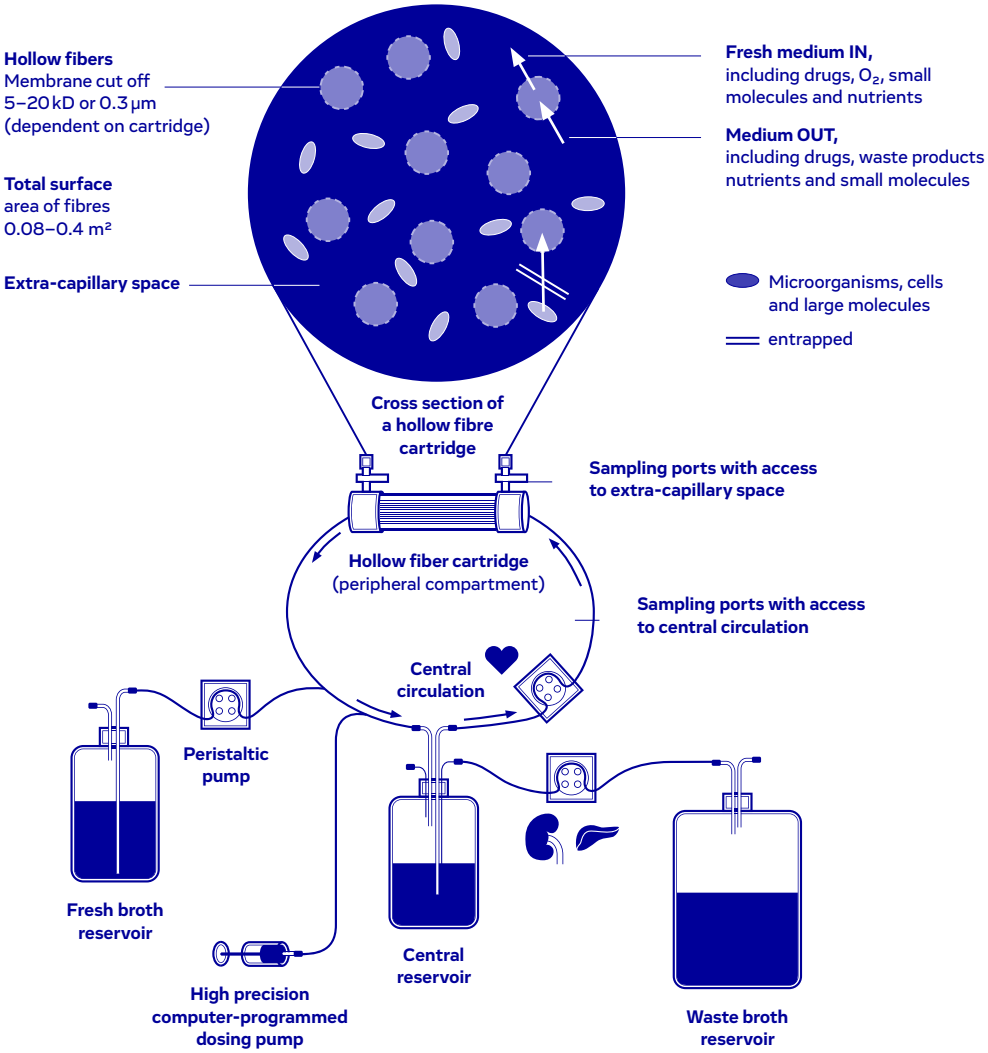
evotec

#RESEARCHNEVERSTOPS

The Hollow Fibre Infection Model (HFIM)

- State-of-the-art BSL2 facilities dedicated to the Hollow Fibre System
- Study duration ranging from a few hours to 6 weeks using a range of microorganisms including Gram negative bacteria, extracellular *M. tuberculosis* and fungal pathogens
- Ability to develop new HFIMs using strains with a wide range of antimicrobial susceptibility profiles and well-characterised resistance mechanisms



The ultimate goal of nonclinical PK/PD in the anti-infectives area is to understand the microbial response to antimicrobial treatment, enabling optimisation of dosing regimens to maximise the efficacy of an antimicrobial compound, minimise toxicity and minimise the risks of antimicrobial resistance.

The HFIM is an *in vitro* system consisting of two principle compartments:

I. A central reservoir and associated tubing, which constitutes a circulating system
II. A hollow fibre cartridge consisting of a sealed tube housing thousands of hollow permeable fibres, representing a peripheral infection site containing the target microorganism.

Evotec's HFIM capabilities

- **Dedicated facilities for *in vitro* PK/PD analysis in the Hollow Fibre Infection Model**
  - HFIM laboratory space at BSL2 with five tall double incubators and a CO_2 incubator
  - Up to 34 cartridges (depending on model type and duration) can be run in parallel for different organisms or variable drug infusion and clearance rates with study duration from hours to 6 weeks
  - A team of scientists trained in setting up and running the system
  - Full microbiology support
  - BioA facilities for LC-MS analysis of PK samples
  - A dedicated PK/PD modelling team

- **Significant experience in establishing models and performing studies**
  - Development of new infection models using reference or clinical isolates of different bacterial and fungal species
  - Mathematical modelling to establish experimental parameters required to mirror human or animal PK profiles in single and multi-drug studies
  - Combination studies with up to four individual compounds
  - Dose-response and dose-fractionation studies to determine pharmacodynamic driver and magnitude of effect
  - Studies to monitor the emergence of resistance in response to treatment, determination of mutant prevention window and identification of mechanism of resistance

- **Can be adapted for a range of organisms including strains that cannot be used for *in vivo* studies.**
  Current experience includes:
  - *Mycobacterium tuberculosis* H37Ra
  - *Acinetobacter baumannii*
  - *Klebsiella pneumoniae*
  - *Escherichia coli*
  - *Pseudomonas aeruginosa*
  - *Aspergillus fumigatus*

- **Hollow Fibre Infection System for TB**
  - Performance of HFIM using *Mycobacterium tuberculosis (M.tb)* avirulent strain (– H37Ra)
  - Single drug or multi-drug combination PK/PD resistance studies
  - Evaluation against replicating and semi-dormant *M.tb*
  - Intracellular system under development