



Abstract

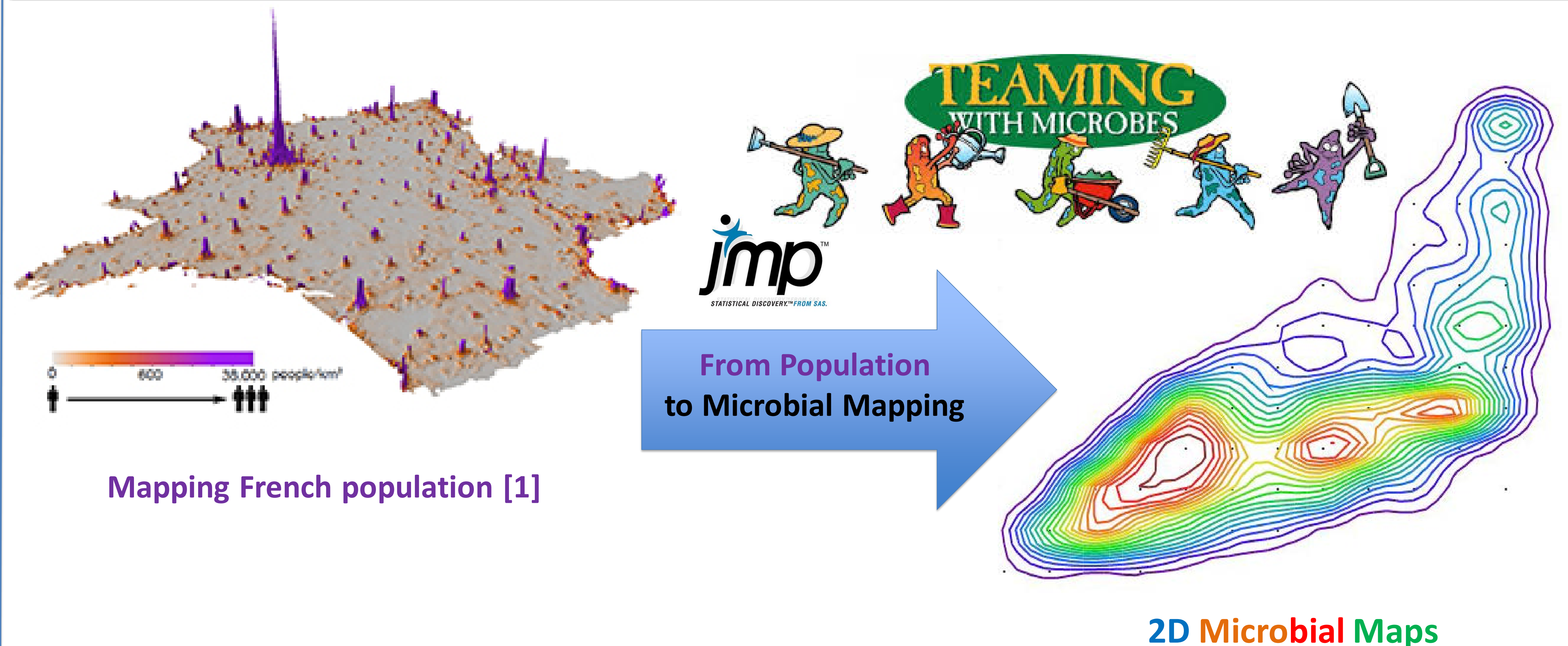
➤ Antimicrobial Resistance is a complex and dynamic process that may involve non-susceptibility to more than one antibiotic, causing what is called multi-drug resistance (**MDR**). Understanding and measuring MDR is critical for drug design, development and for assessing the clinical situation.

➤ The susceptibility of bacteria to antibiotics is usually assessed by appropriate *in vitro* test systems in which we determine the so-called minimal inhibitory concentration (**MIC**; a lower MIC denotes a more active antibiotic)

➤ Cross-resistance to two antibiotics is usually reported on Y-X graphs, on which the distribution of the population of microorganism collected in a given environment is shown by numbers (see Results; Figure A). These graphs are not visually appealing and the information cannot be easily grasped.

➤ JMP software has allowed to present the data in an innovative, informative and eye-catching form.

The basic idea: using known mapping approaches to describe cross-resistance



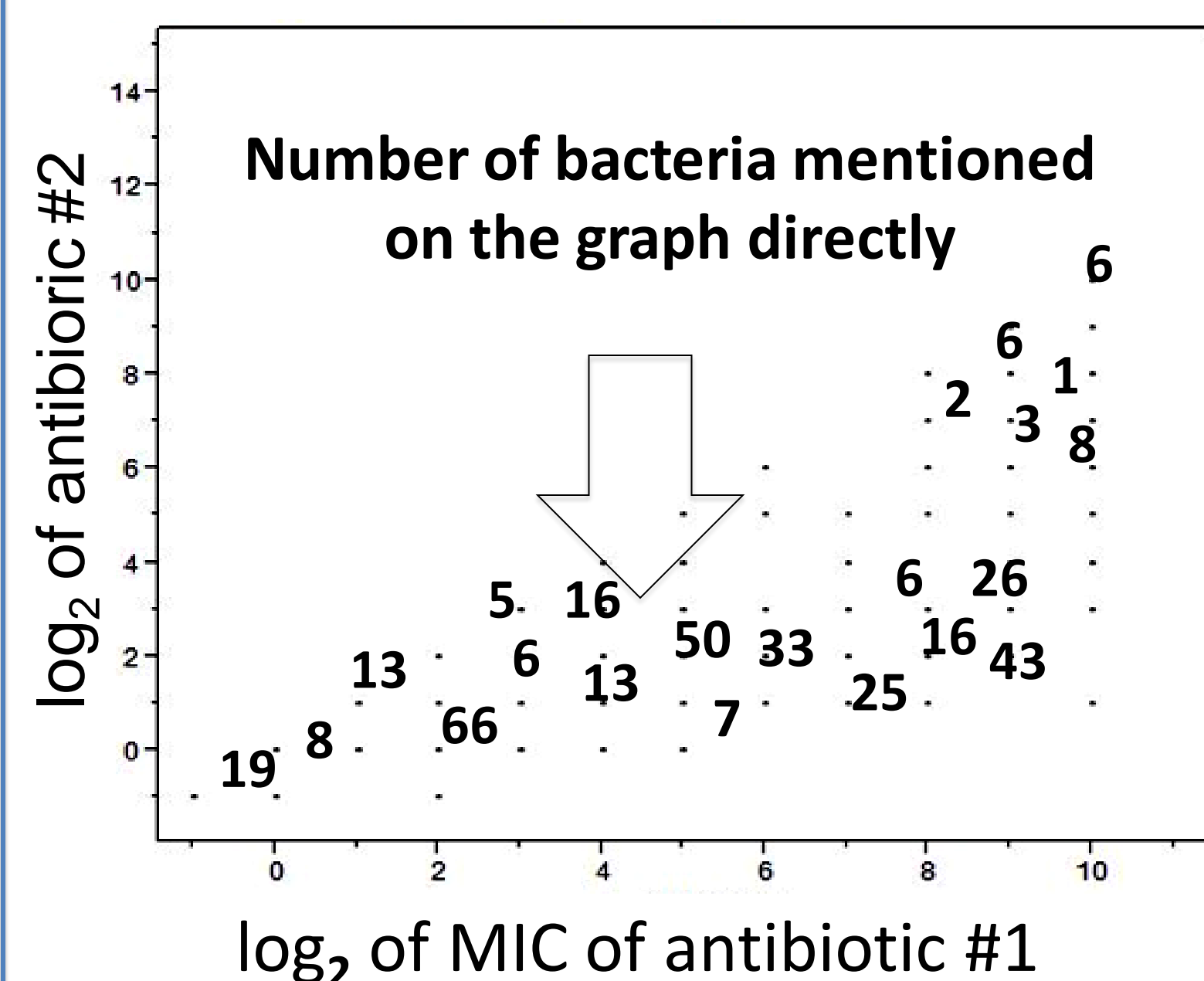
- ❑ Generation of **2 Dimensions Microbial Maps (2DMM)** against pairs of antimicrobials to quantify cross-resistance (basic studies)
- ❑ Use of the **2DMM** as a basis for clinical practice guidelines about antimicrobial efficacy in specific bacterial population (e.g. bacteria isolate from patients with community-acquired pneumonia)
- ❑ Assessment of the corrective action of inhibitors/modulators of bacterial resistance (drug development studies)

Methods

- Maps were fitted using quantile density contour analysis (JMP® versions 10.0.2, SAS Institute Inc, Cary, NC).
- Contour interval analysis can be generated in colored or black and white density levels using JMP® Graph Builder.

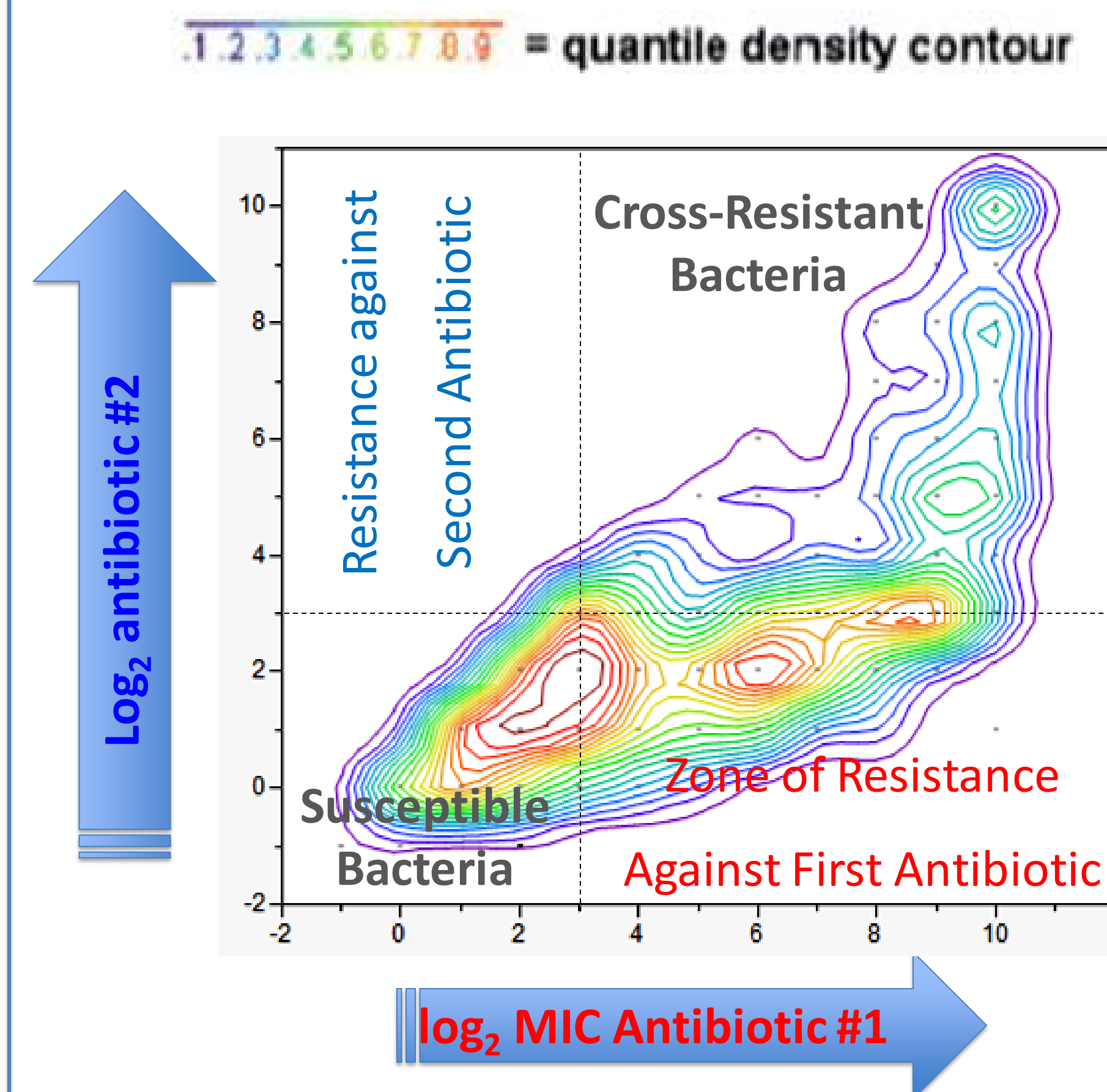
Results

Figure A.
Basic Method for plotting the microbial cross resistance.



- Foggy Method with difficult reading and interpretation.

Figure B. Microbial Resistance Mapping using the *In Vitro* antimicrobial activity data using the Contour Interval Analysis JMP® Method . This method was published for the first time in the *Journal of Antimicrobial Chemotherapy* [2].



- The colors (from cold to warm) show the density (from low to high) of the bacteria with respect to their MICs for the 2 antibiotics (abscissa and ordinate)
- The vertical and horizontal show the limits of clinical susceptibility
- Bacteria that are in the left lower quadrant susceptible to both antibiotics, while bacteria in the right upper quadrant are resistant to both antibiotics.
- This type of graph shows immediately that there are two main populations in this sample of 390 isolates, with about half being susceptible to both antibiotics and the other half only susceptible to antibiotic #2. Only a small proportion of bacteria is resistant to both antibiotics.

Conclusions

- ✓ Simple presentation of the distribution of the bacterial population *vis-à-vis* existing as well as novel antimicrobials.
- ✓ Easy tracking for the fluctuations of antimicrobial resistance when new resistance mechanisms are emerging.
- ✓ As for population cartography, **2D Microbial Maps (2DMM)** could be established by research centers and communicated to clinicians as guidelines for efficient antimicrobial usage.

References and Acknowledgments

- [1] <http://www.uclouvain.be/481519.html>
- [2] Chalhoub *et al.* Journal of Antimicrobial Chemotherapy, 2014, *in press*.
 - Other microbial mapping studies done by our laboratory (Lemaire *et al.*, Chalhoub *et al.*) are available at: <http://www.facm.ucl.ac.be/posters.htm>
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