Supplementary section

Formation of droplets: Aqueous droplets containing bacteria are formed injecting the bacterial suspension, mineral and hydrofluoroether (HFE) oils into the cross junction CrossB with the bore diameter 0.5mm (P-634, Upchurch Scientific), as shown in Fig.1a and on the photo in Fig.1S(a). The linear dimensions of the junction achieves 25mm. To avoid the coalescence of the neighboring reservoirs and the wetting on the tube's wall, 0.006% of highly biocompatible tri-block copolymer surfactant is added to the HFE oil[6]. Mineral oil droplets are aimed to separate the reservoirs with bacteria. Mineral oil was chosen for this purpose, as it is immiscible with continuous phase oil and the aqueous medium. The resulting length of the droplets is about ~0.75mm, volume is about~100nl, polydispersity of the droplets is less than 3% in a tube with an inner diameter of 0.5 mm. Further, droplets are stored and manipulated in the transparent tubing (see Fig.1S(b)).

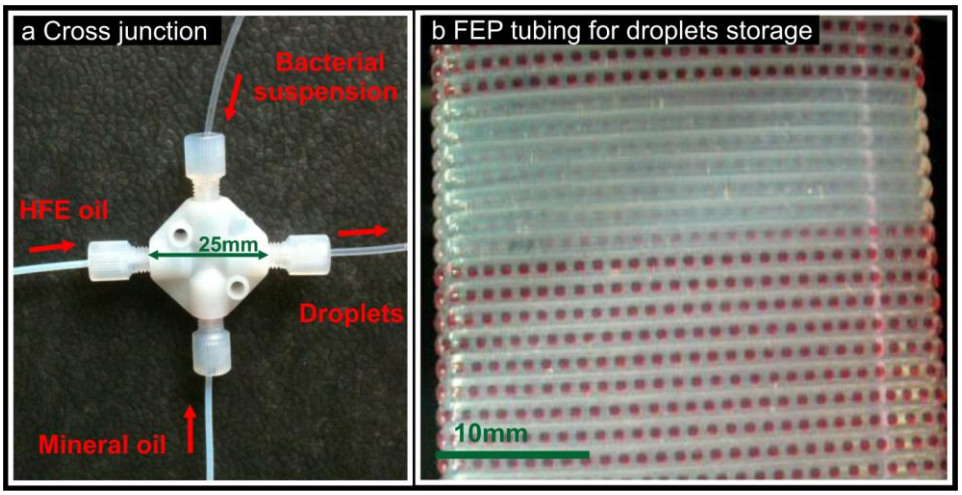

Fig.1S Formation and storage of the droplets in the MDA. (a) Droplets are formed in the cross junction, injecting through the inlets the bacterial suspension, HFE oil and mineral oils. The (b) The holder for the FEP tubing - to store and to manipulate the train of droplets. The length of the FEP tubing is about 7m.

The direction of the fluid flow during droplets formation and further operation of the device is controlled by the electric valves V1, V2, V3 (3-Way LFRX0500500B and 2-Way LFVA1230413H, Lee Company).

FEP tubing characteristics: We use tubes made of Teflon (FEP) for ensuring a good wettability of the continuous phase, and therefore to prohibit that droplets stick on the wall when they are manipulated and stored inside the tubes (see Fig.1S(b)). Note that the total length of the FEP tube necessary to operate 10^3 droplets lies in the range of 6 - 7 m, which induces a non-negligible hydraulic resistance. Because of the elastic properties of the tube (elastic modulus close to 0.34 GPa), the pressure needed for creating and manipulating the droplets causes a substantial inertia of the device, i.e. a transient phase has to be taken into account before obtaining a regular train of monodisperse droplets and a constant droplet velocity.

Bacterial incubation: First, the MC4100-YFP strain was streaked out on Luria Broth (LB) agar[36] containing 100 μg/mL ampicillin (the strain carries an ampicillin resistance gene) and then grown overnight at 37°C. The next day, a few colonies were picked and used to inoculate 5ml LB medium, containing ampicillin. The incubation is performed in test tubes under agitation at 600 rpm for 5-6 h at 37° C. The incubation is stopped when the bacterial populations reach mid-exponential growth phase with an optical density (OD_{600}) of the culture close to 1, equivalent to ~ 4 x 10^8 cells/mL.

Bacterial inocula of varying size were prepared by diluting pre-incubated exponential-phase cells in LB medium followed by encapsulation in drops for the calibration of the detection module. The MIC assays were done using cefotaxime (CTX), a 3rd generation cephalosporin that belongs to the β-lactam antibiotics[23]. To prepare CTX solutions of varying concentrations, a stock CTX solution of 100 μg/mL was diluted in LB medium.

Comparison of the step sizes (MDA vs 96 microplate): The precision of the determination of MIC is substantially increased compared to the standard techniques, because the step-size of the changes of the antibiotics concentrations between the neighboring cultures in our device is much smaller. For instance, MDA provides the step-size about ≤1% of the initial concentrations, according to the empirical formula $\Delta C \sim (C_{MAX}\text{-}C_{MIN})/N^g_D$. The microplate technique allows to form 100% differences of the concentrations during the serial 2-fold dilutions. This statement is displayed in Fig.2S, where the cefotaxime concentration is calibrated against number of droplets for MDA (shown in blue) and number of dilution steps for the microplate (shown in red).

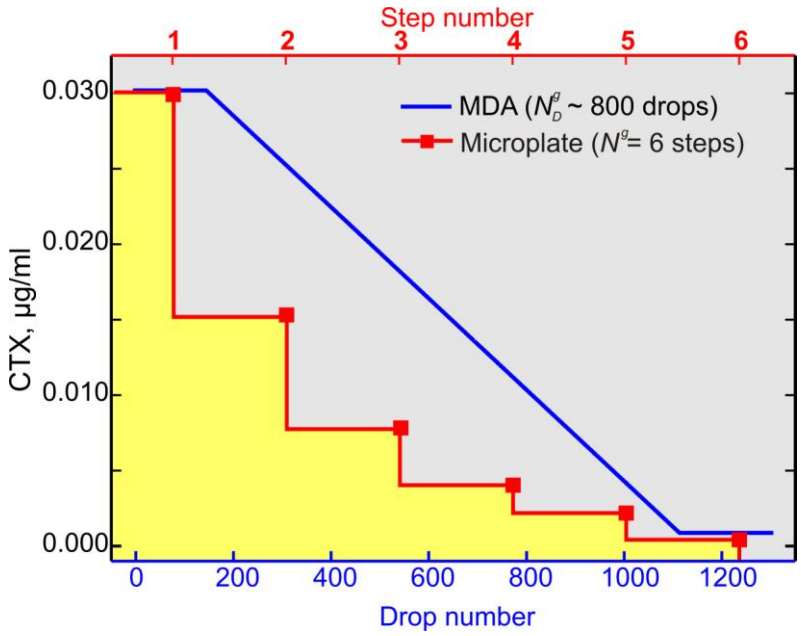

Fig.2S Comparison of the dilution steps in MDA and 96 microplate.

One can see that the concentration range of 0.03-0.0015μg/ml is covered by N^g_D ~800 droplets using MDA and only by six 2-fold dilution steps using a microplate method. This fact undoubtedly helps to increase substantially the performance of the MIC assays.