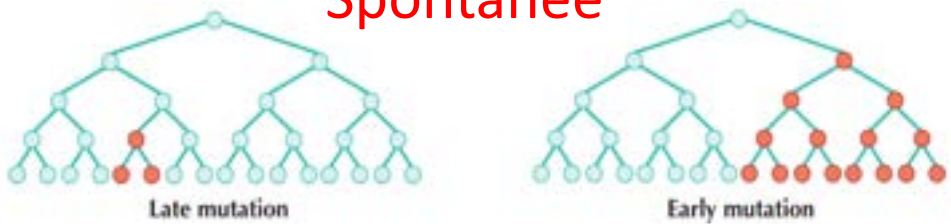


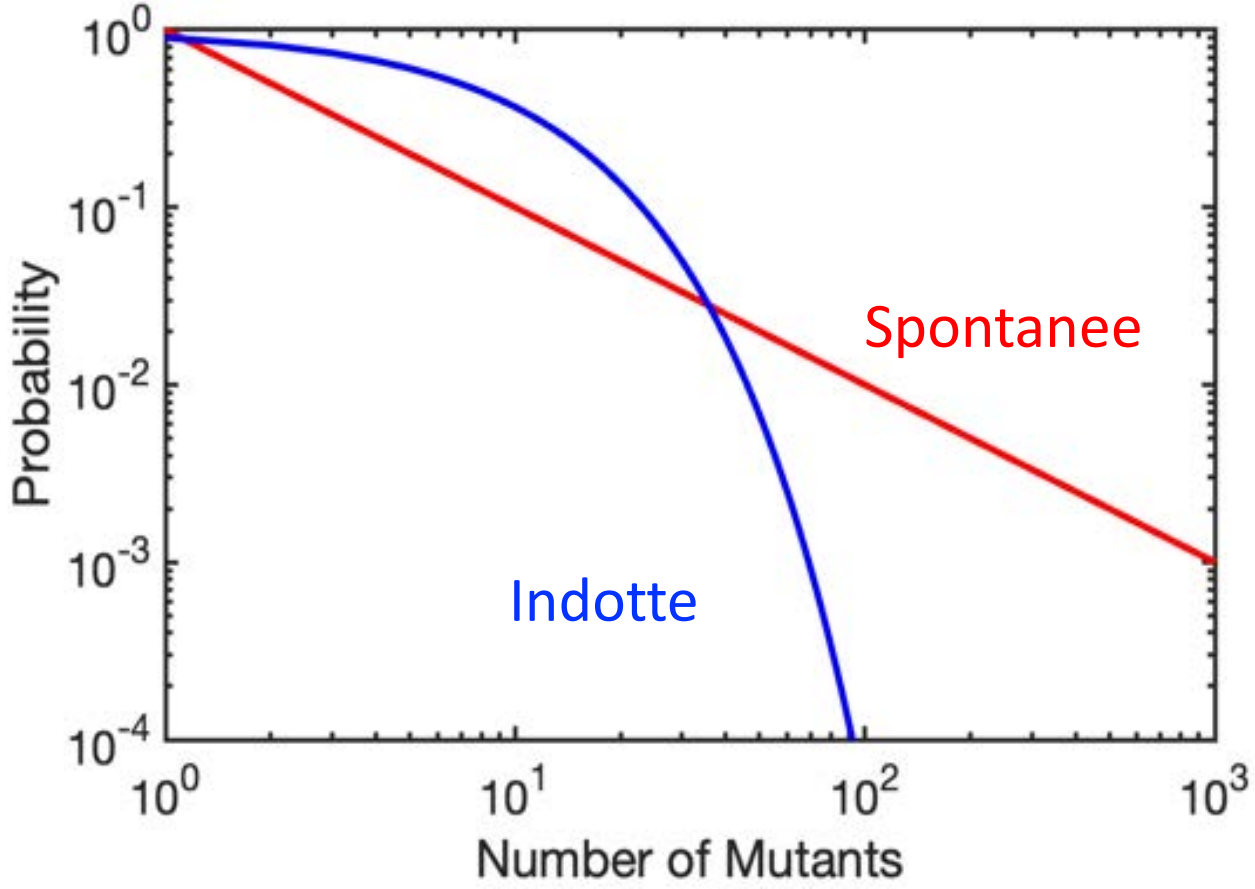
Trasferite in un piatto che contiene l'agente



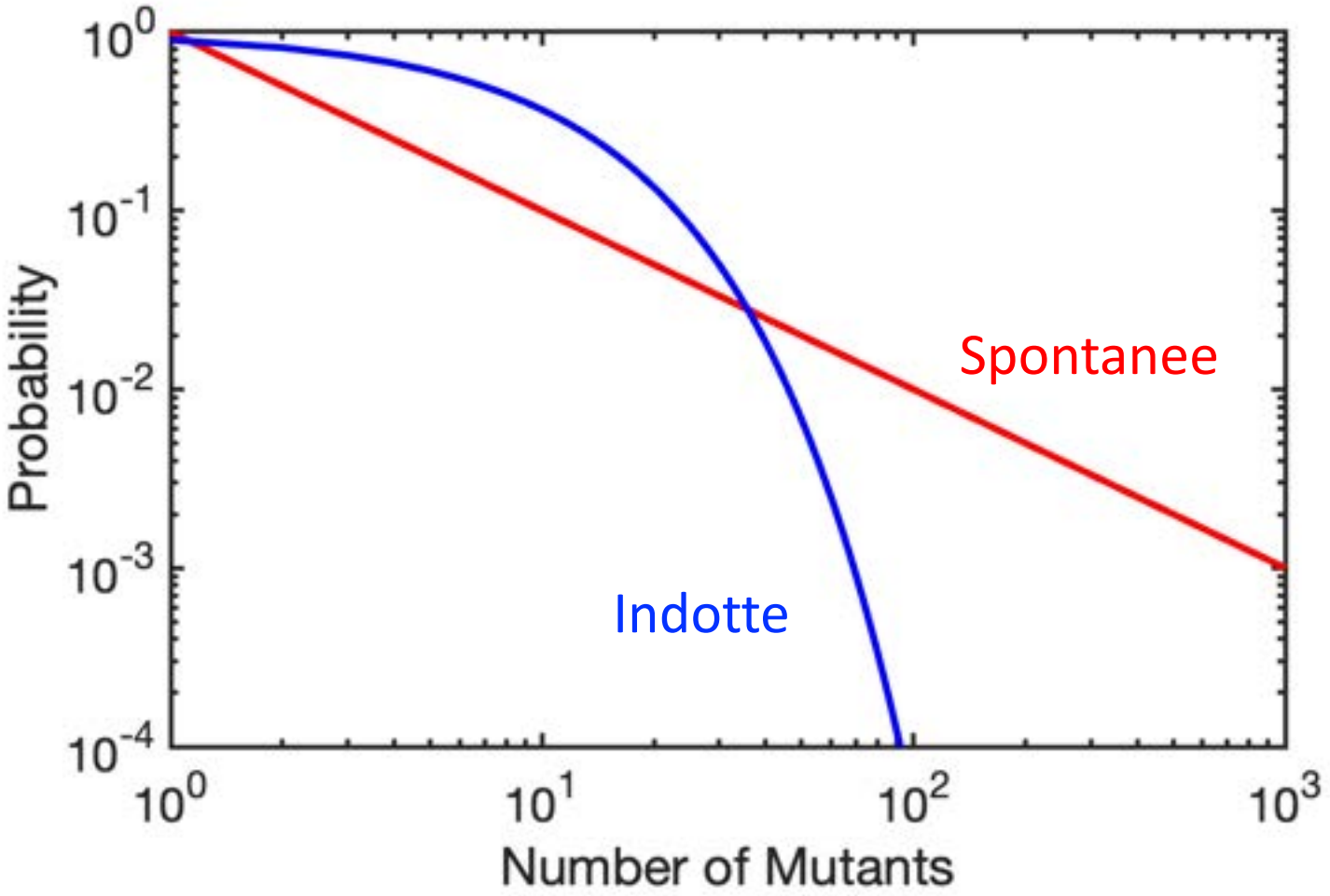
Indotte

Spontanee





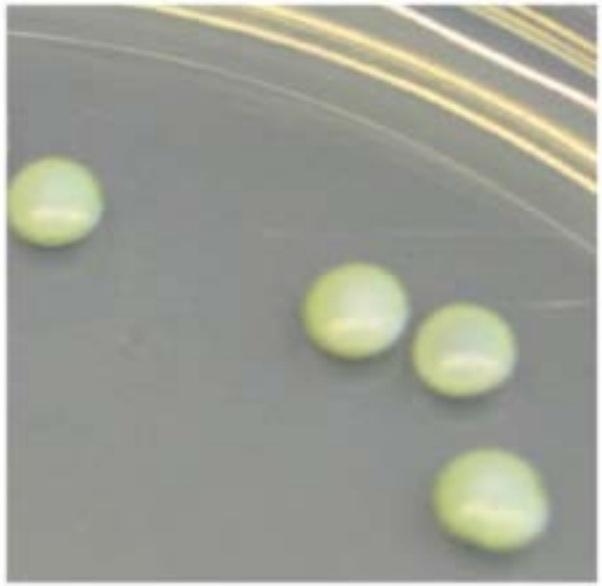
Cosa dicono i dati sperimentali?



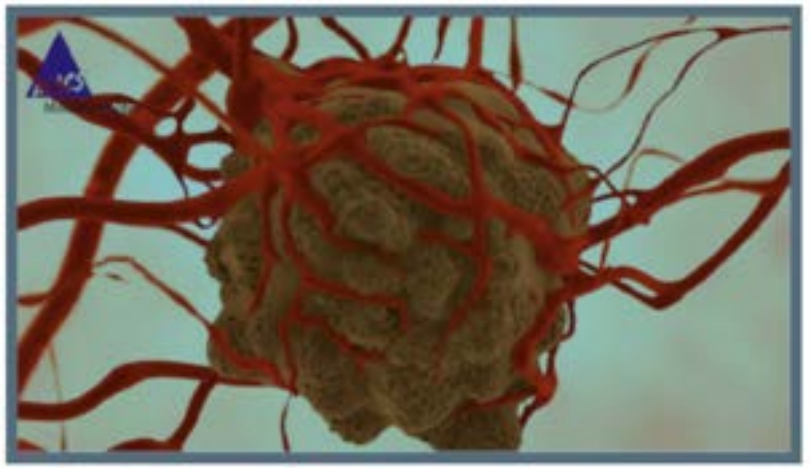
Resistant bacteria	*Number of cultures*
0	29
1	17
2	4
3	3
4	3
5	2
6– 10	5
11– 20	6
21– 50	7
51– 100	5
101– 200	2
201– 500	4
501–1000	0

Spontanee!

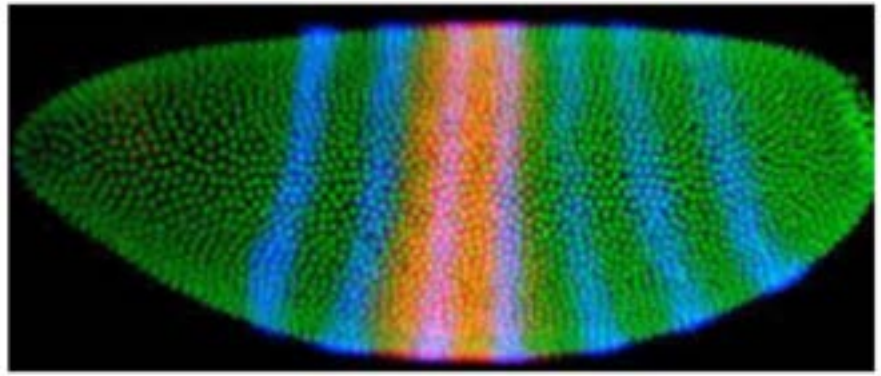
Quando la crescita non e’ esponenziale?



In colonie e biofilms

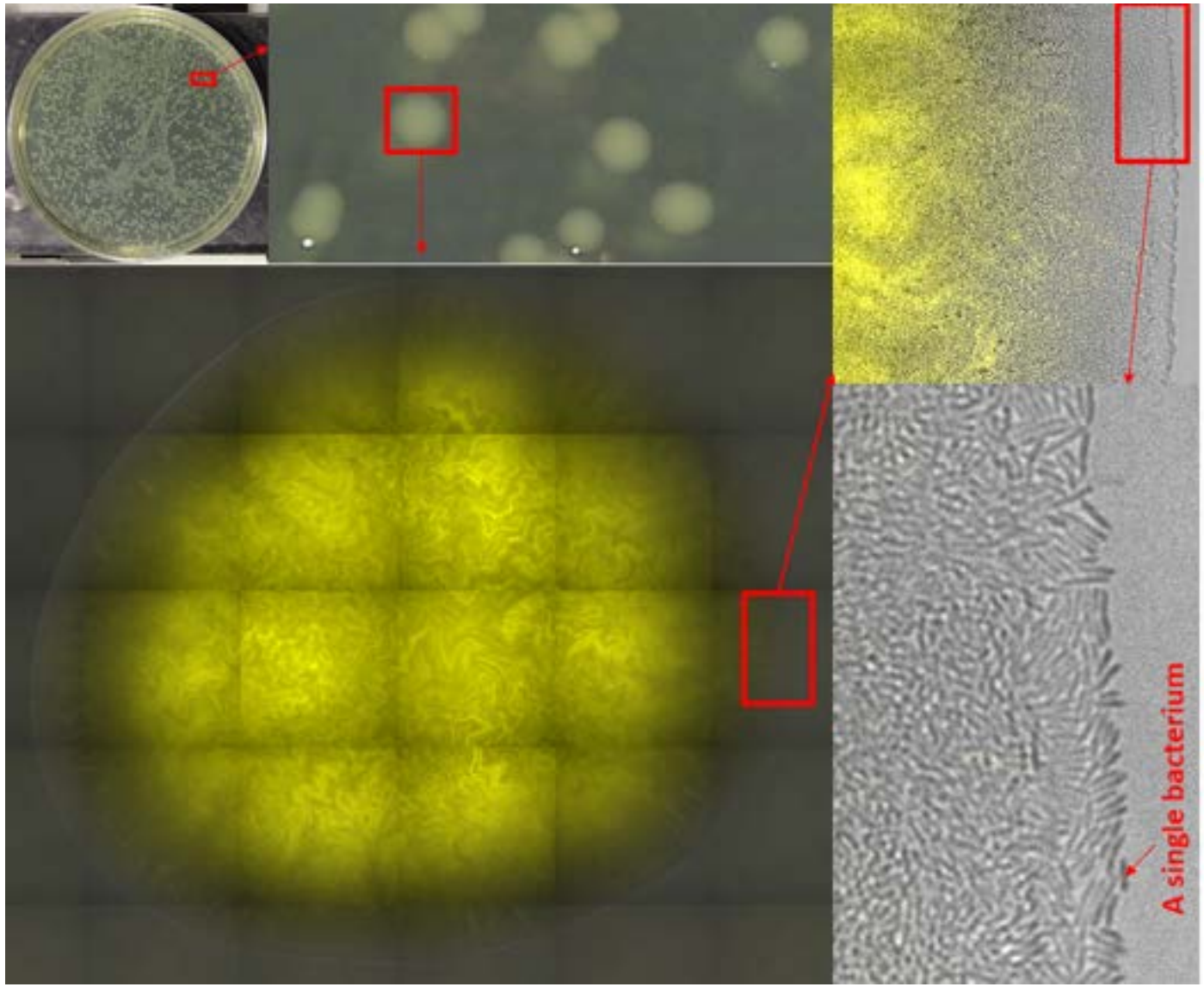


Nei tumori



Negli organismi multicellulari

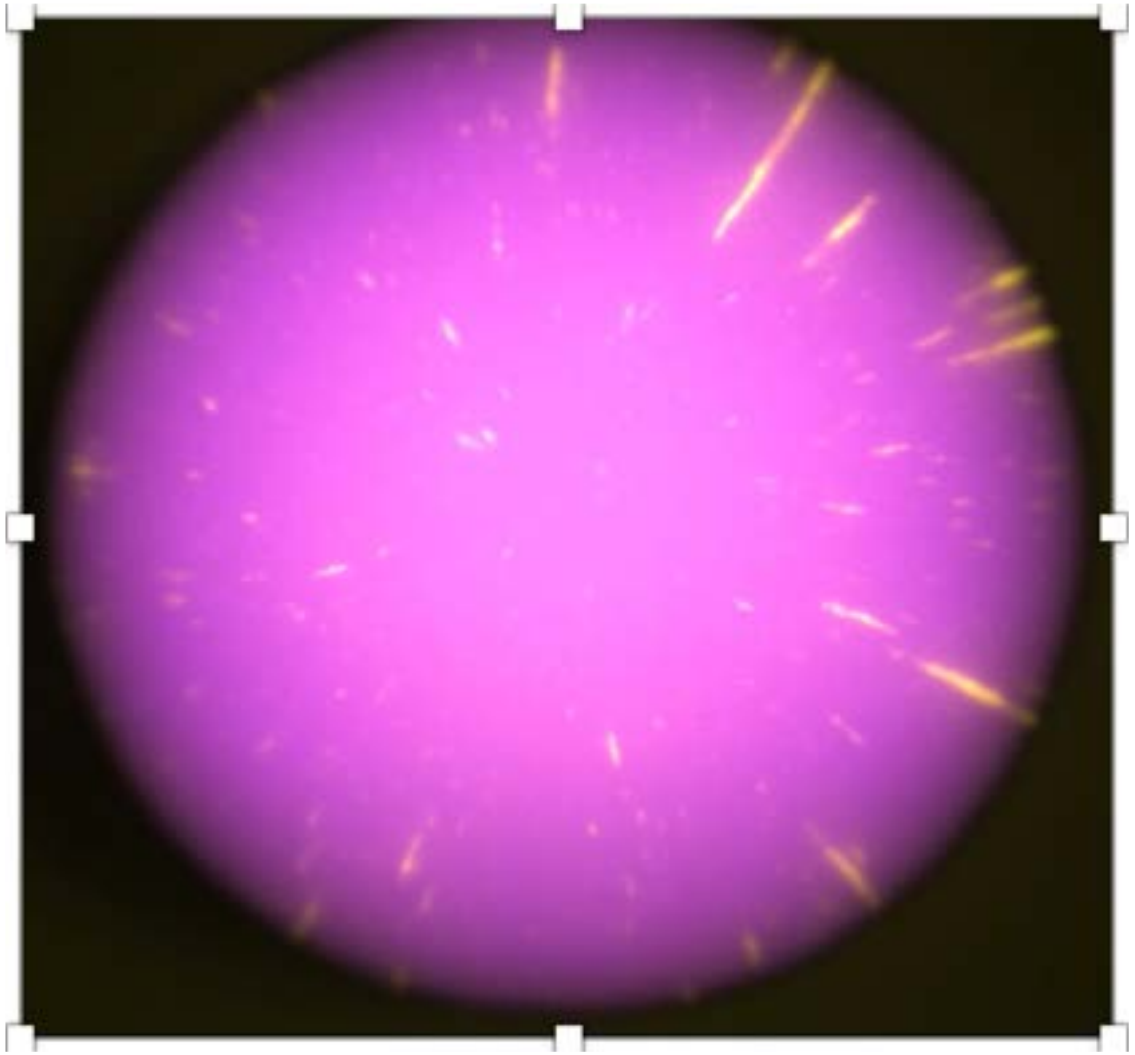
Il caso piu’ semplice: una colonia batterica

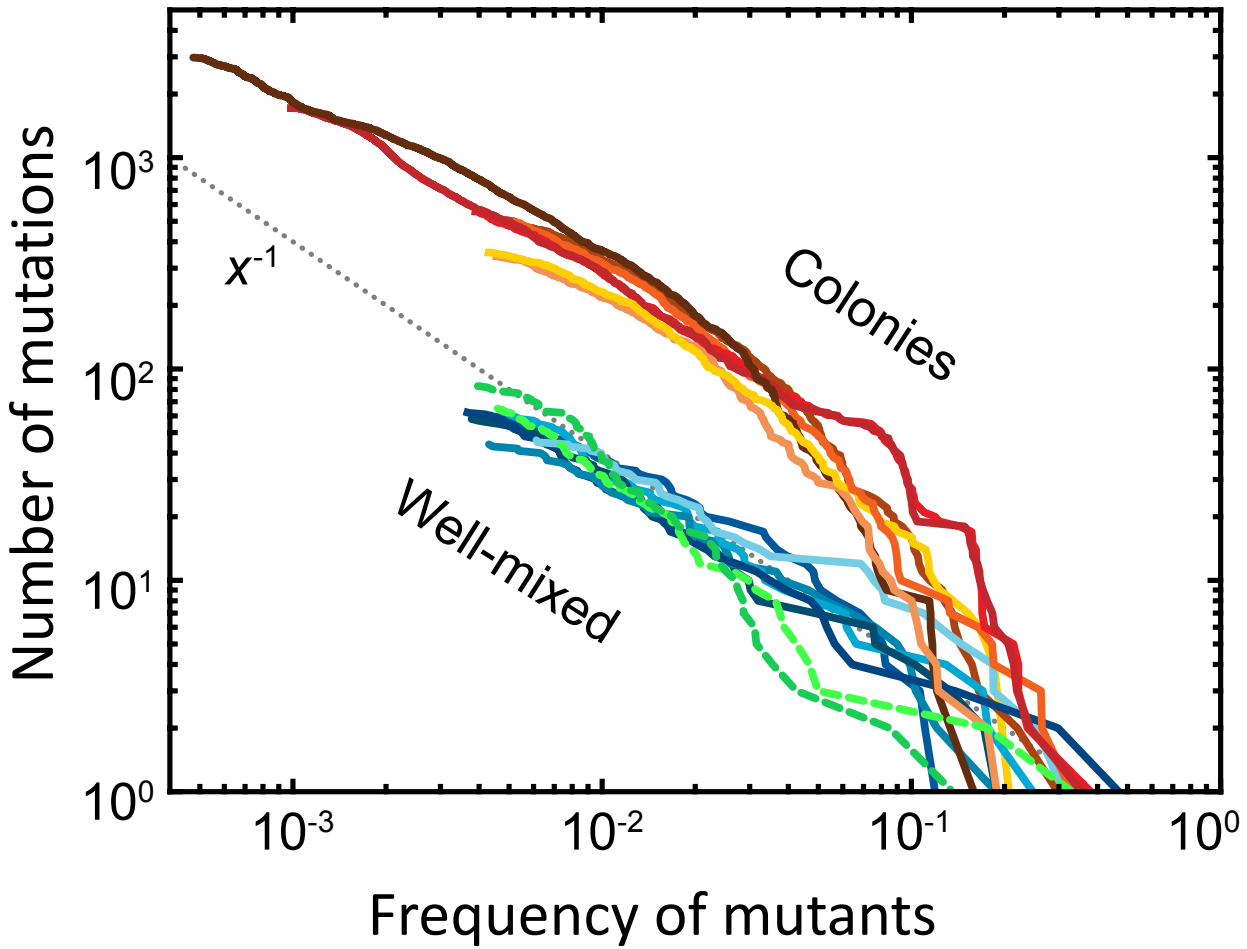


Solo le cellule vicino al bordo possono crescere

Grazie a Somenath Bakshi, Engineering, Cambridge

Il caso piu’ semplice: una colonia batterica

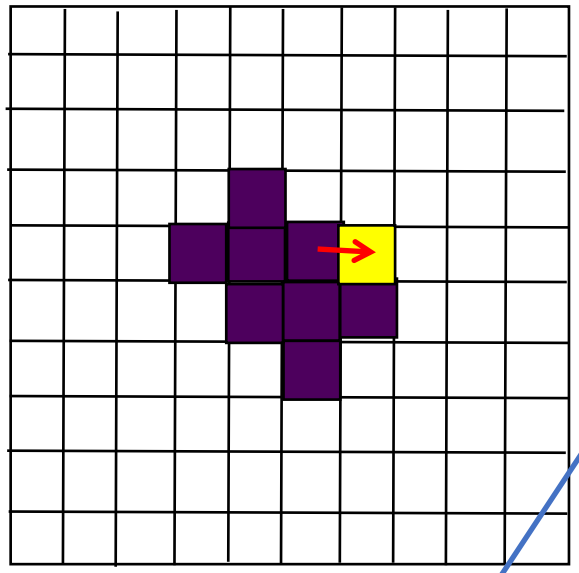


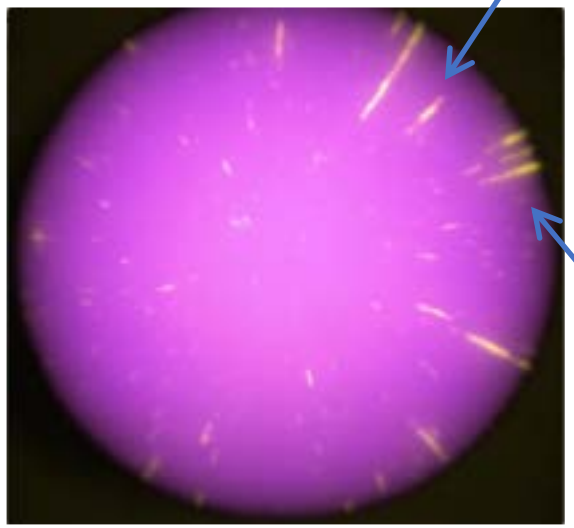


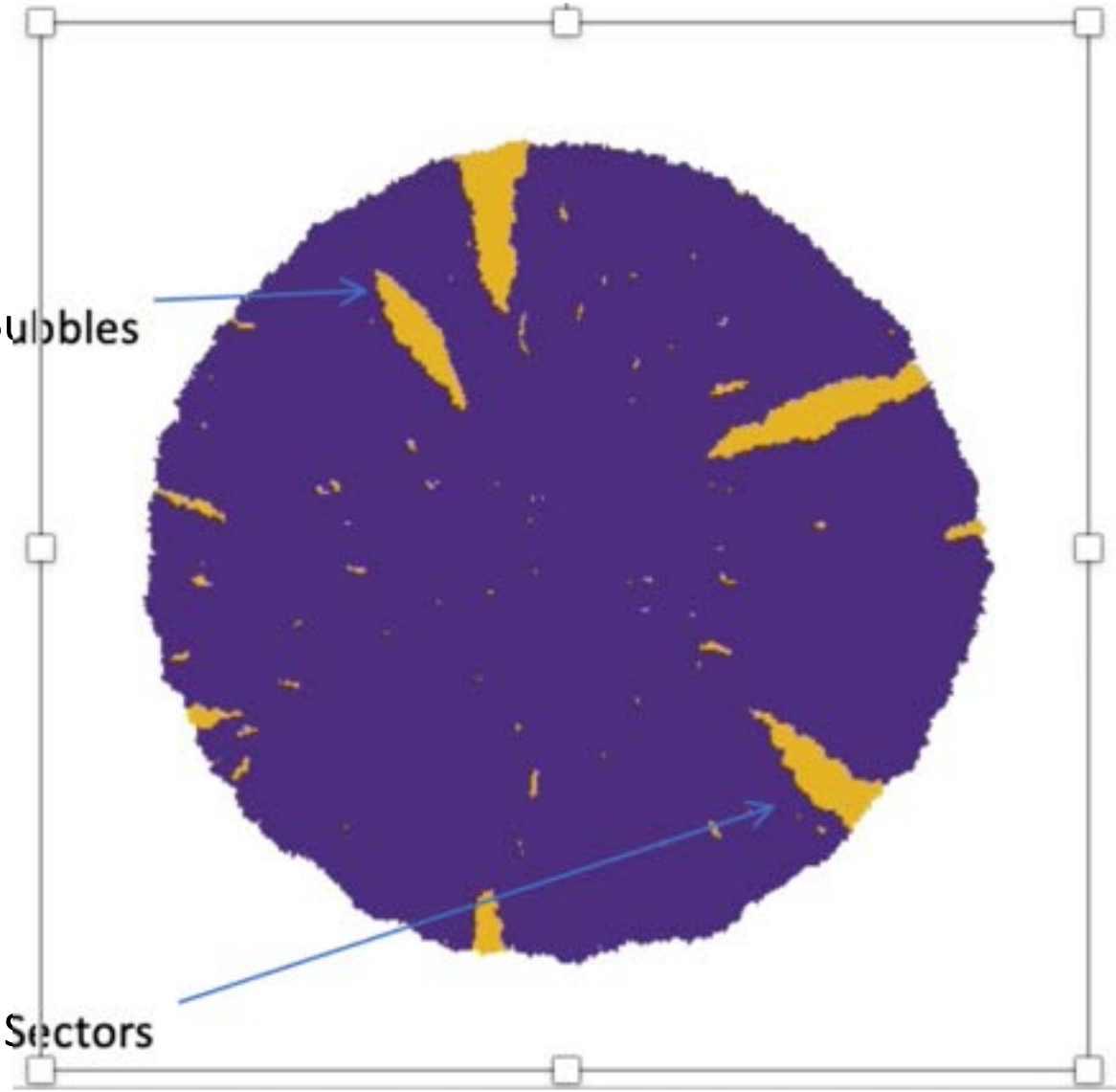
Fusco et al., *Nat. Comm.,* 2016

Crescita al bordo e' l'unico ingrediente necessario

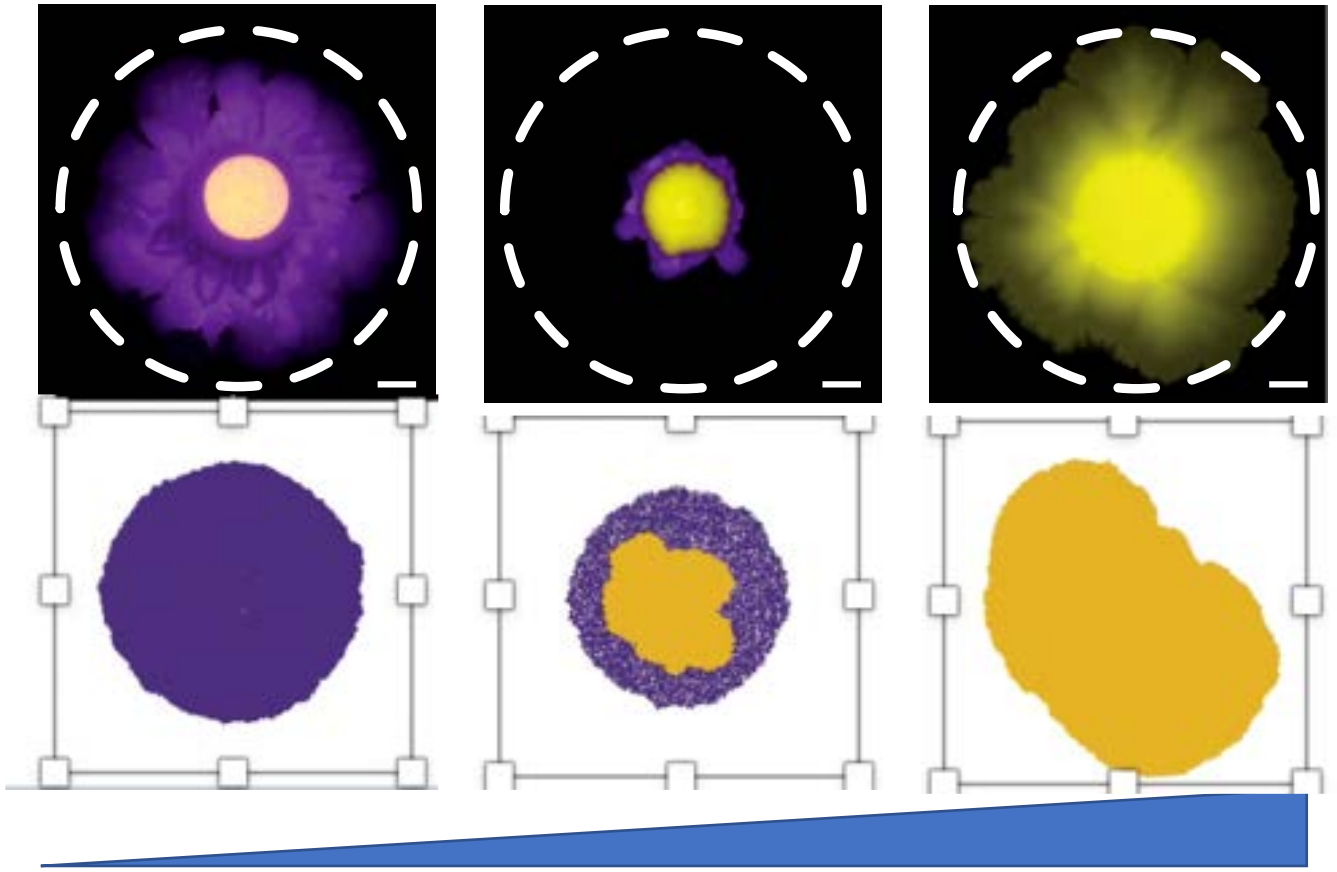
Eden model





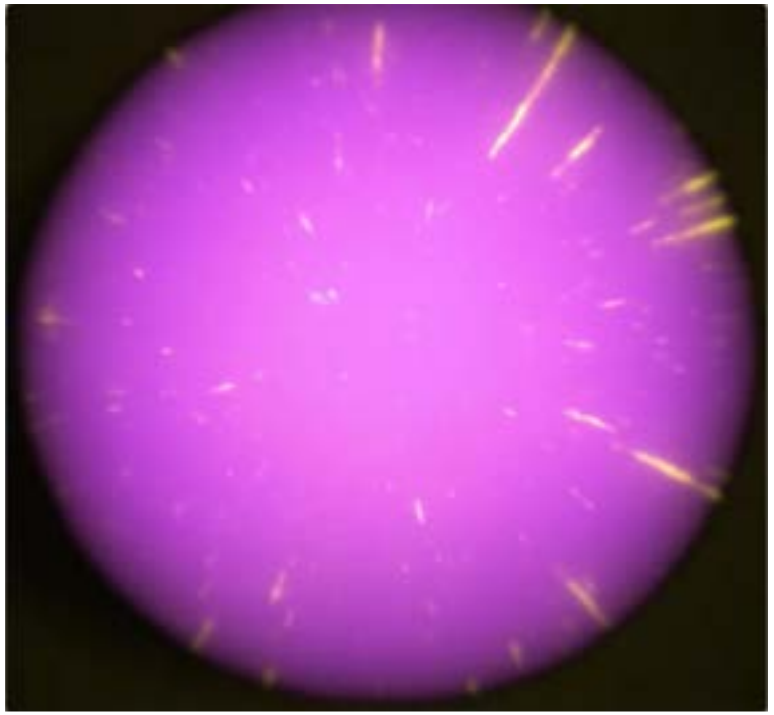


La maggioranza delle mutazioni sono quiescienti all’interno della colonia

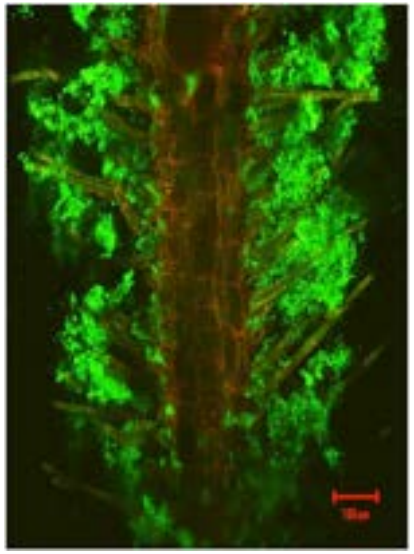


Concentrazione di antibiotico

Le colonie sono dei biofilm? Si’ e no



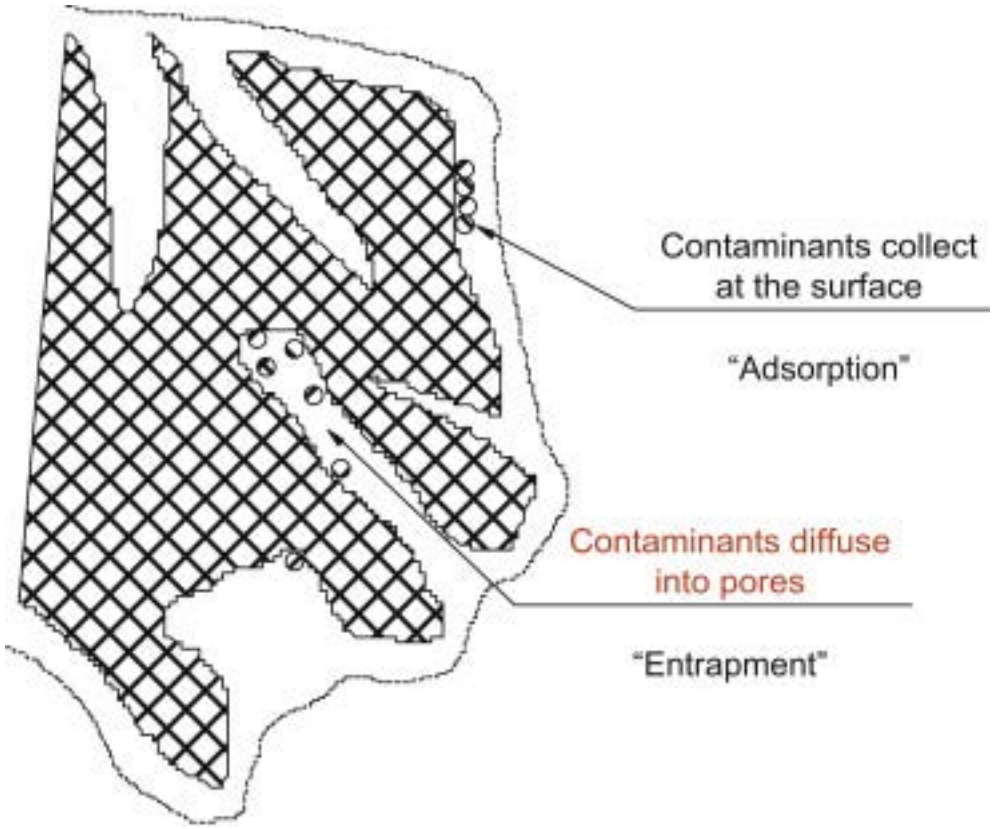
L’obiettivo e’
la crescita

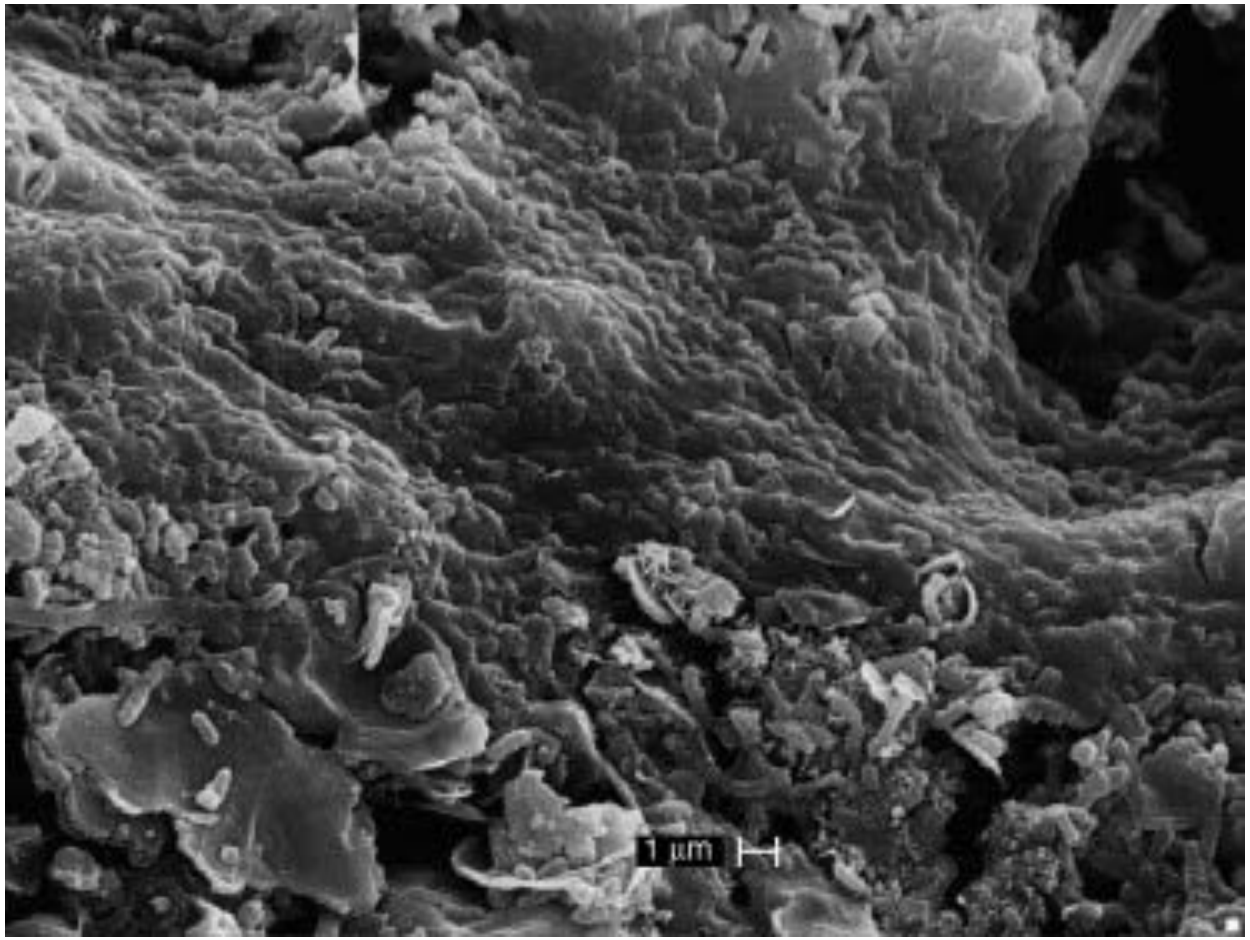


L’obiettivo e’
la sopravvivenza

Spesso hanno effetti indesiderabili

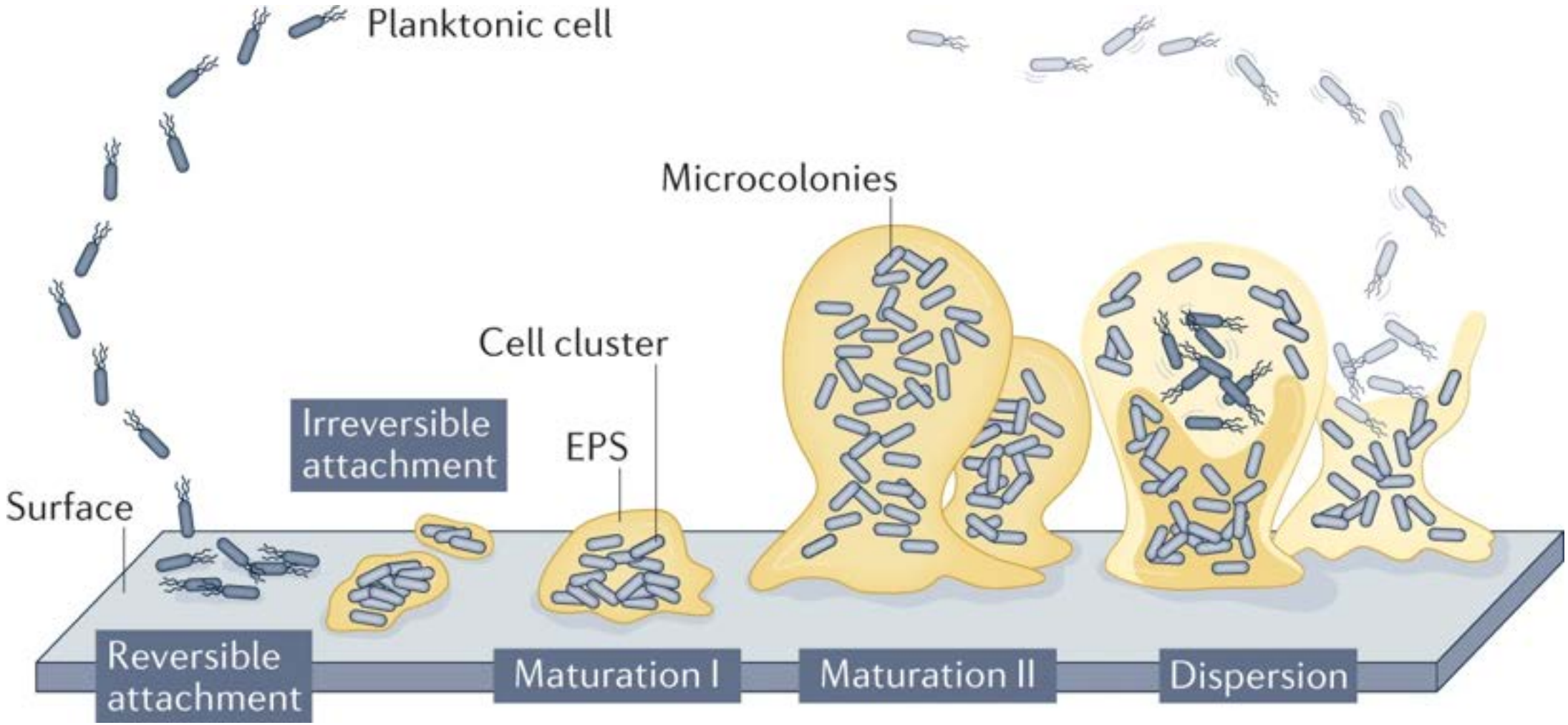
Ma possono anche essere utili





Simpson, *et al. 2018*

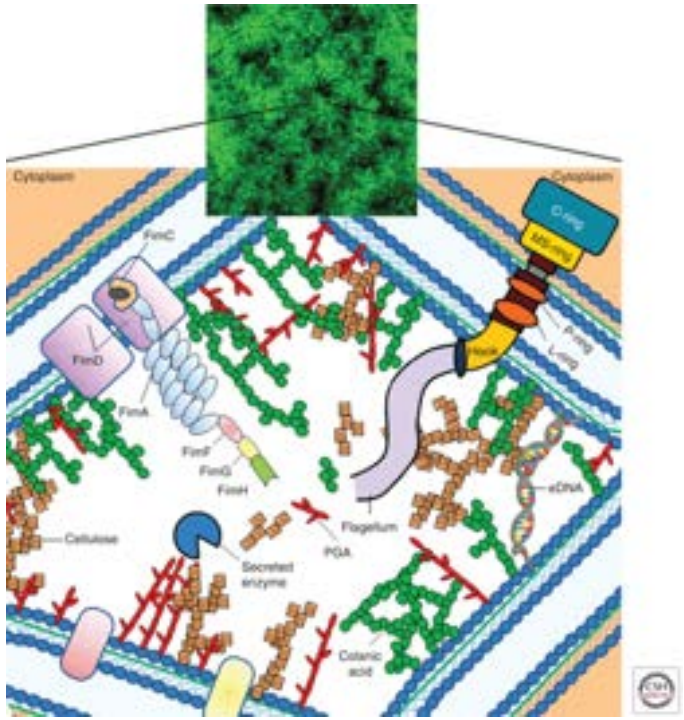
Il biofilm e’ una risposta allo stress

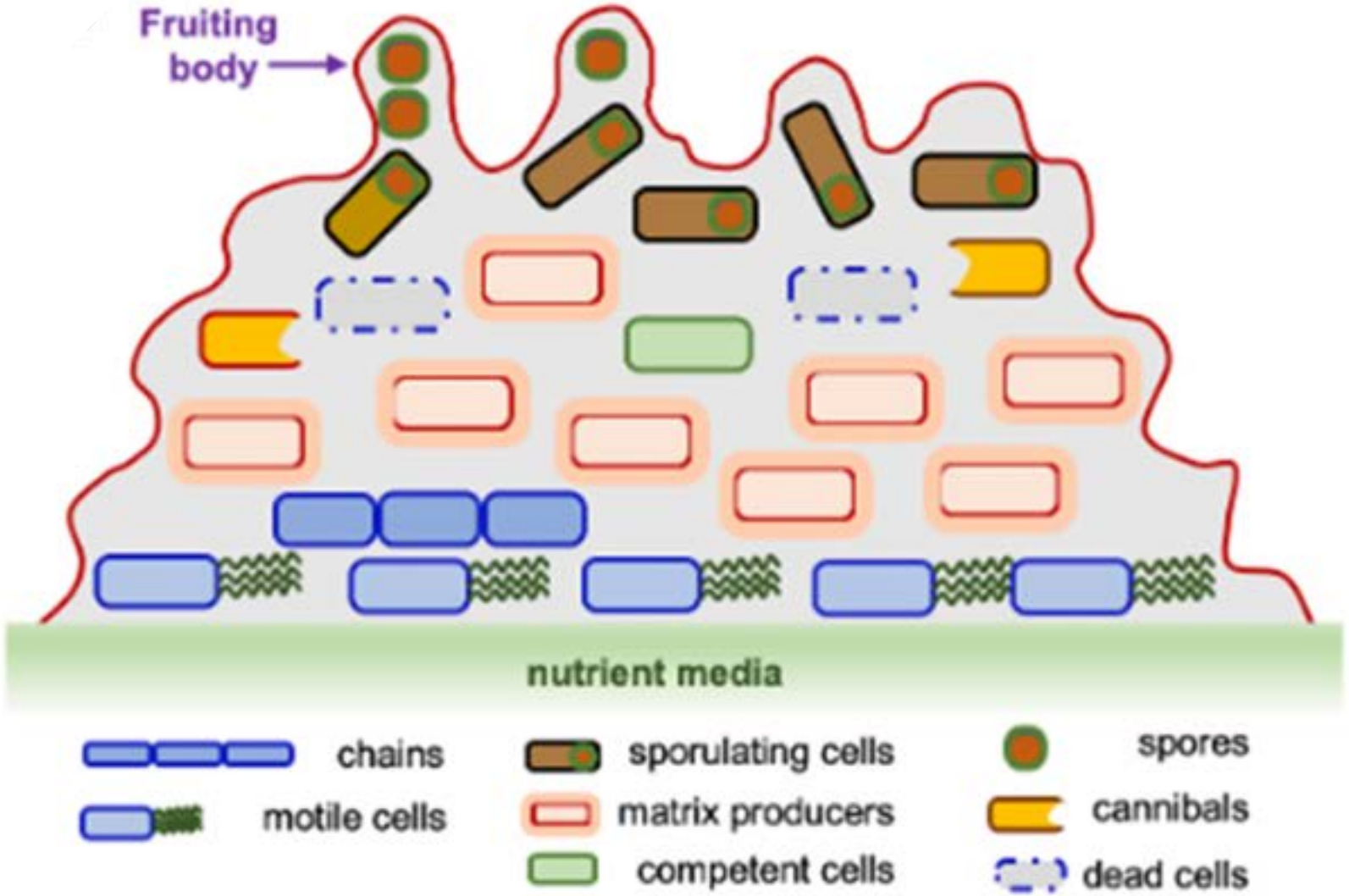


Sauer et al., 2022

Cosa rende un biofilm un vero biofilm?

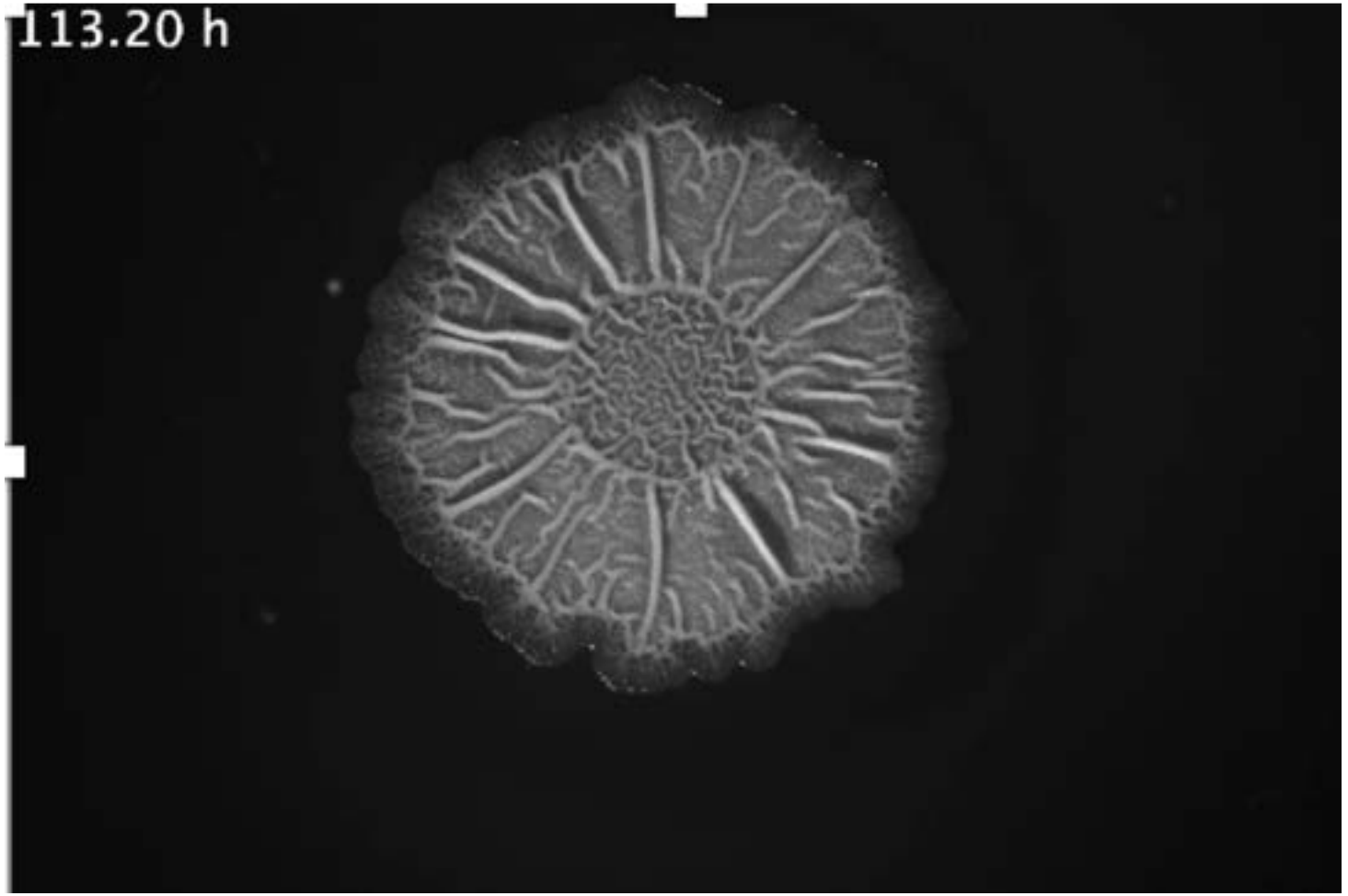
1. Differenziazione
2. Matrice extracellulare





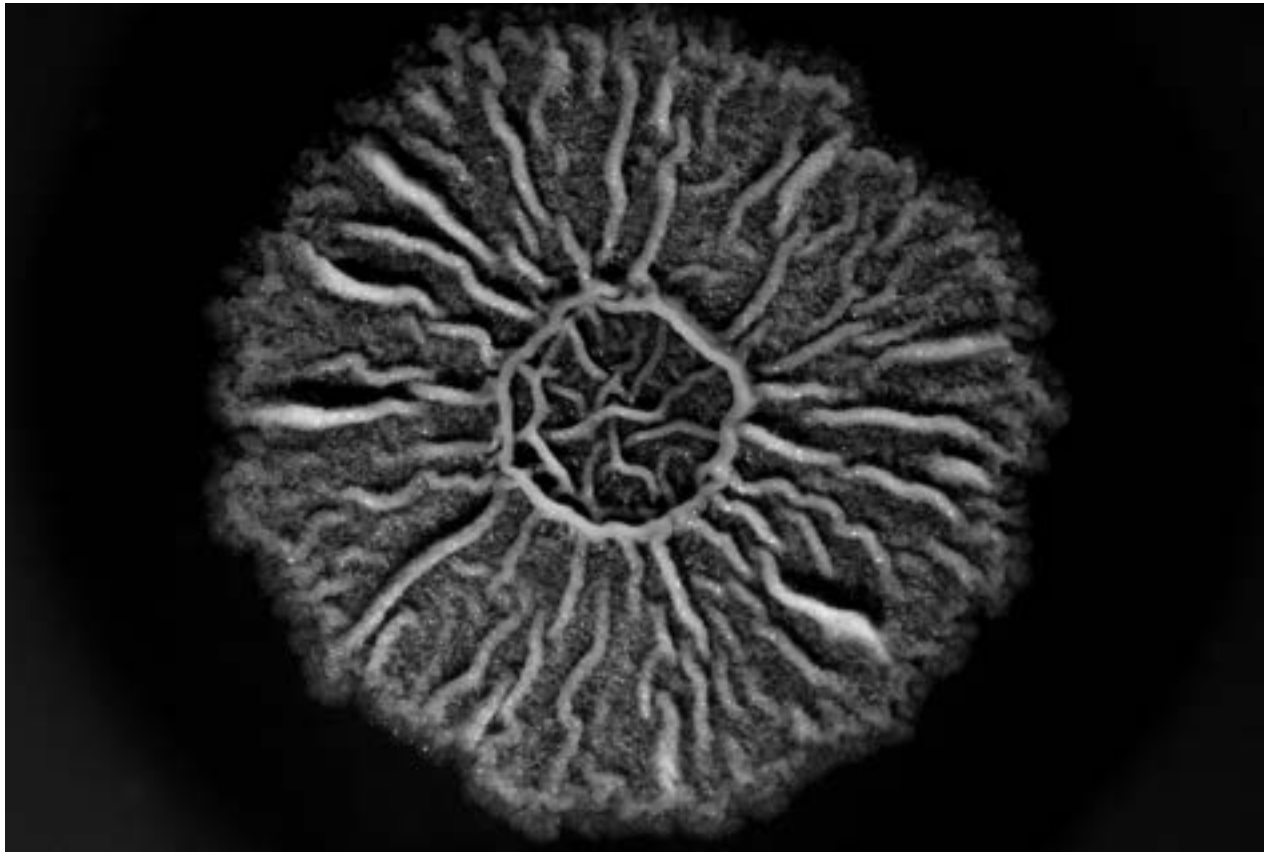
Qin, Y.; Angelini, L.L.; Chai, Y. (2022)

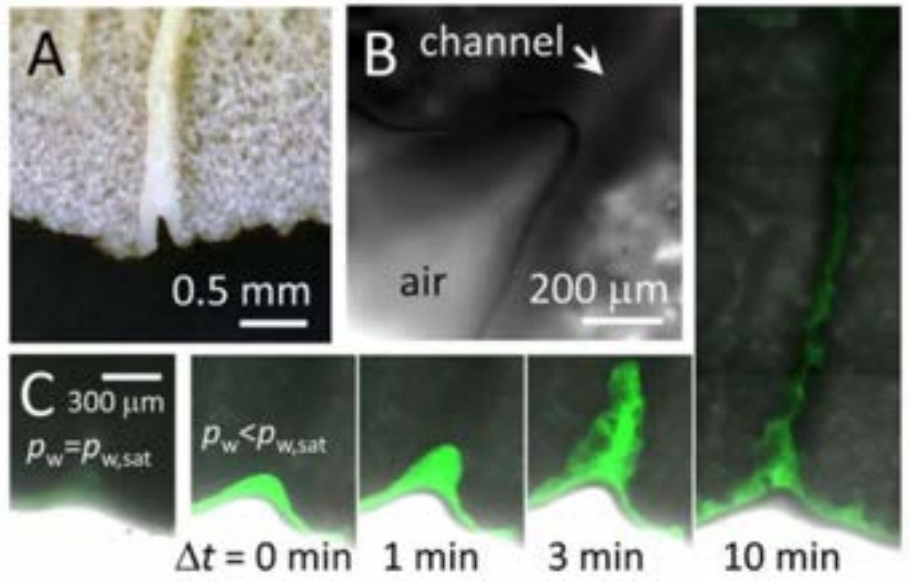
Le conseguenze della matrice

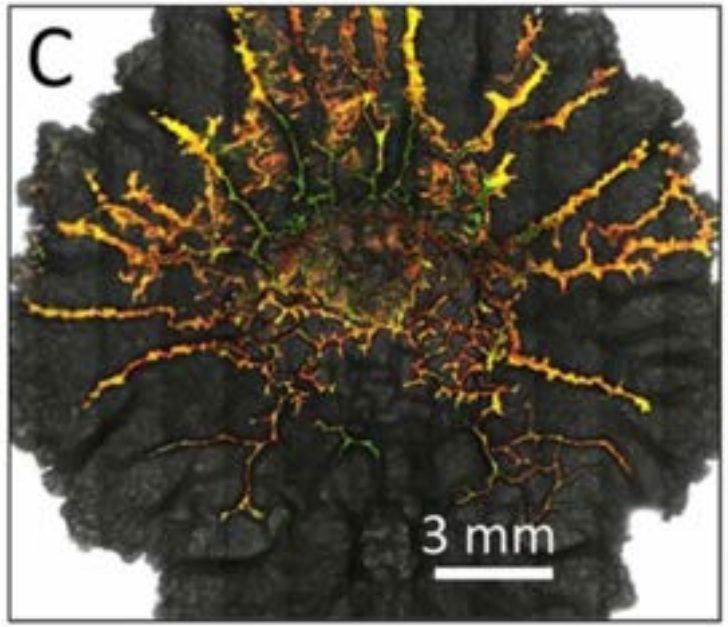


Cairns et al, 2014

L’emergenza di un sistema vascolare

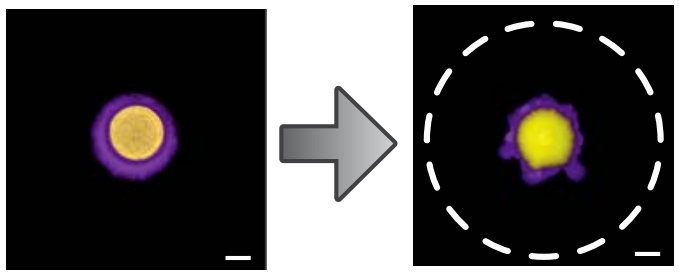


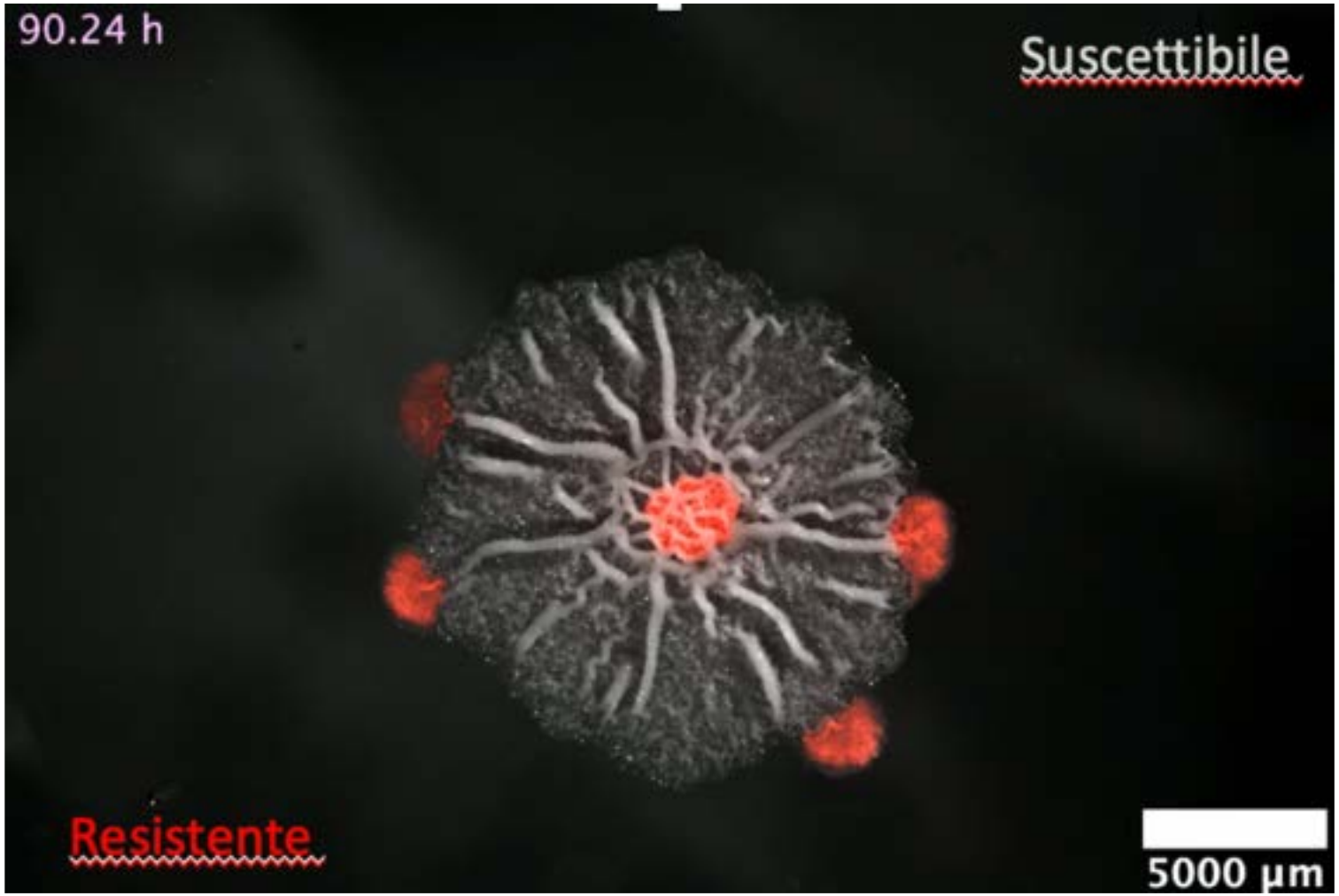




Wilking *et al*. PNAS **110** (2012)

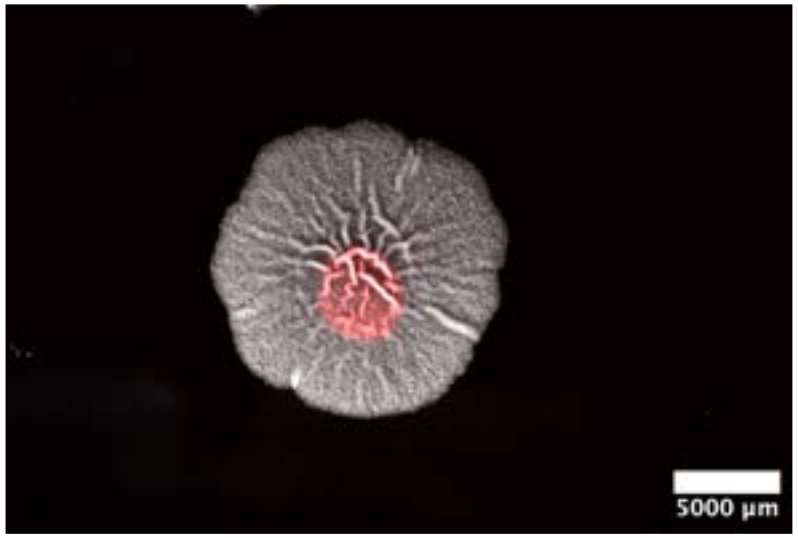
Conseguenze per la resistenza e la creazione di vie di fuga

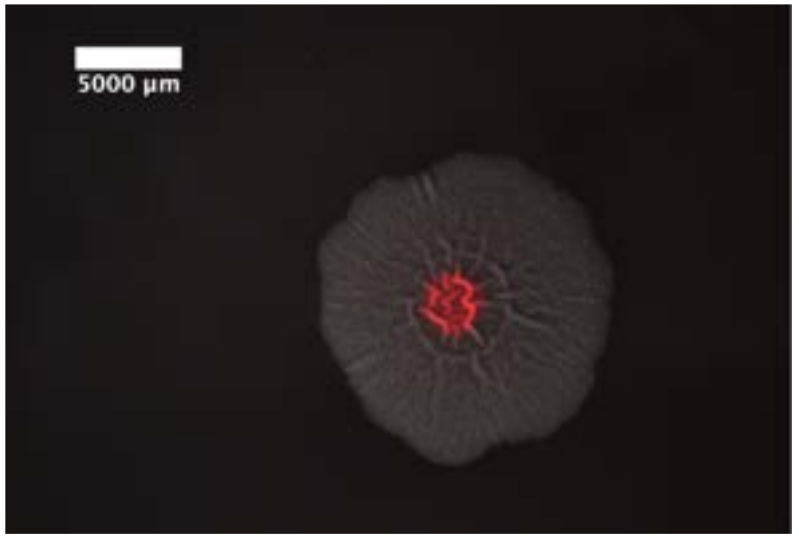


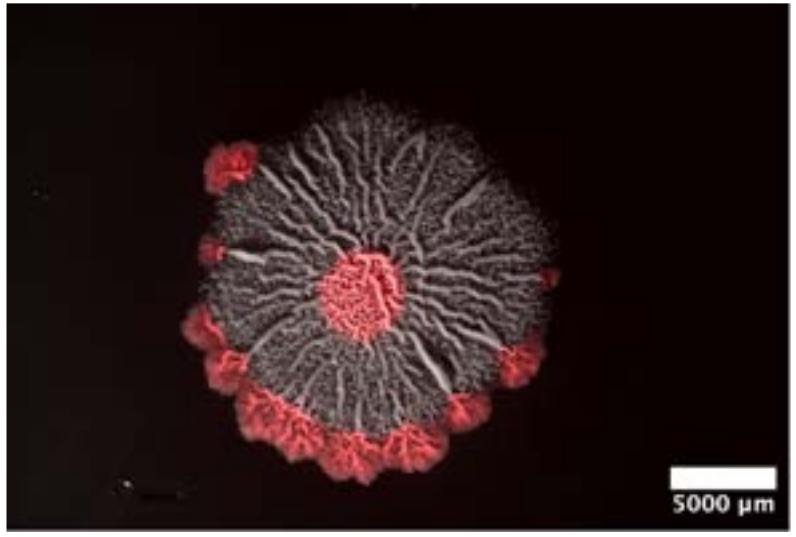


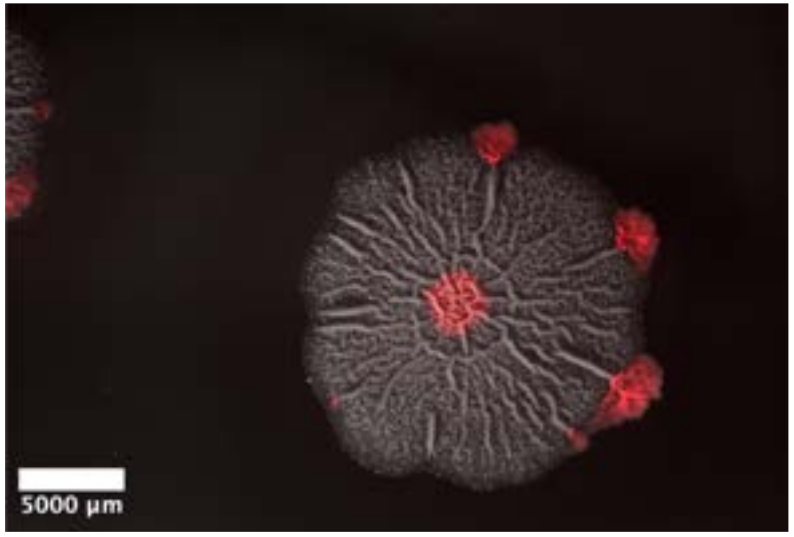
Krishnan et al, 2023

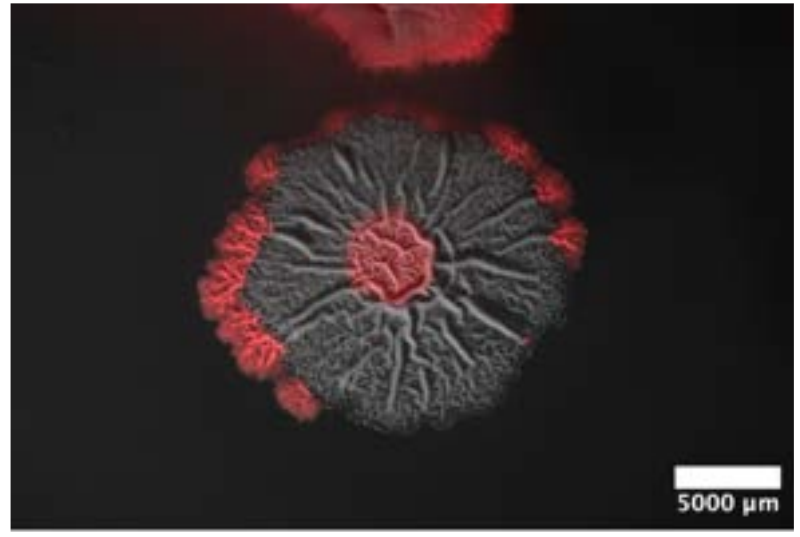
La fuga e’ riproducibile





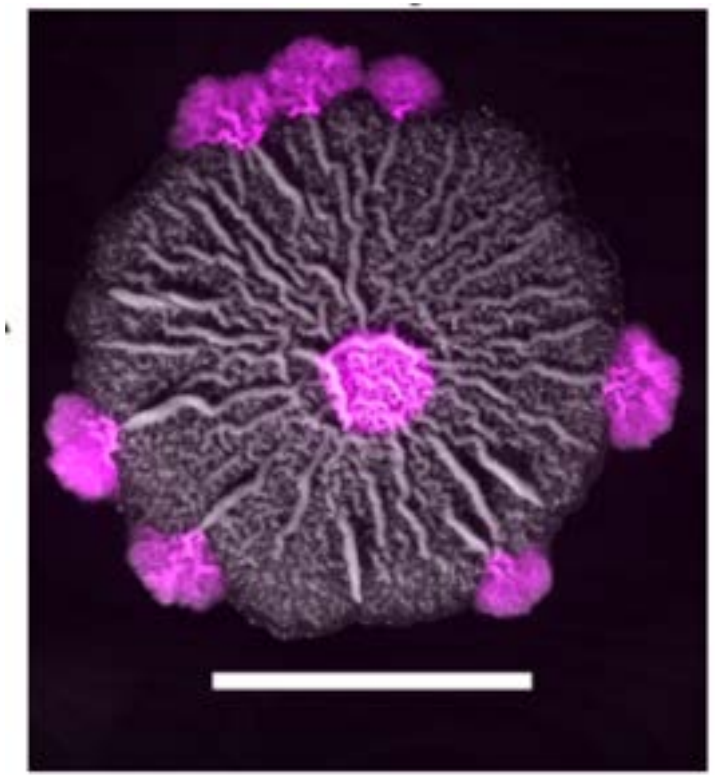




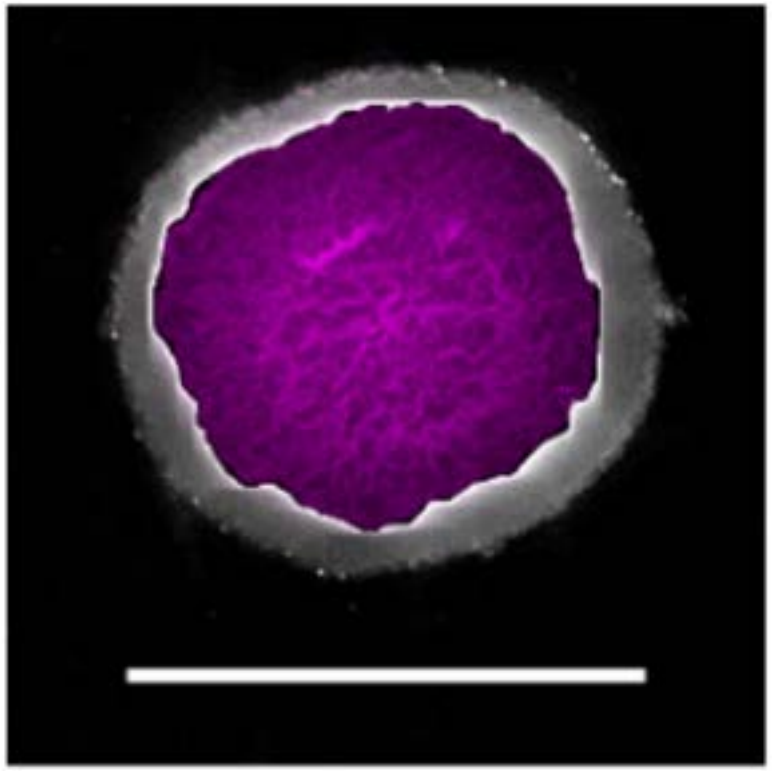


Ma non avviene senza matrice o senza cellule mobili

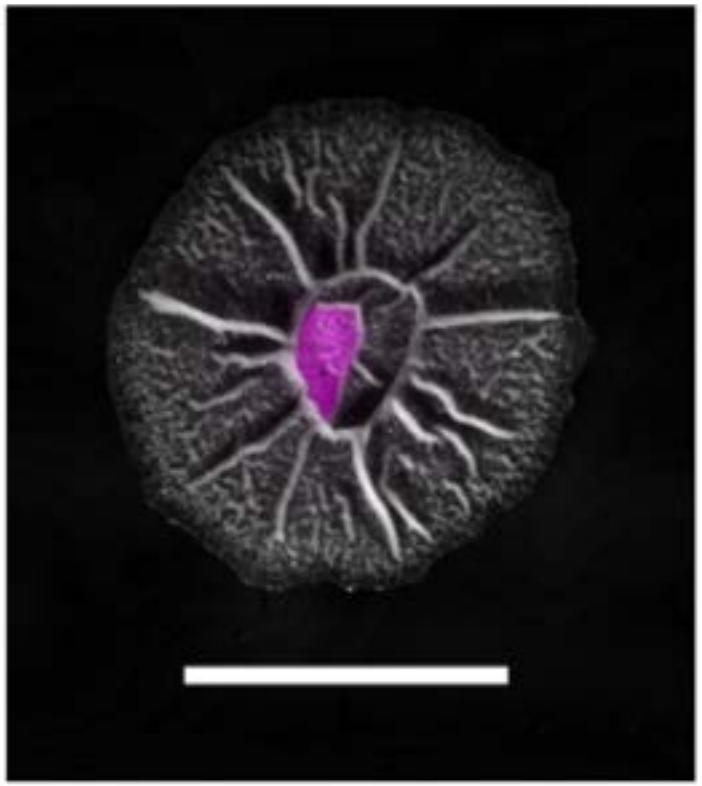
Controllo



Mancanza di matrice all'esterno



Mancanza di motilita' all'interno



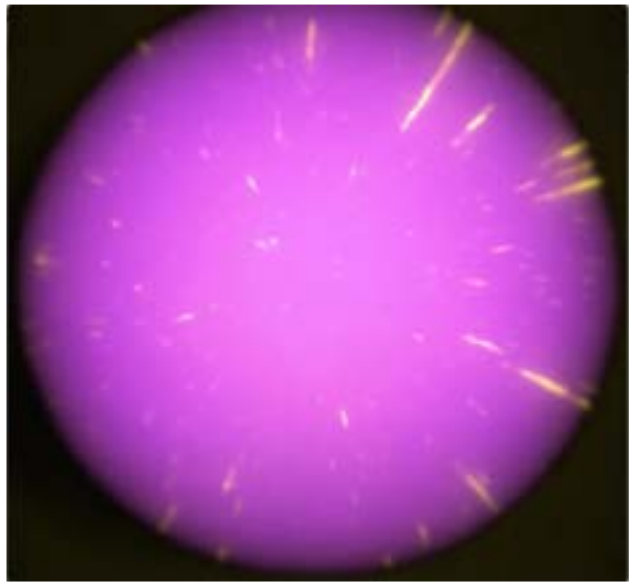
Differenziazione necessaria

Di cosa ho parlato

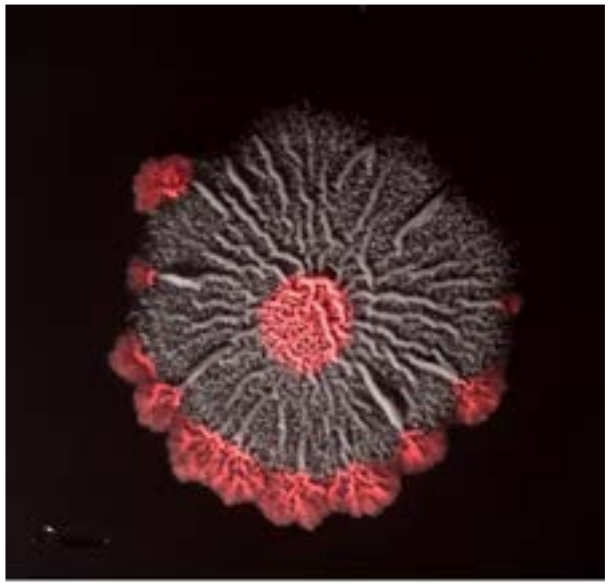
Usare batteri e modelli per capire fenomeni biologici

Resistant bacteria	*Number of cultures*
0	29
1	17
2	4
3	3
4	3
5	2
6– 10	5
11– 20	6
21– 50	7
51– 100	5
101– 200	2
201– 500	4
501–1000	0

Come la crescita spaziale genera una particolare distribuzione di resistenza



Come la differenziazione tipica dei biofilm permette loro di trovare sempre una via di fuga



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Aaron Smith
Hassan Alam
Joe Knight
Anna Tarodi
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Carolina Tropini, UBC
Joe Larkin, Boston U.
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