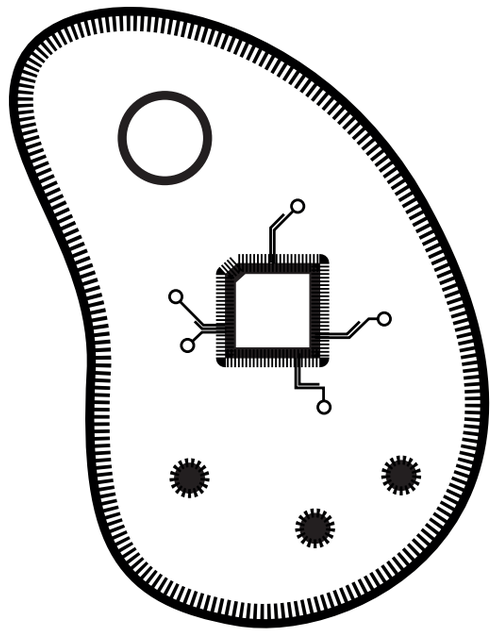
Ingénierie de bactéries programmables pour le diagnostic



Jerome Bonnet

Synthetic biology Group

Centre de Biologie Structurale (CBS), INSERM, CNRS, Université de Montpellier, France

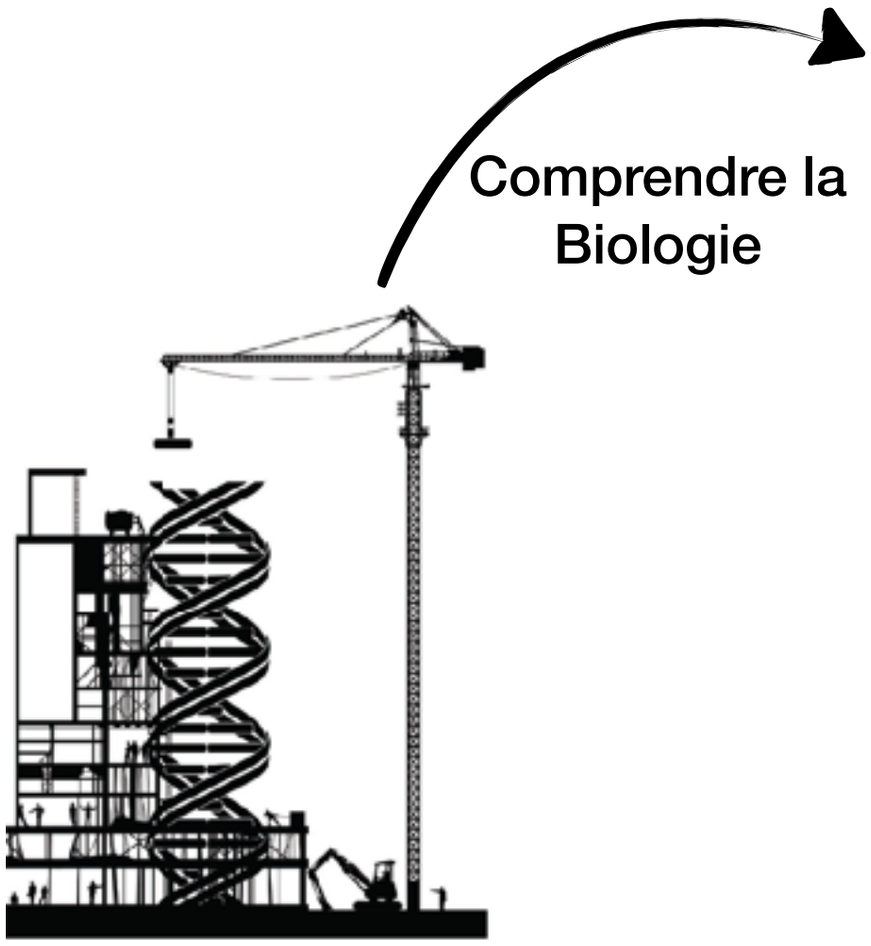
jerome.bonnet@inserm.fr

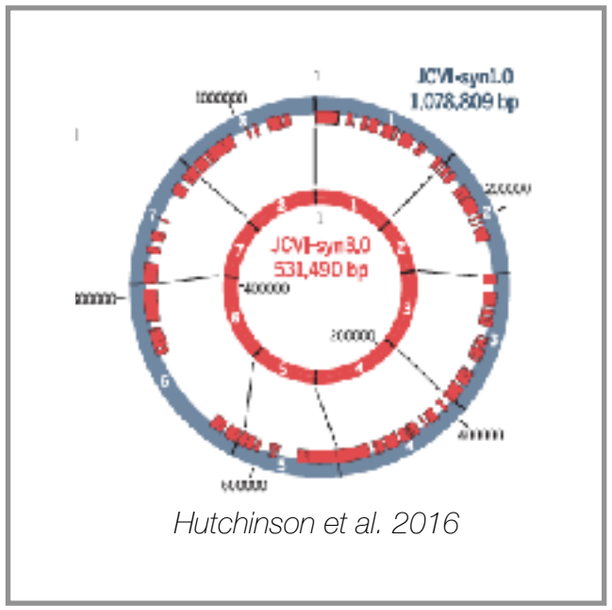
13eme journées ITS 7 & 8 Novembre 2022

aviesan
alliance nationale
pour les sciences de la vie et de la santé

CBS Inserm cnrs

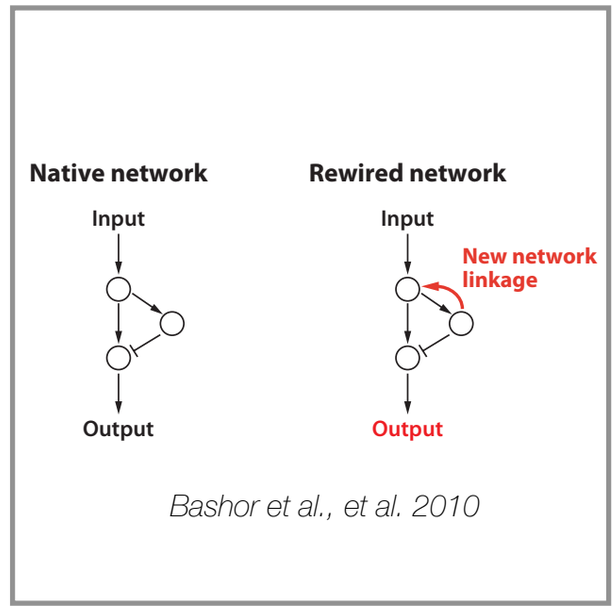
Biologie synthétique: ingénierie de nouveaux systèmes et fonctions biologiques





Hutchinson et al. 2016

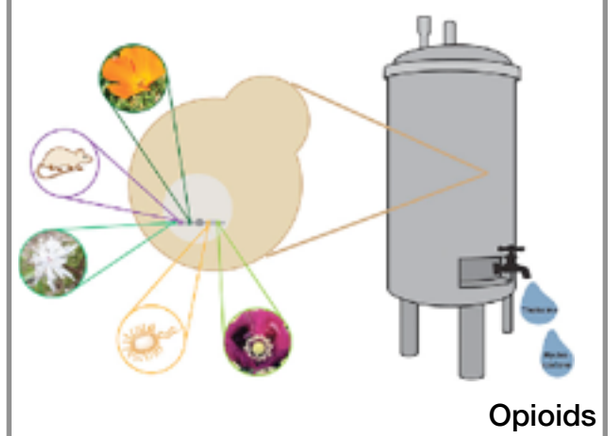
Synthetic genomes



Bashor et al., et al. 2010

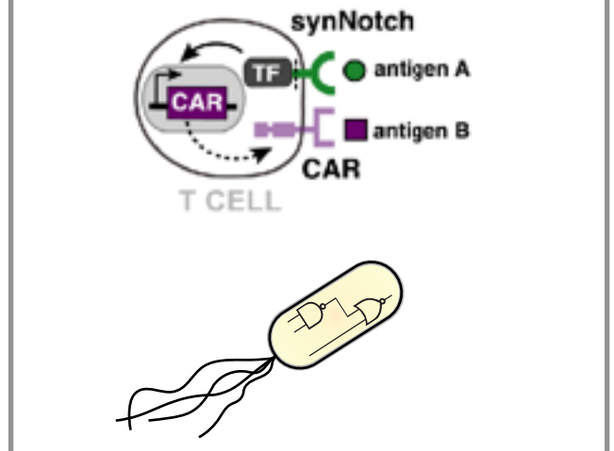
Synthetic signaling

Drug production



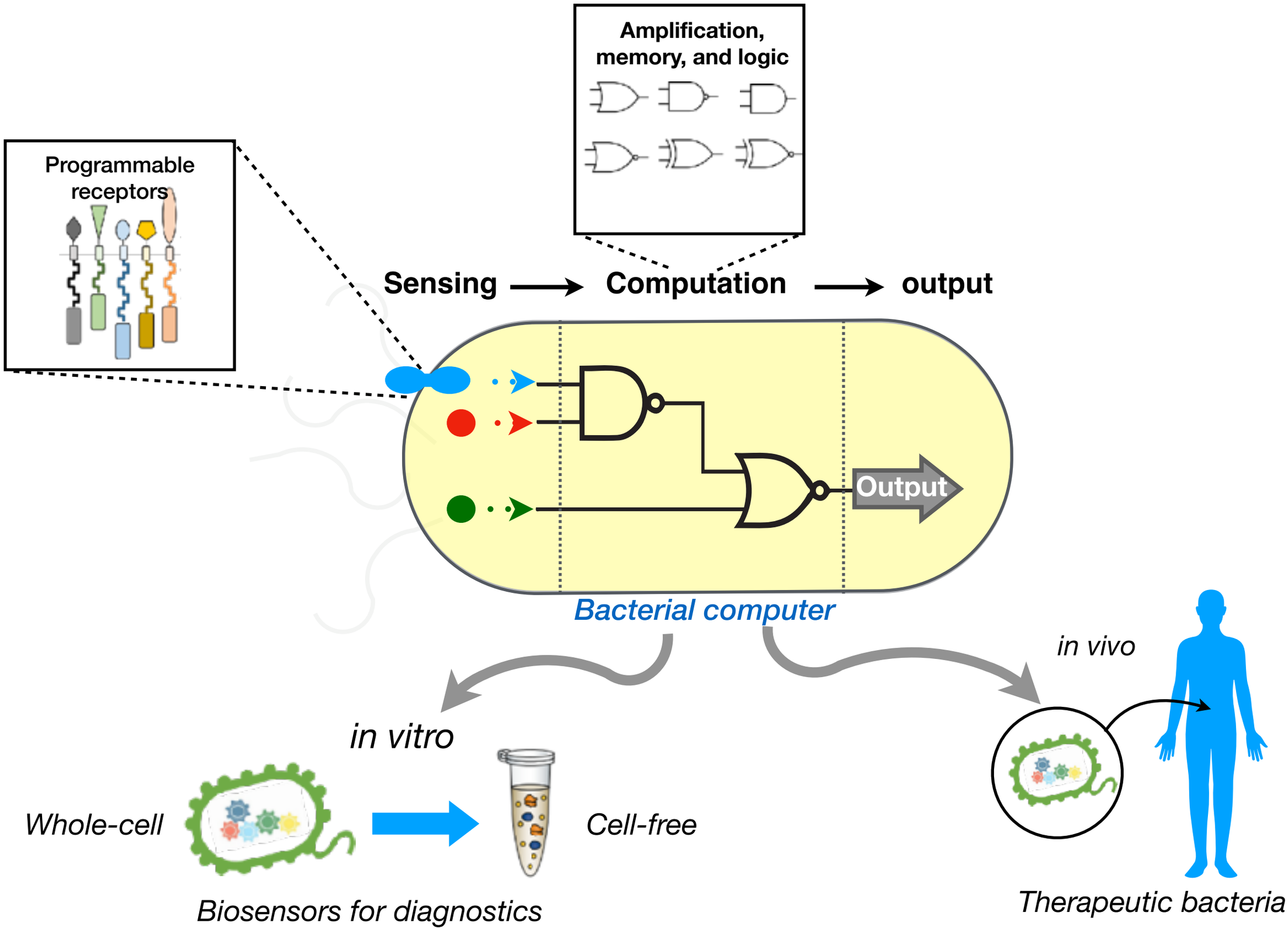
Galanie et al. 2016

Diagnosis and Therapeutic cells

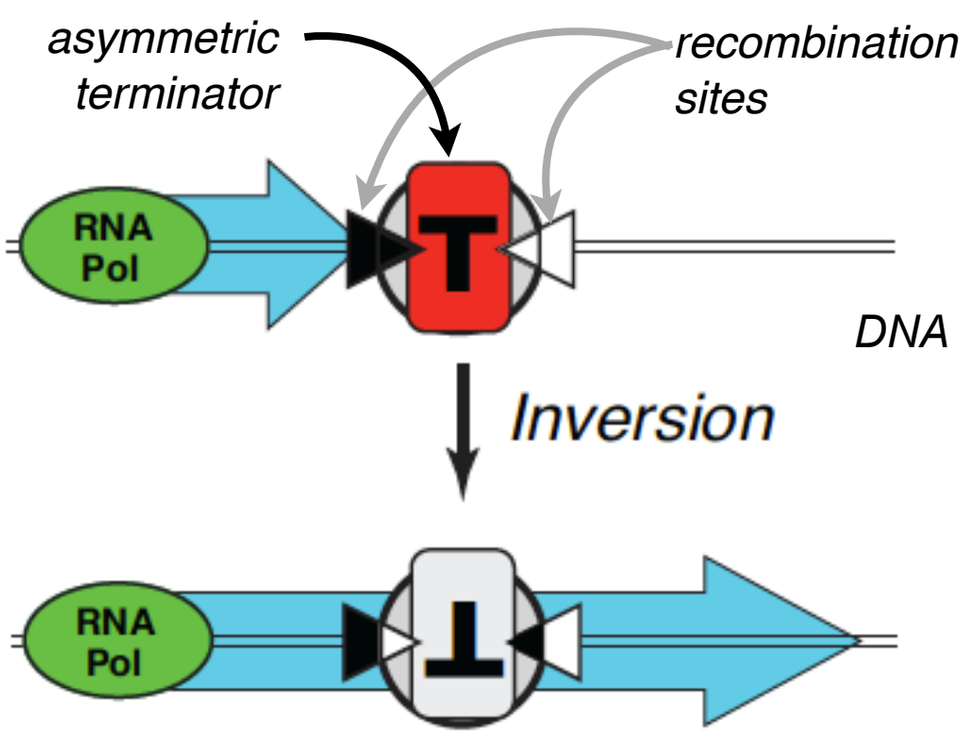


Roybal et al. 2016

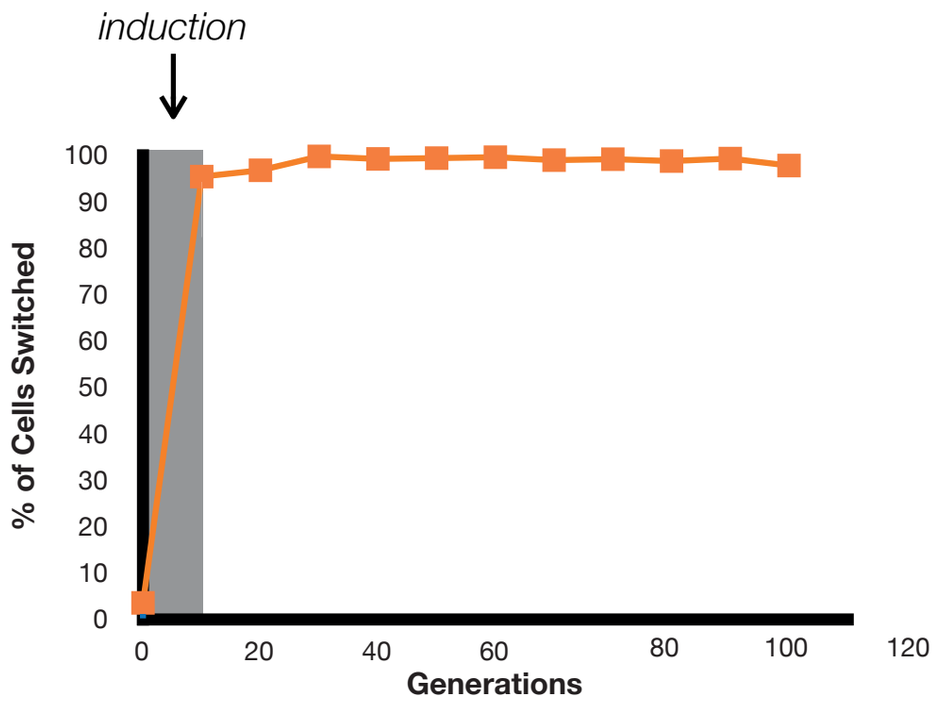
Des bactéries programmables pour le diagnostic et la thérapie



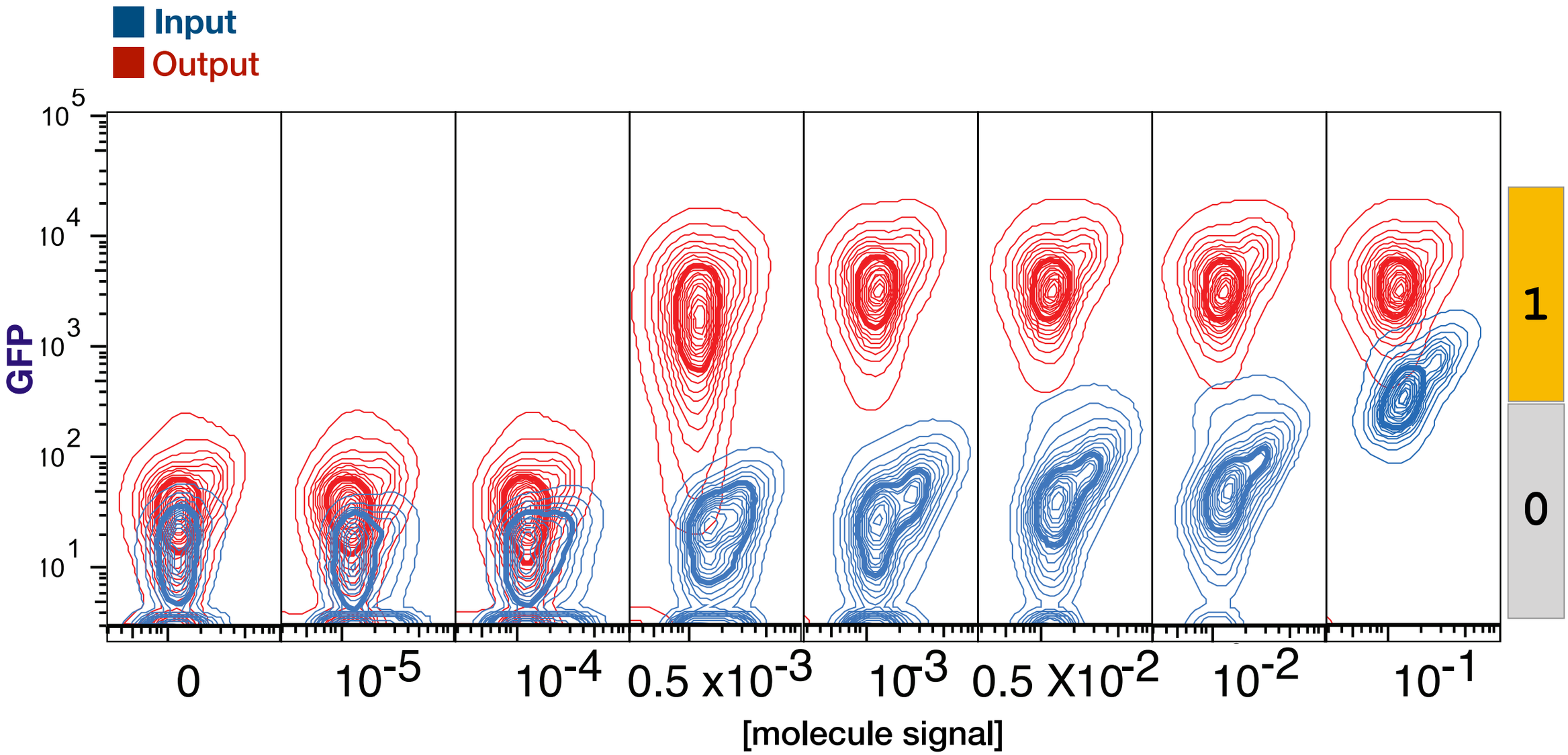
Interrupteurs génétiques a recombinases



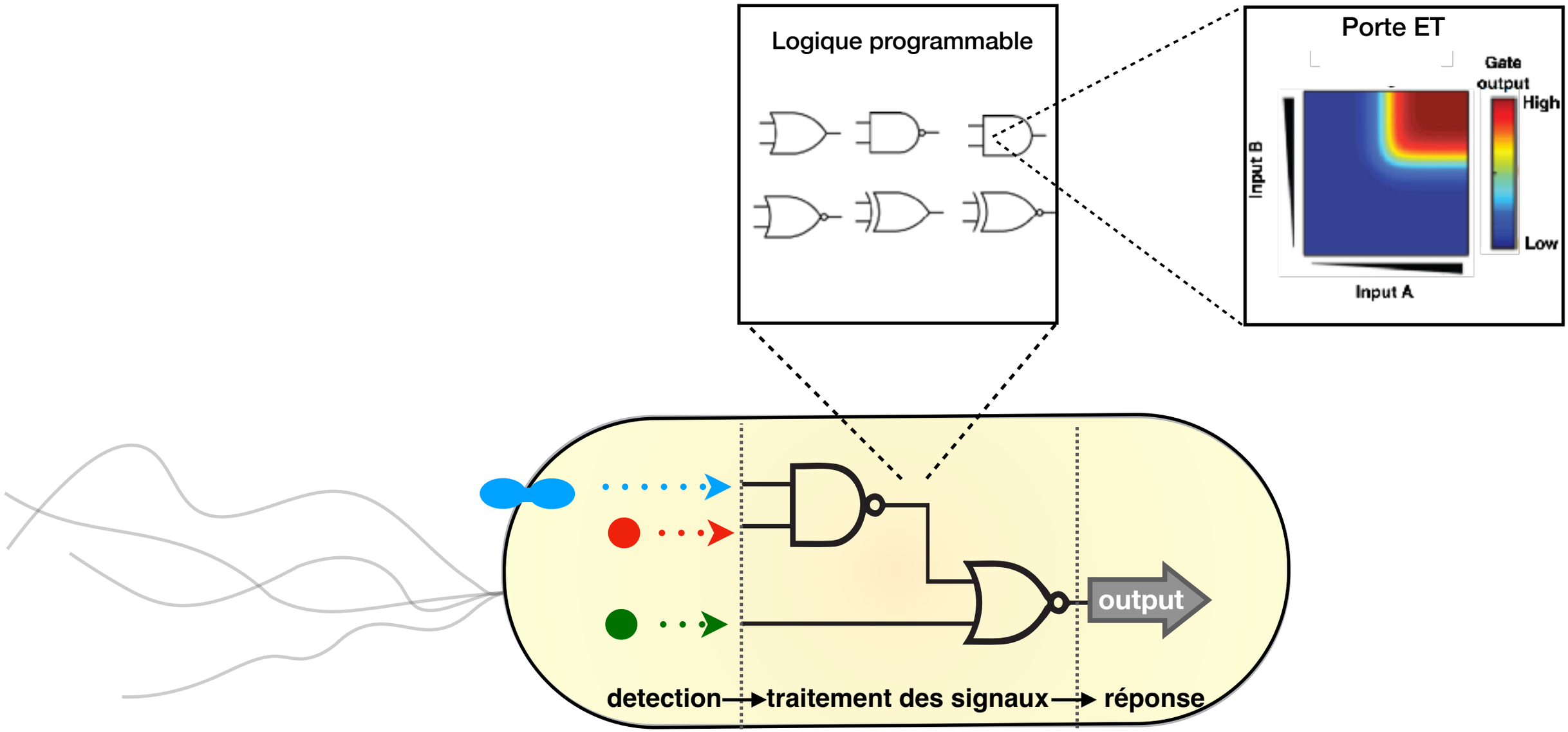
Stockage ADN > 100 generations



Amplification et Numérisation



Programmer le comportement cellulaire

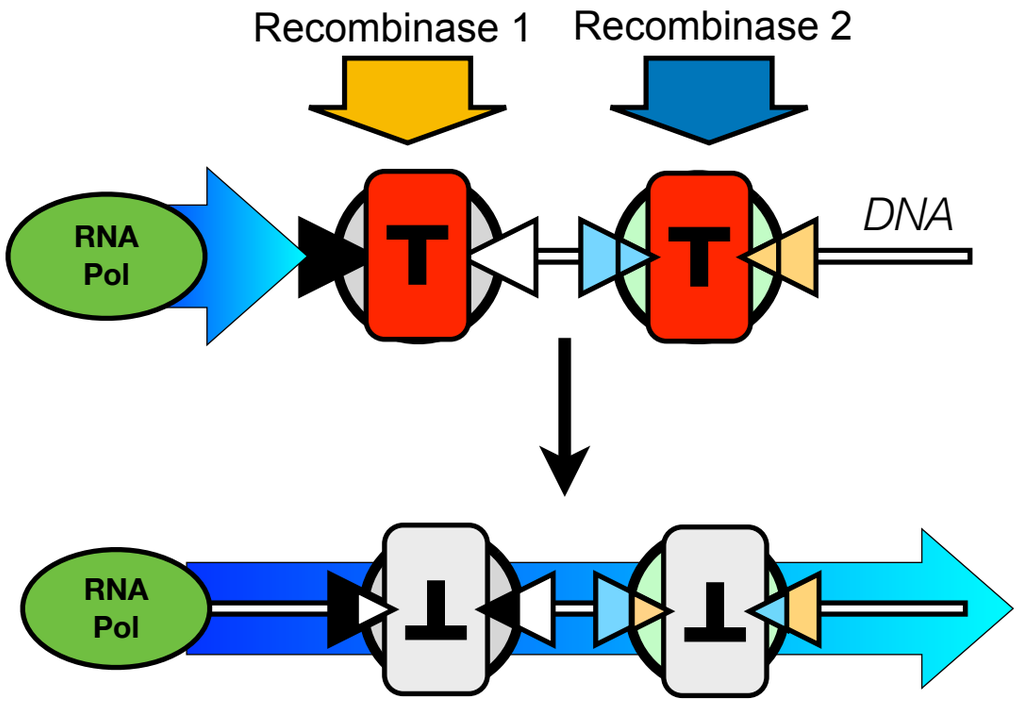


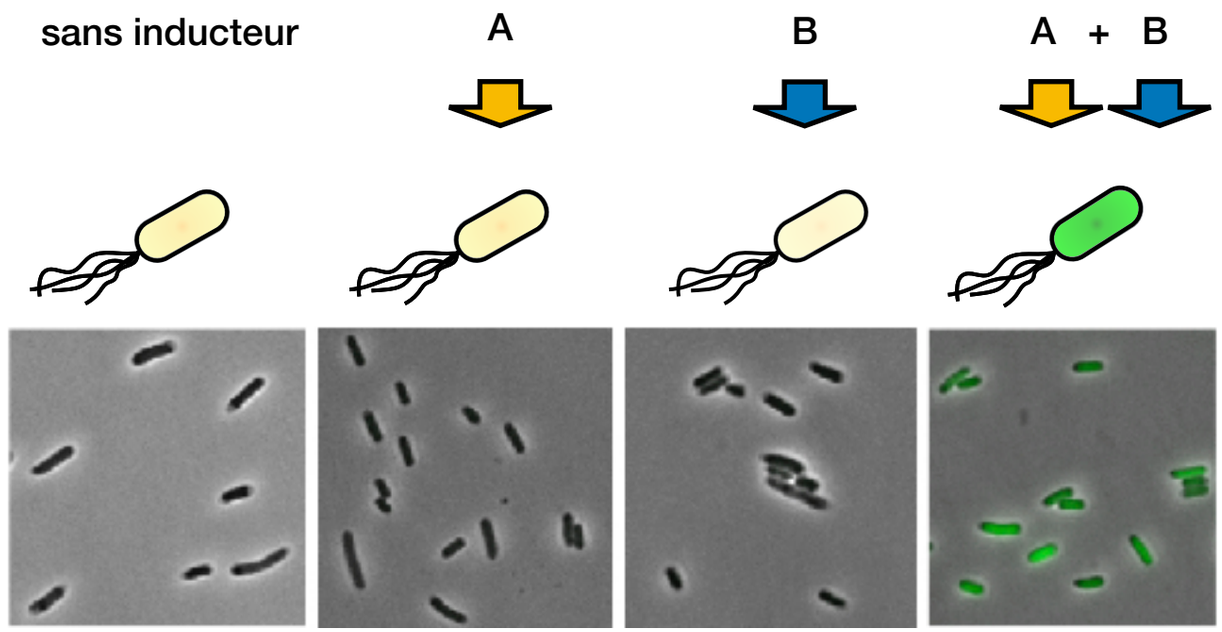
Bacterial computer

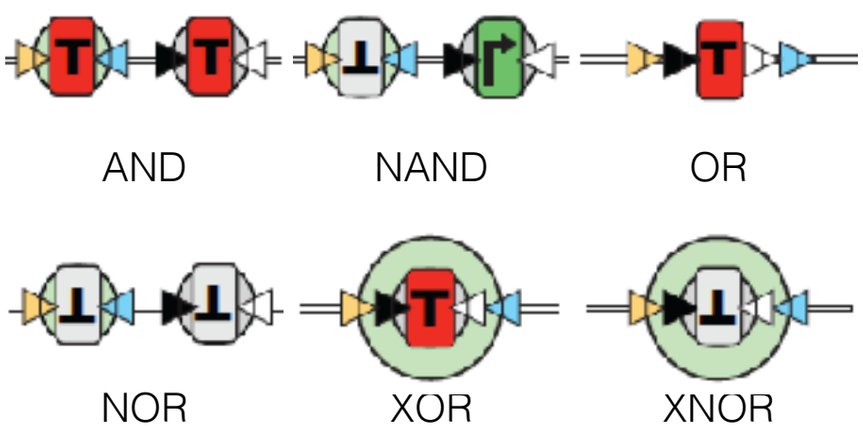
Logique Booléenne génétiquement encodée

A.Zuniga S.Guiziou

Porte logique AND







Logiciels de design automatisé

CALIN

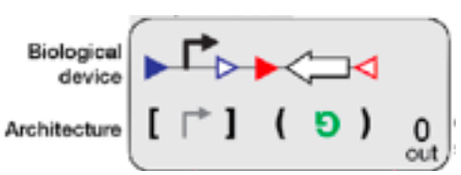
COMPOSABLE ASYNCHRONOUS LOGIC USING INTEGRASE NETWORKS

CALIN is a software tool for automated design of multicellular recombinase logic circuits. CALIN was developed in the Synthetic Biology Group at the CBS, Montpellier, France.

ANY FEEDBACK ?

synbio.cbs.cnrs.fr/calin

Recombinator



LIRMM

G. Peruthion-Khili, M. Leclere, F. Ulliana

http://recombinator.lirmm.fr/

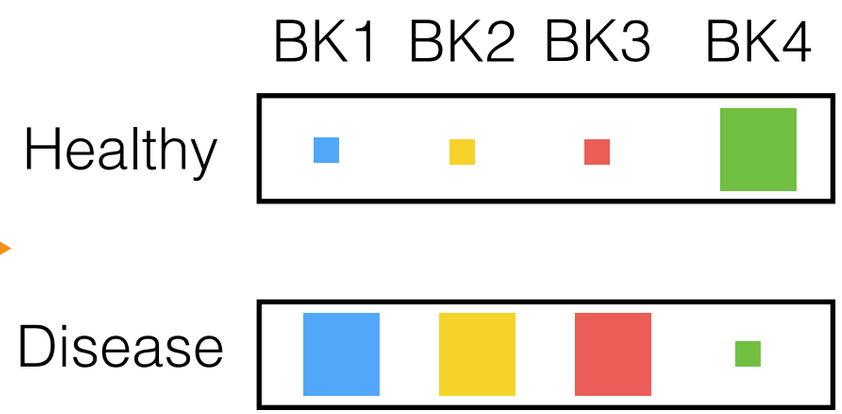
*Bonnet et al., **Science**, 2013, Guiziou et al., **ACS Synthetic Biology**, 2018 , Zuniga et al., Guiziou et al., **Nature Communications**, 2019, 2020*

Les Bactéries programmables pour le diagnostic

Les défis du diagnostic médical

Biomarkers (BKs)

Multiplexing



Hopital ou laboratoire


Equipement lourd

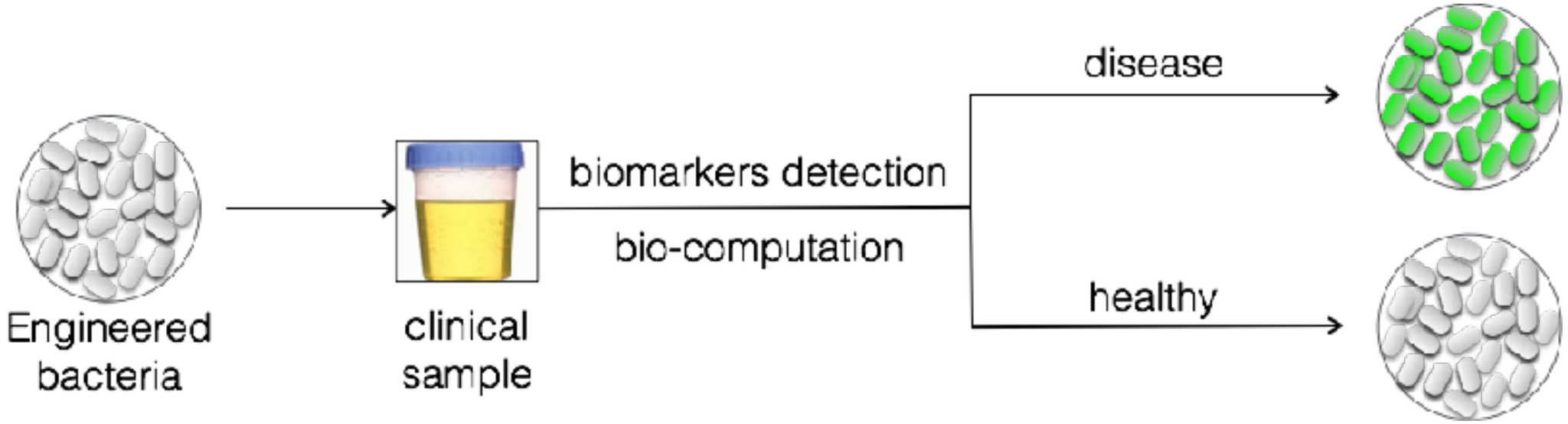

Personnel


Onereux

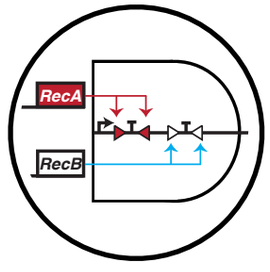
?

point-of-care / maison

Des bactéries programmées pour le diagnostic médical



Sensitivity specificity



Computation

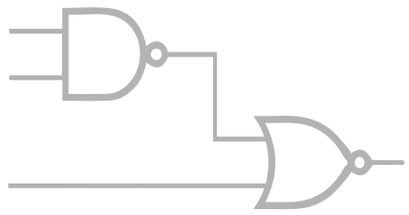
Self-manufacturing Technology

~10^9 cells/ml

Défis des bactéries programmables pour le diagnostic

1. **Robustesse dans des milieux complexes**

2. **Detection à façon de biomarqueurs pertinents chez les patients**

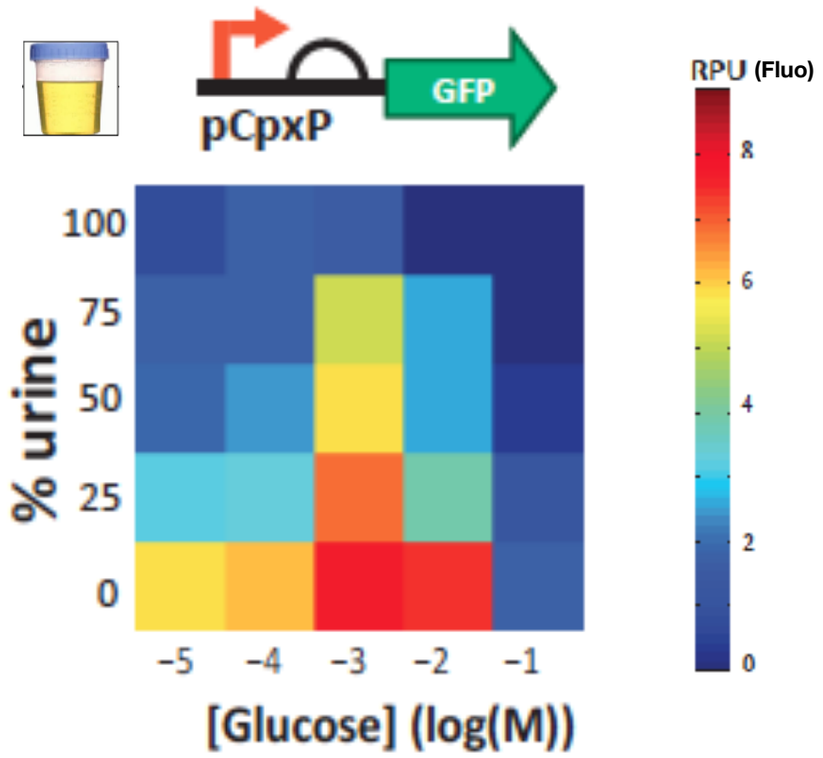


3. **Assurer le confinement physique et génétique**

4. **Valider les preuves de concept en contexte clinique**

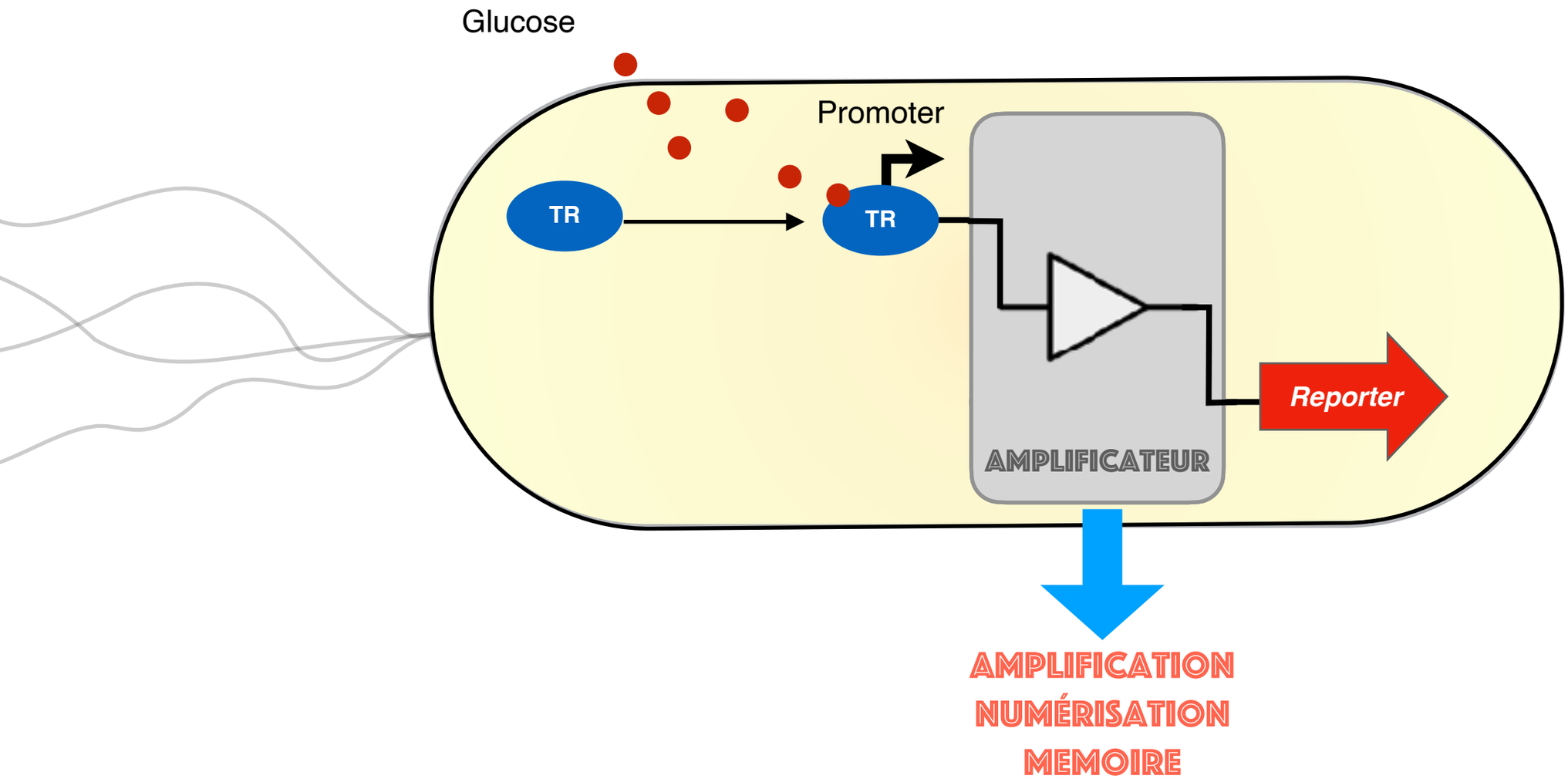
Les échantillons cliniques inhibent les capteurs bactériens

Alexis Courbet

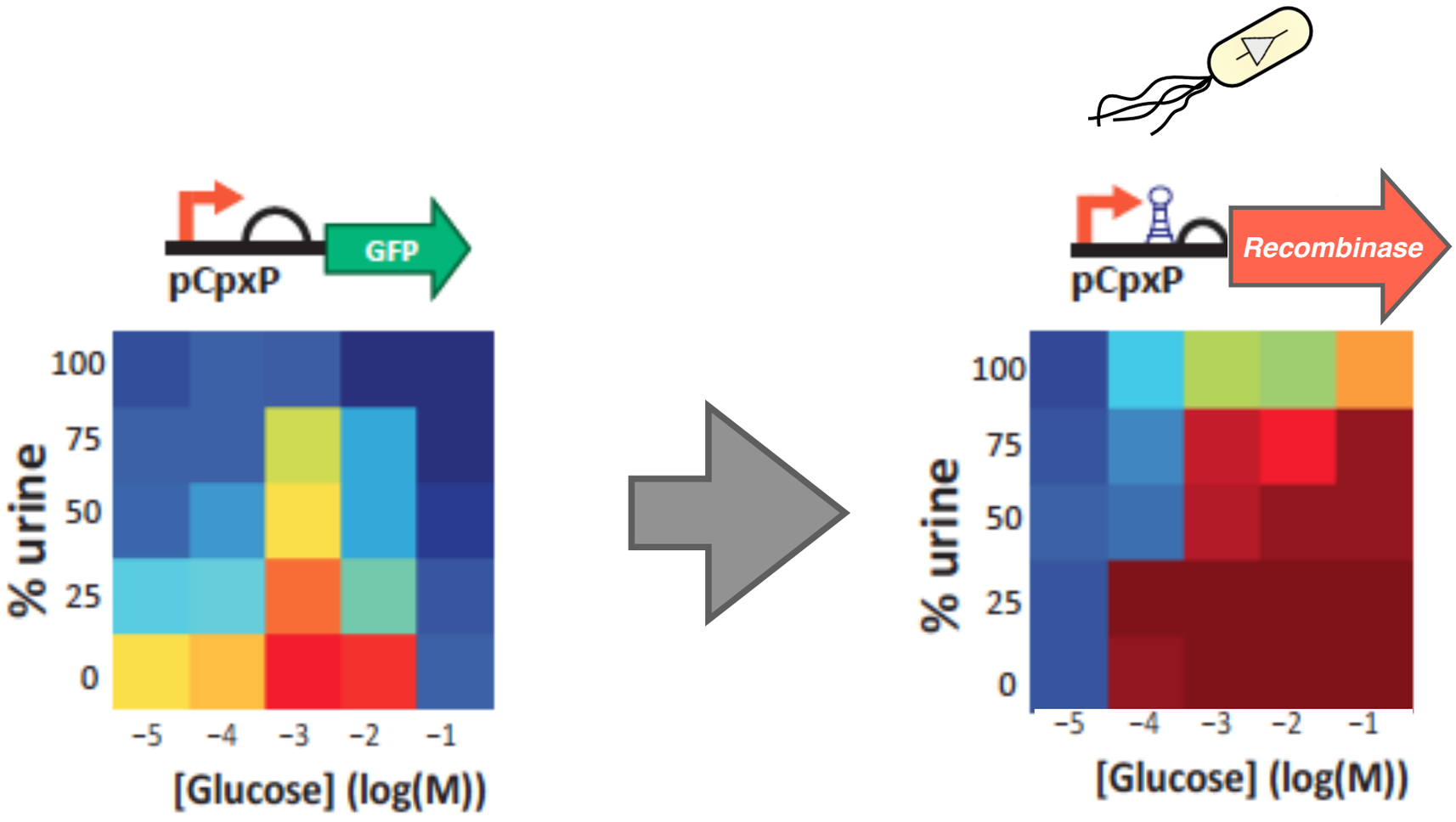


Coll. E. Renard (CHU) F. Molina (CNRS)

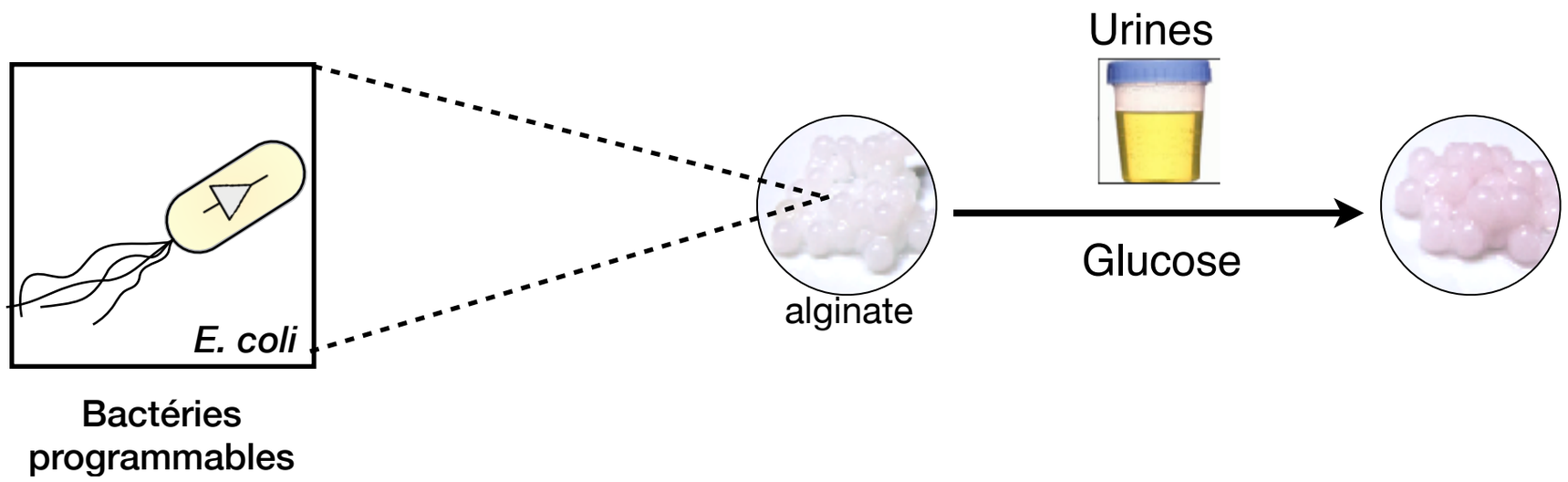
Améliorer la robustesse des biocapteurs avec les interrupteurs génétiques

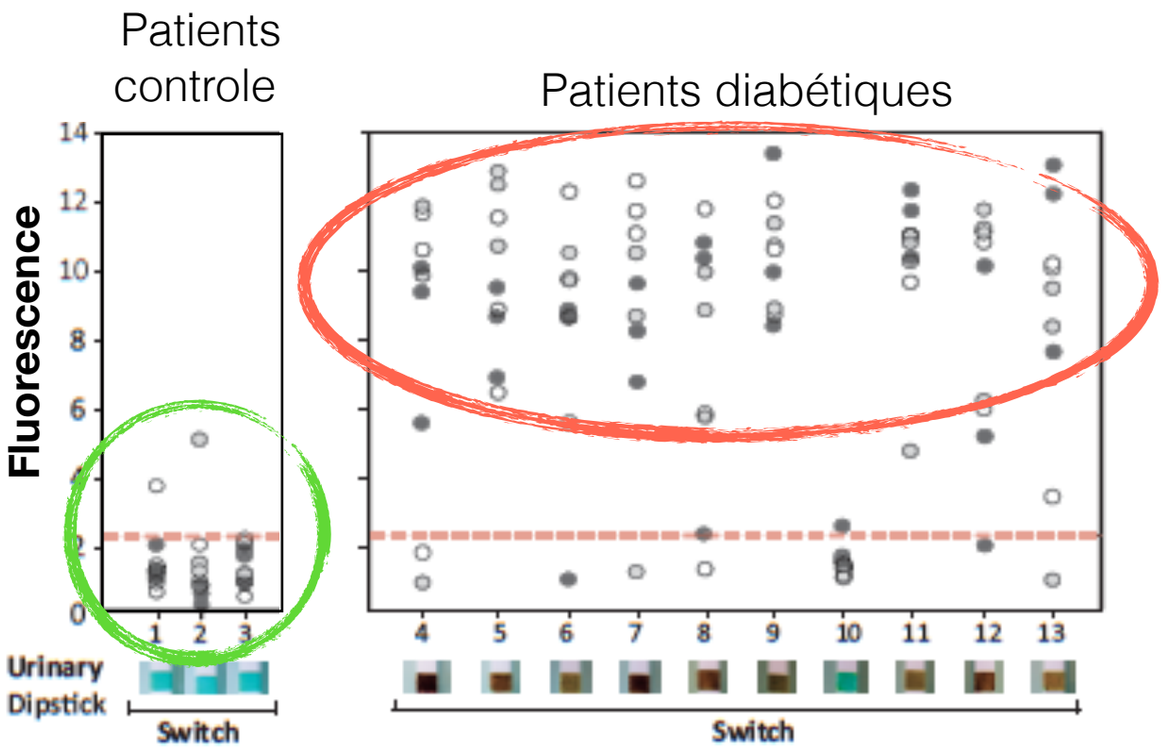


Amplification et numérisation du signal en échantillons cliniques

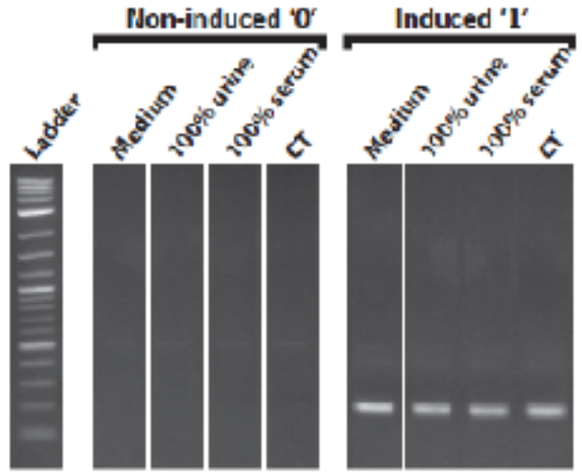


Detection de glycosurie pathologique dans les urines de patients diabétiques





Memoire a ADN du test diagnostic

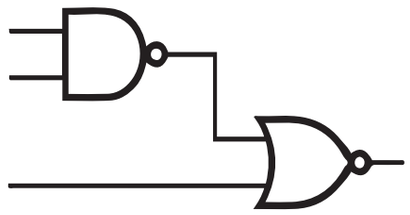


8 mois

*Courbet et al., **Science Translational Medicine**, 2015* *Coll. E. Renard (CHU) F. Molina (CNRS)*

Défis des bactéries programmables pour le diagnostic

1. **Robustesse dans des milieux complexes**

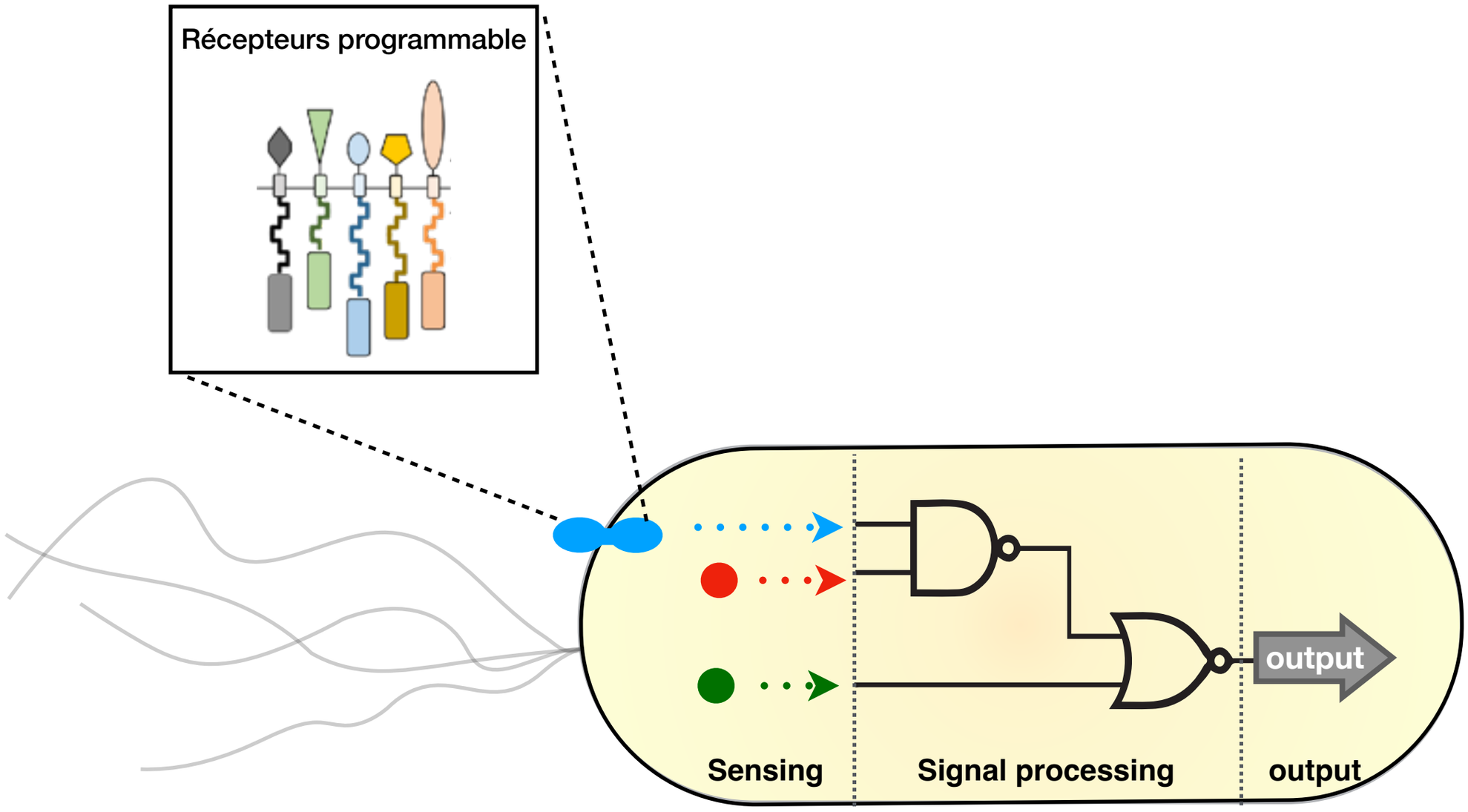


2. **Detection à façon de biomarqueurs pertinents chez les patients**

3. **Assurer le confinement physique et génétique**

4. **Valider les preuves de concept en contexte clinique**

Ingénierie de récepteurs a spécificité programmable

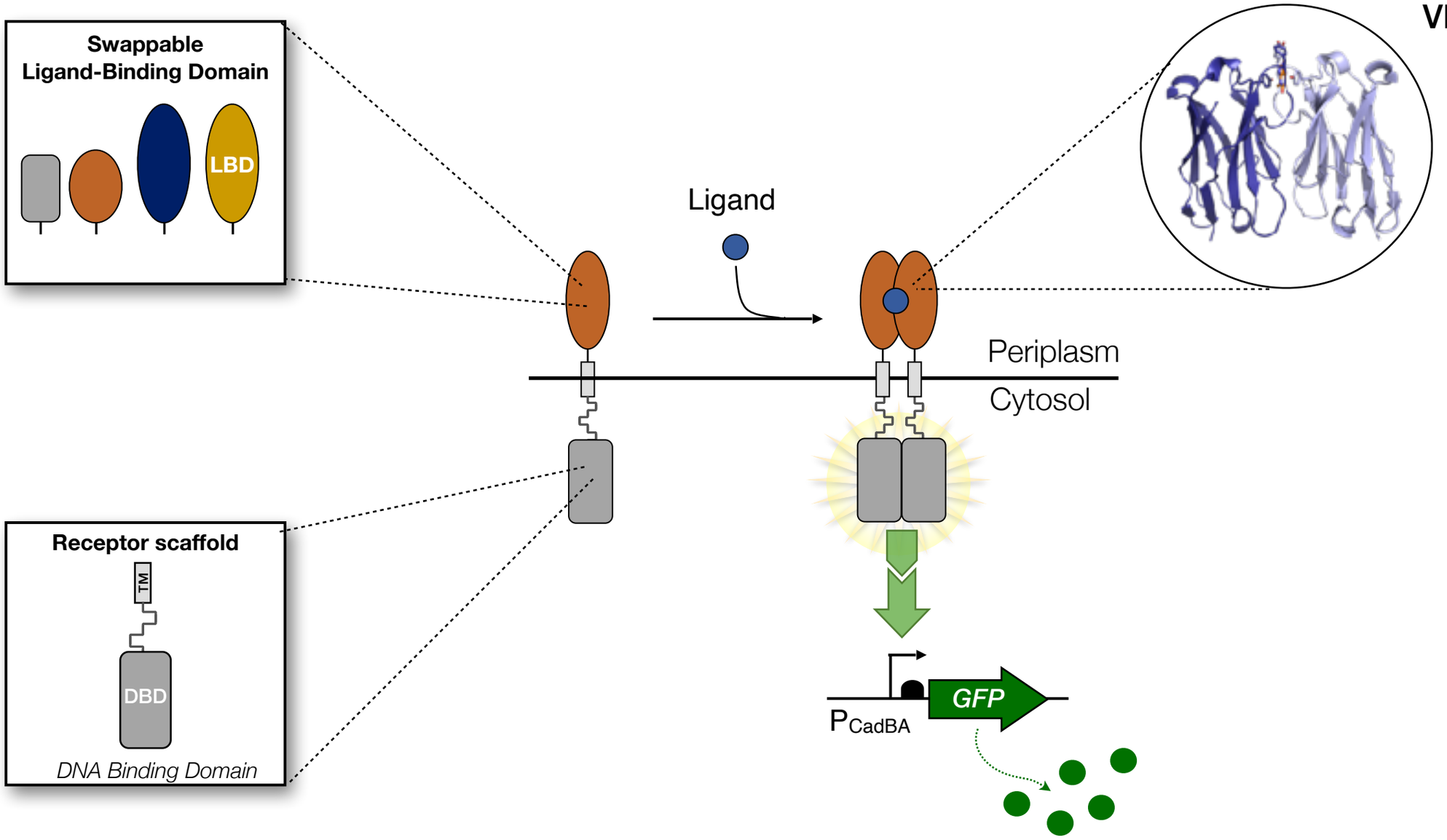


Récepteurs synthétiques activé par dimérization

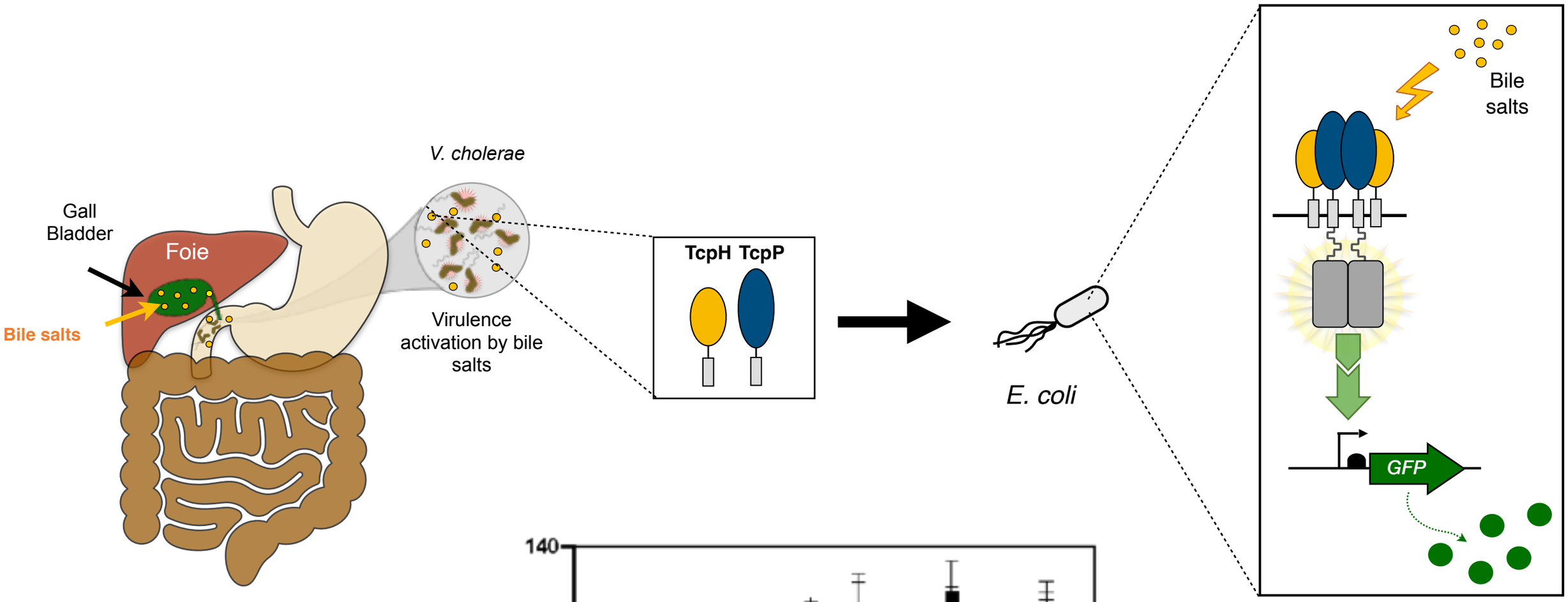

Hung-Ju Chang

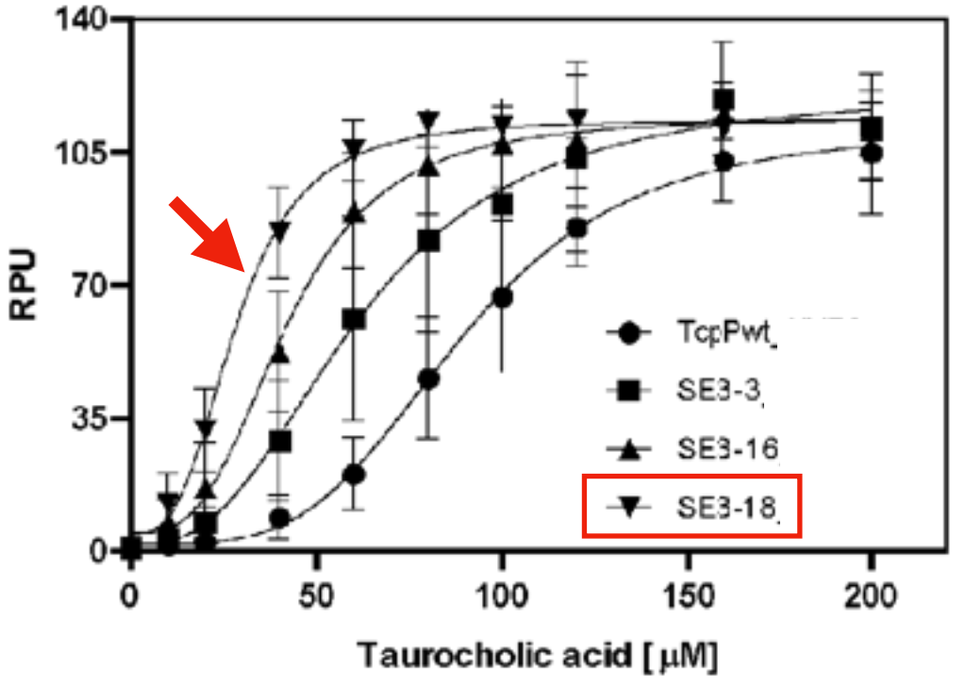

Pauline Mayonove


Estelle Grosjean



Recablage des récepteurs pour détecter les sels biliaires



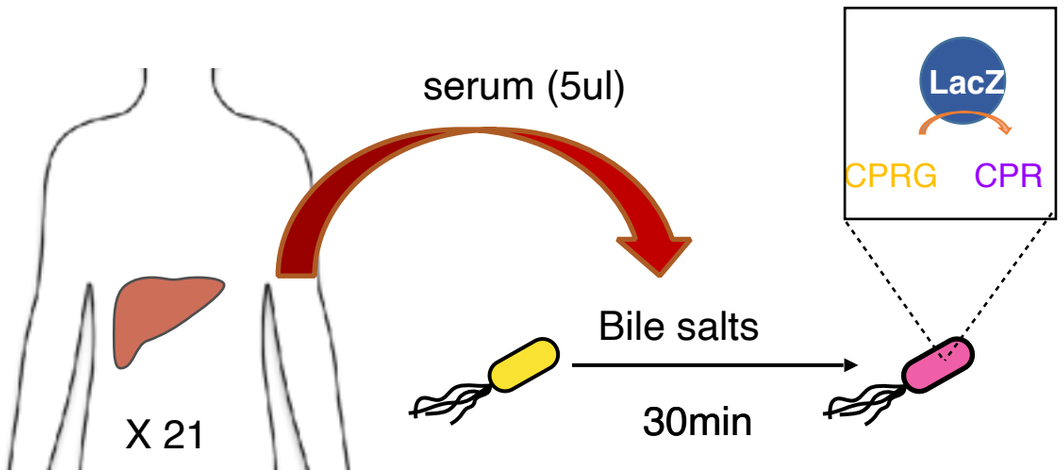


Chang et al. ***Nature Communications,*** *2021*

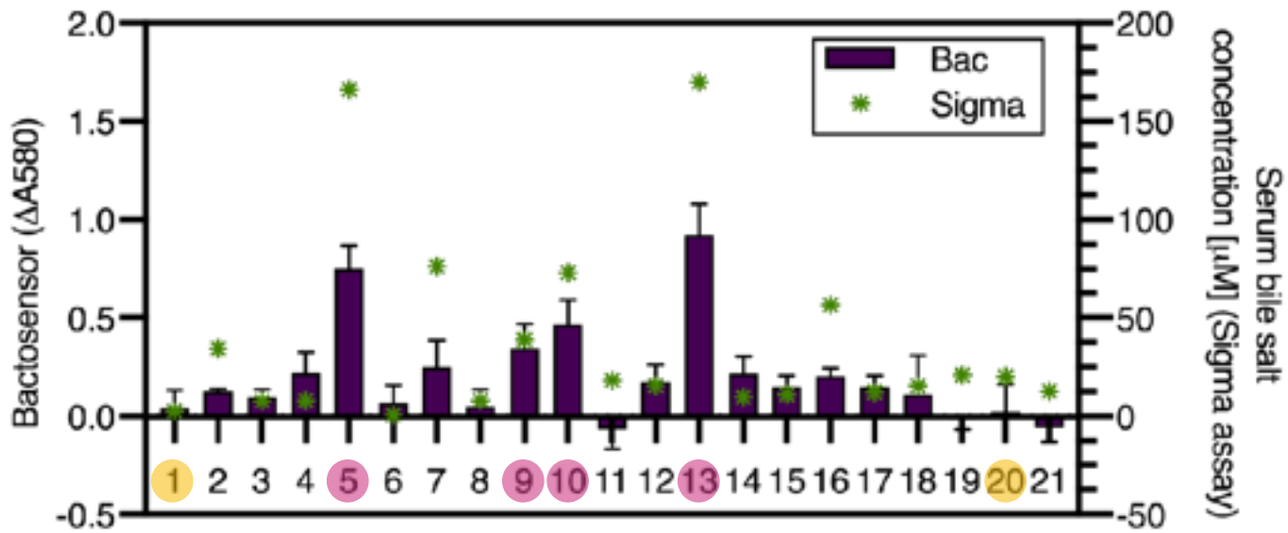
Fast serological detection of liver dysfunction with a colorimetric assay

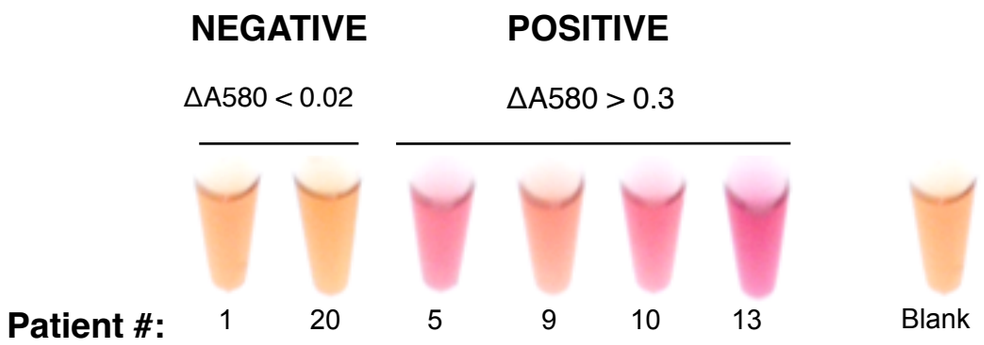
Coll. L. Meunier, M. Meszaros, G.P. Pageaux Hepatology Dpt, (CHU Montpelli

Bile salts in serum
= liver dysfonction



Liver transplant patients

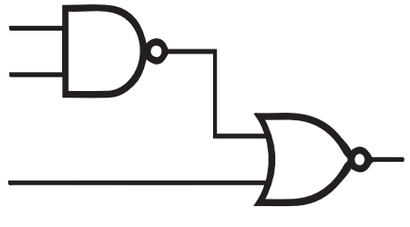




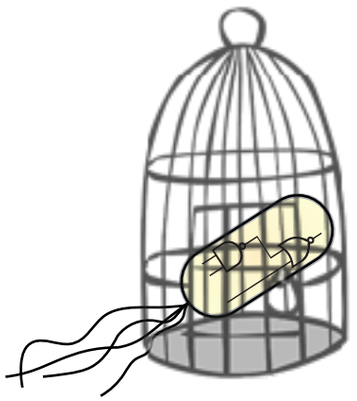
Chang et al. ***Nature Communications****, 2021*

Défis des bactéries programmables pour le diagnostic

1. **Robustesse dans des milieux complexes**
   Amplification, memoire, encapsulation, integration chromosomique



2. **Detection à façon de biomarqueurs pertinents chez les patients**
   More to come



3. **Assurer le confinement physique et génétique**
   Encapsulation, integration chromosomique, auxotrophies, kill-switches…

4. **Valider les preuves de concept en contexte clinique**
   Variabilité des effets de matrice, psychologie, reglementation, éthique.

Collaborations and funding

Montpellier

CBS

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Josephine Lai-Kee-Him

Aurelie Ancelin

Aurelien Fouillen

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IRCM

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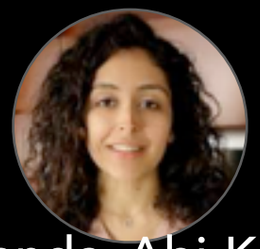

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