

# Persistent Maximum of Loops in Bacterial Protein Interaction Networks

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Joint work with Tim Downing (The Pirbright Institute, UK),  
being presented at the  
4th Workshop on Topological Methods in Data Analysis  
September 21, 2023, 3 p.m. Heidelberg, Germany  
– 3 a.m. in French Polynesia

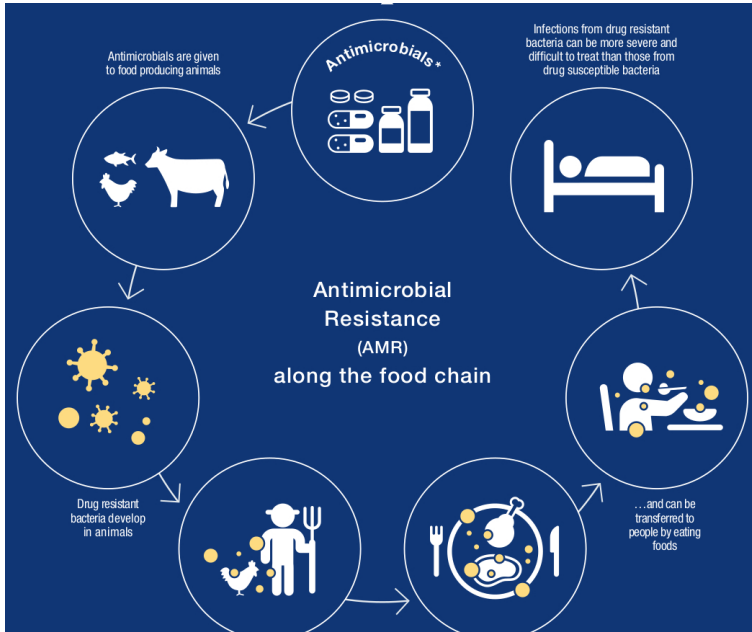
# Unleashing bacteria with antimicrobial resistance (AMR)



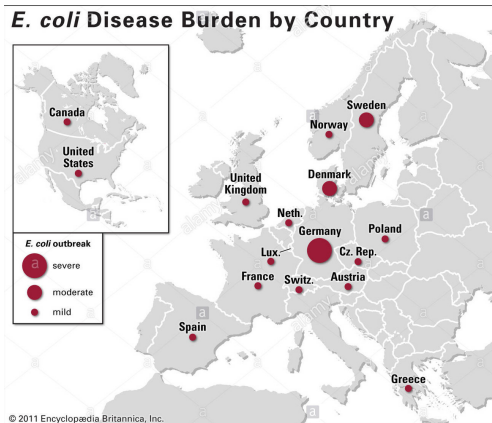
Wastewater from the Gud-dapatharam Industrial Area near Hyderabad, flowing into the Isnapur Lake. An antibiotics manufacturing facility owned by Au-robindo (Unit V) stands on the skyline.

There are quality standards for antibiotics, but no environmental standards for their production.

# Spread of antimicrobial resistance according to the WHO



# Escherichia coli ST131 spread in 2011

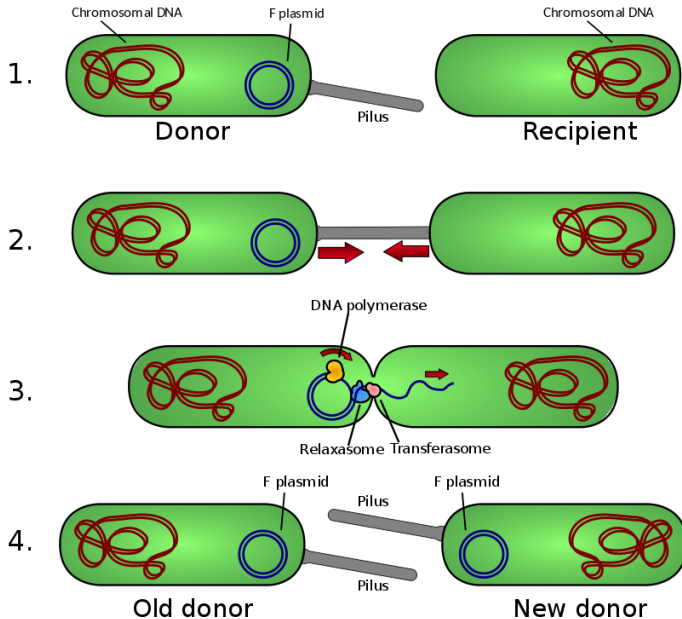


Key aspects in the pandemic spread of *E. coli* ST131:

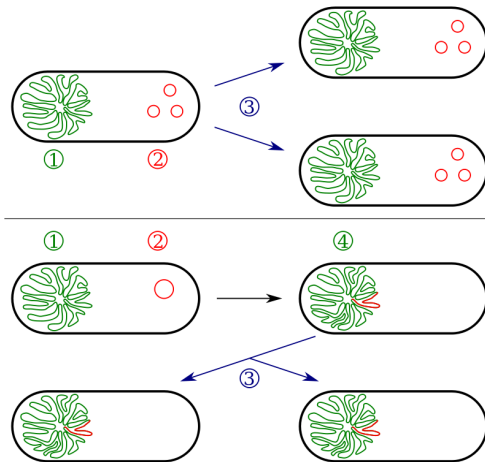
- ▶ Plasmid conjugation,
- ▶ recombination
- ▶ AMR gene repertoire.

⇒ Co-Evolvability of plasmids in the bacterial genome plays an important role.

# AMR transfer by plasmid conjugation



# Co-evolvability of plasmids in the bacterial genome

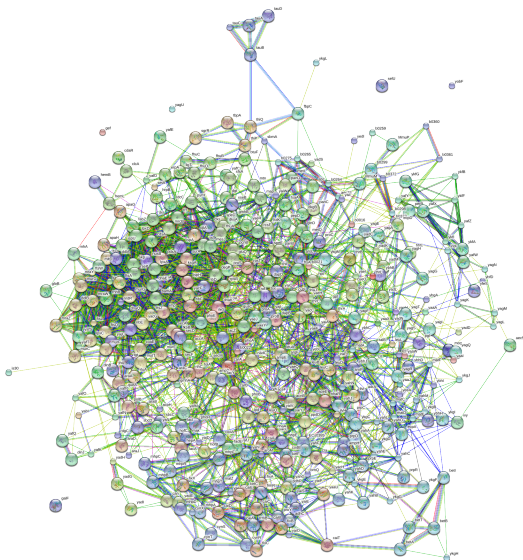


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Key aspects of the pandemic spread of *E. coli* ST131 :

- ▶ Plasmid conjugation,
- ▶ Integration of plasmids into the chromosome (co-evolvability)
- ▶ AMR gene pool.

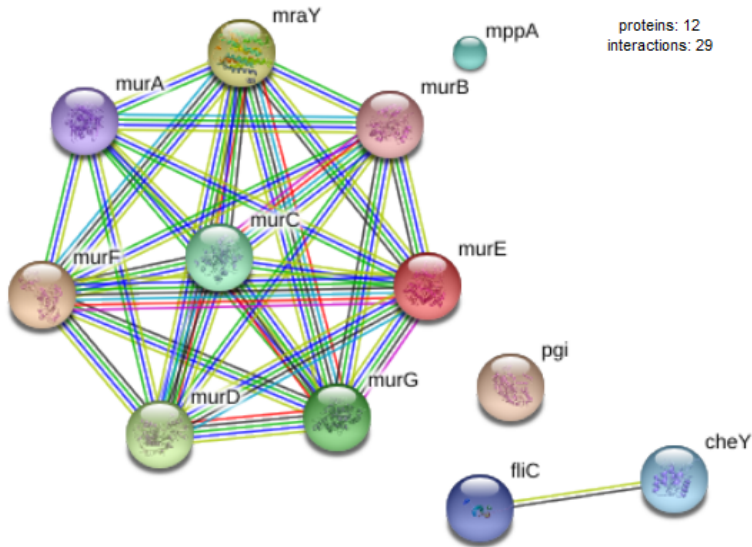
⇒ The co-evolvability of plasmids in the bacterial genome is playing an important role.



Protein-Protein Interaction Network (PPIN) of the *E. coli* ST131 chromosome. 4.146 proteins, 105.457 interactions.

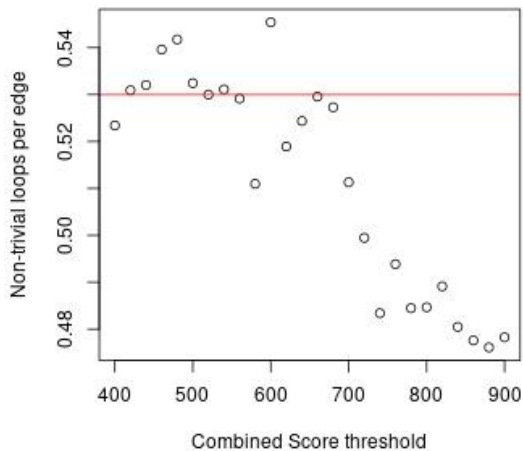
How to measure the integration of plasmids?

The “interactions” are edges weighted according to several biological criteria in a combined score





# Non-Trivial Loops per edge plotted vs. threshold



NLE = Non-Trivial Loops per Edge (interaction).

**Persistent Maximum of NLE (PMNLE):**

maximal value equal or less than NLE for an interval of 100 combined score units on the cut-off threshold, hence 6 consecutive NLE values in this coarse resolution.

# Scientific achievements

Work of Downing & R. shows: *PPINs are generally robust to the loss of plasmid proteins.* We examined:

$P_{\text{all}} = \text{PMNLE}$  for all proteins

and  $P_{\text{chromosomal}} = \text{PMNLE}$  for chromosomal proteins only.

$\Rightarrow P_{\text{all}} - P_{\text{chromosomal}}$  indicates plasmid-driven effects.

471 out of 489 samples had very low  $P_{\text{all}} - P_{\text{chromosomal}}$

$\Rightarrow$  plasmid-encoded proteins had no large effects on the PPIN structure.

71% more connected components when passing from full PPIN to chromosomal PPIN.

18 out of 489 samples had  $P_{\text{all}} - P_{\text{chromosomal}}$  exceeding two standard deviations.

327% more connected components when passing from full PPIN to chromosomal PPIN.  $\Rightarrow$  *Plasmid-encoded proteins play a central role in the PPIN, high co-evolvability in these 18 bacteria.*

## What can be done against AMR spread?

Constructive answers to this question are not scientific, but political. For instance:

- ▶ Impose environmental standards upon importation of antibiotics,
- ▶ Revert from industrial meat production to traditional ways of keeping livestock, with lower density, hence lower output but no necessity to give antibiotics to farm animals,
- ▶ etc.

Identification of plasmid genes is prone to errors:

- ▶ Typically plasmid-bound genes can have already entered the chromosome in certain bacteria,
- ▶ Different names can have been given to the same plasmid, when the classifying lab did not see the match.

⇒ Maybe the noise is stronger than the signal.

Thank you

Thank you very much  
for your attention !