PROGRAMMABLE SINGLE-CELL MAMMALIAN BIOCOMPUTERS

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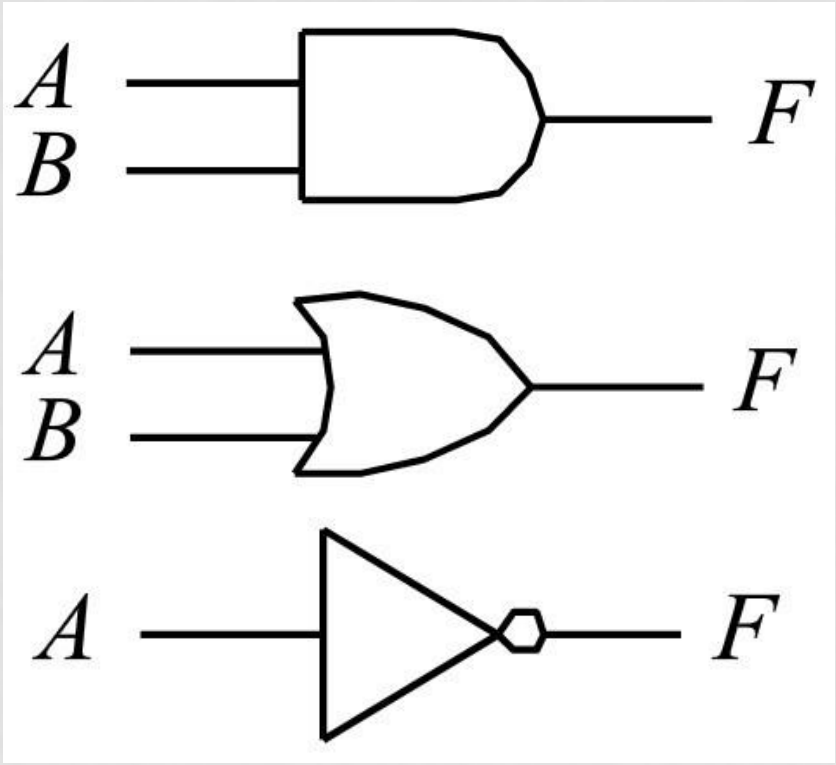
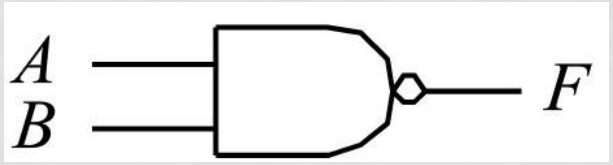
BACK GROUND

- Boolean operation
  - AND
    - AB or A ·B or A∩B
  - OR
    - A+B or A ∪ B
  - NOT
    - $\overline{A}$

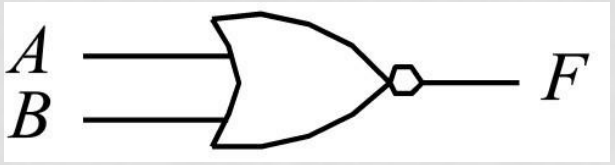


BACK GROUND

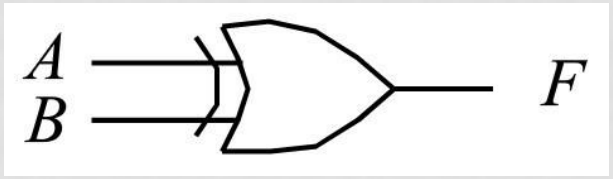
- **Boolean operation**
  - **NAND**
    - $\overline{AB}$
  - **NOR**
    - $\overline{A+B}$



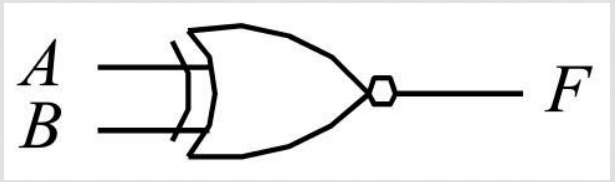
与非（F = $\overline{AB}$ ）



或非（F = $\overline{A+B}$ ）

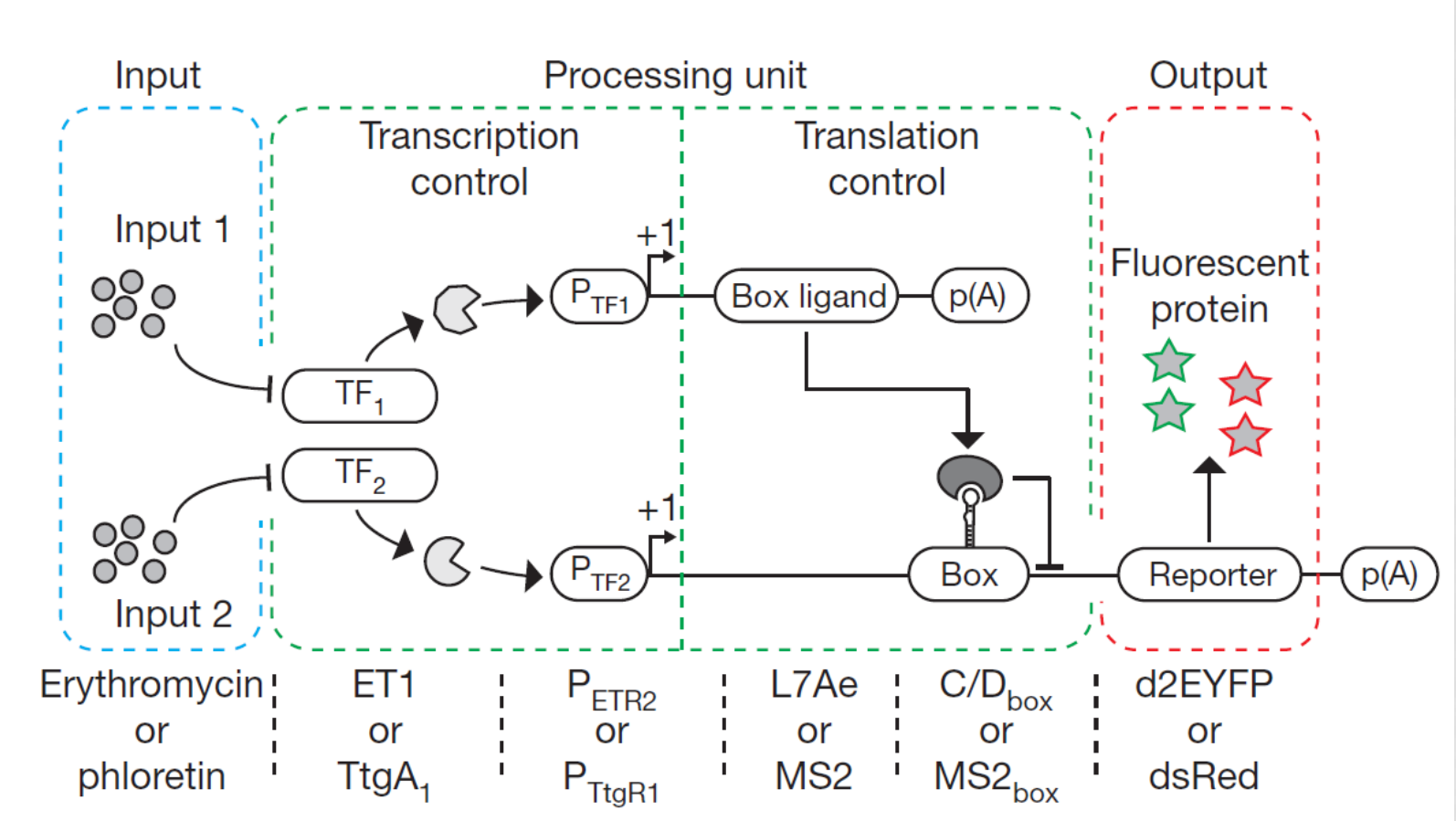


异或（F =A ⊕ B = $\overline{A}B + A\overline{B}$ ）



同或（F =A⊗B =$\overline{A}\,\overline{B}$ +AB）

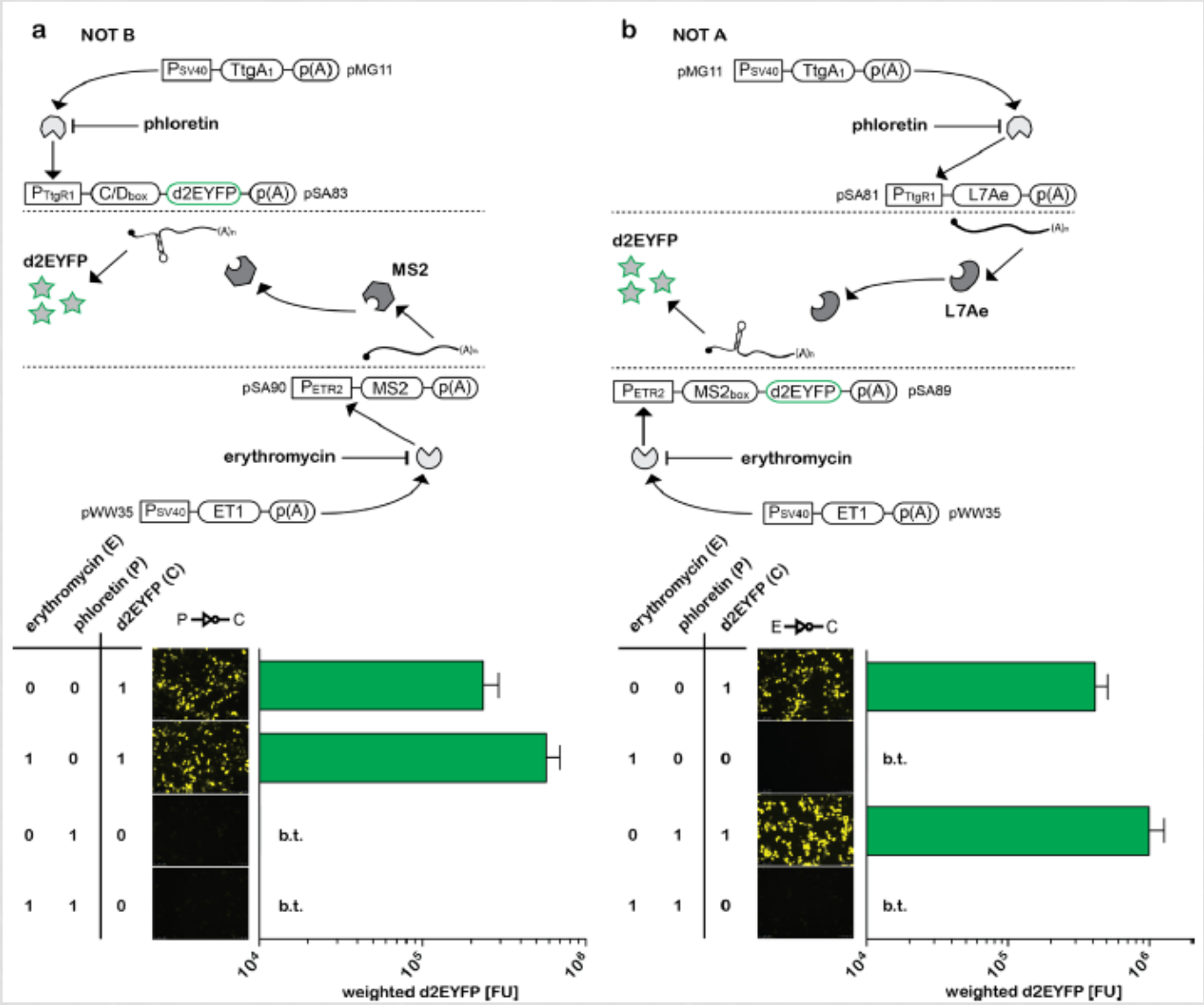
BASIC BIOLOGICAL PRINCIPAL



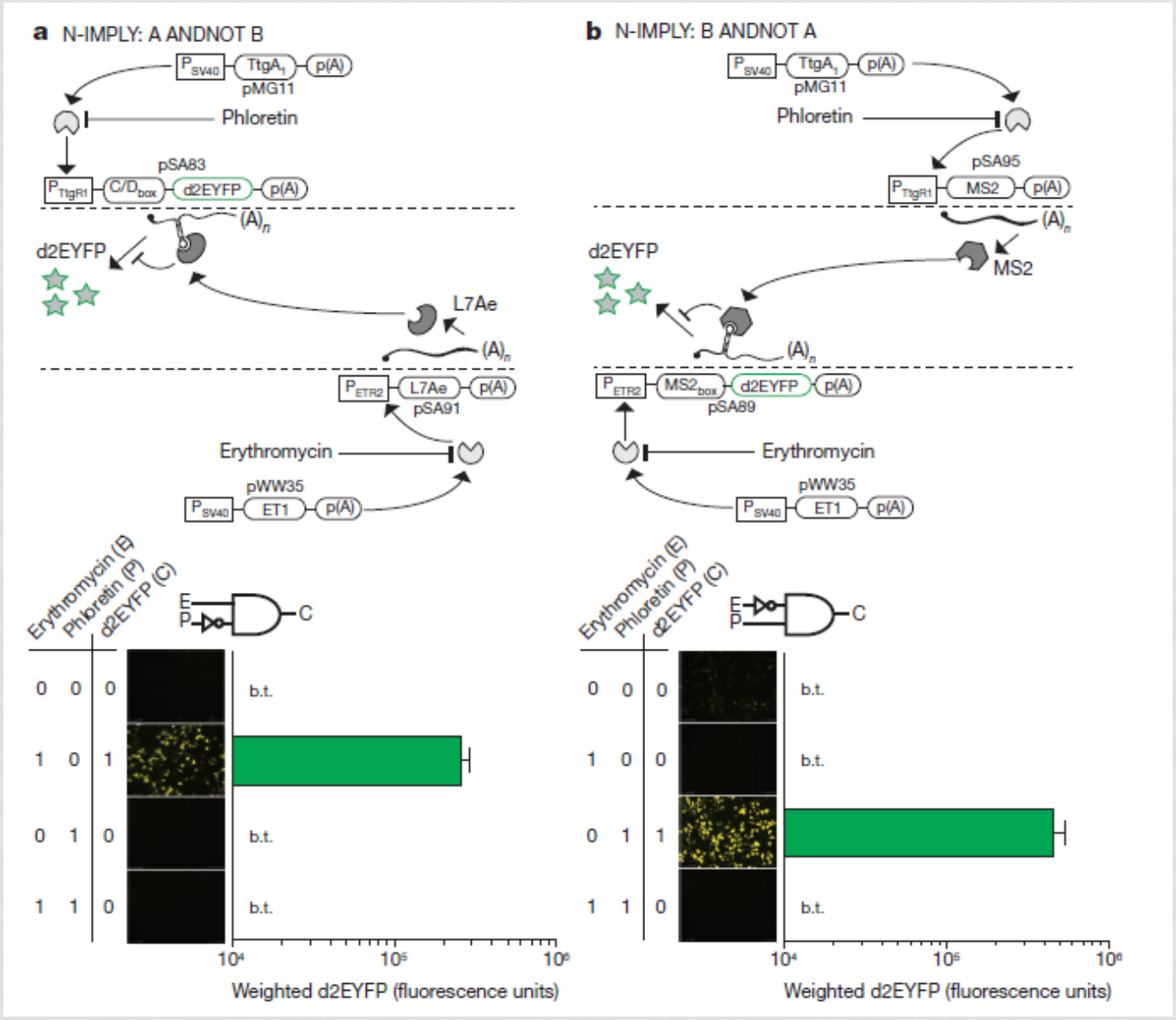
Erthromycin: 红霉素； Phloretin:根皮素；

RNA Controller: binding to complementary natural or synthetic RNA motifs

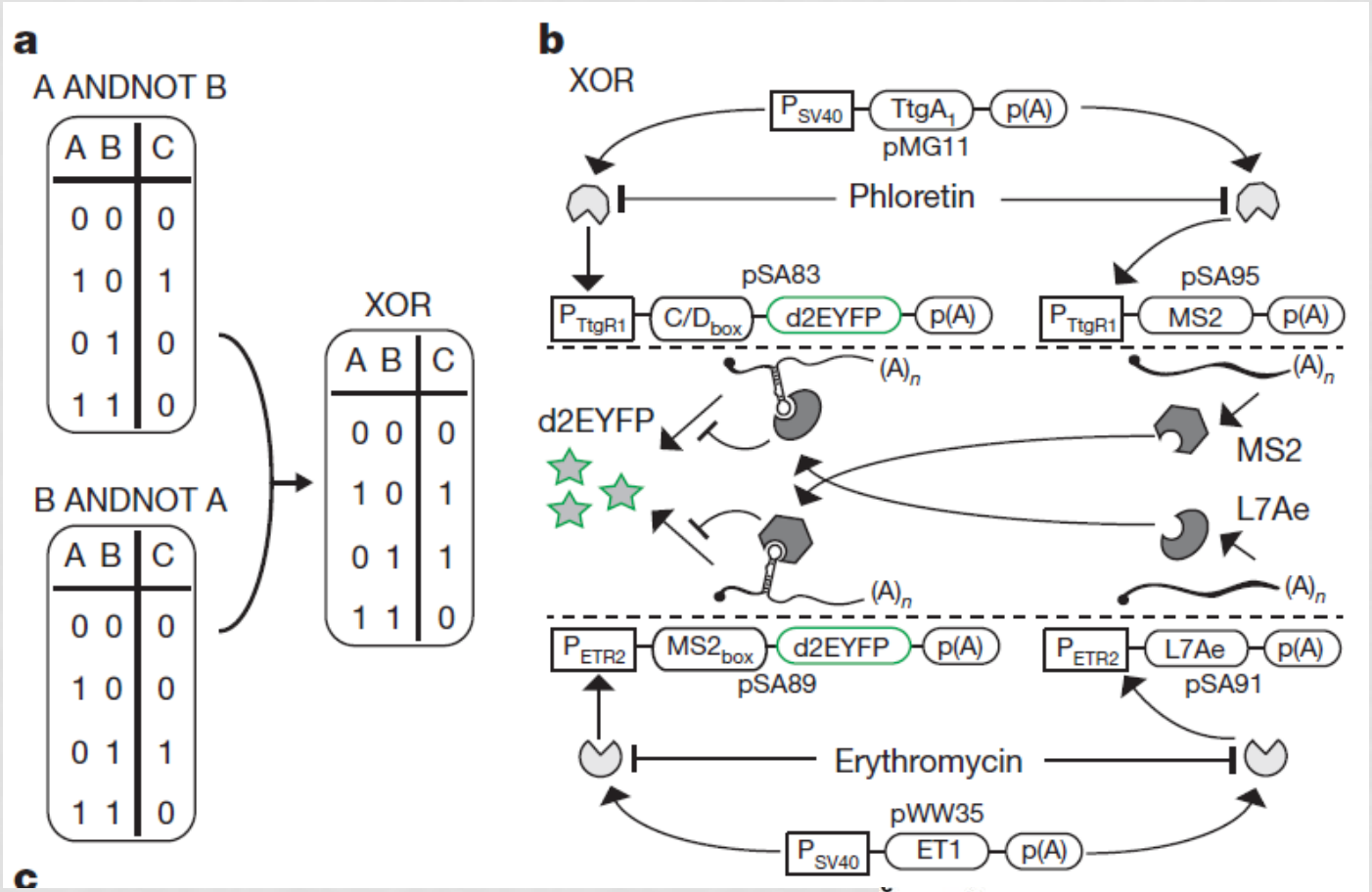
IMPLEMENT OF NOT



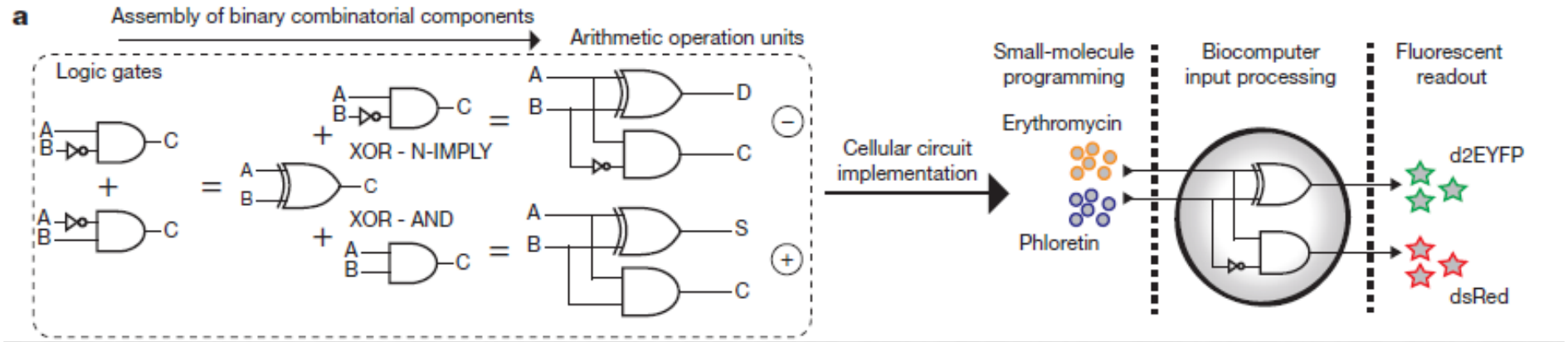
IMPLEMENT OF N-IMPLY



IMPLEMENT OF X-OR

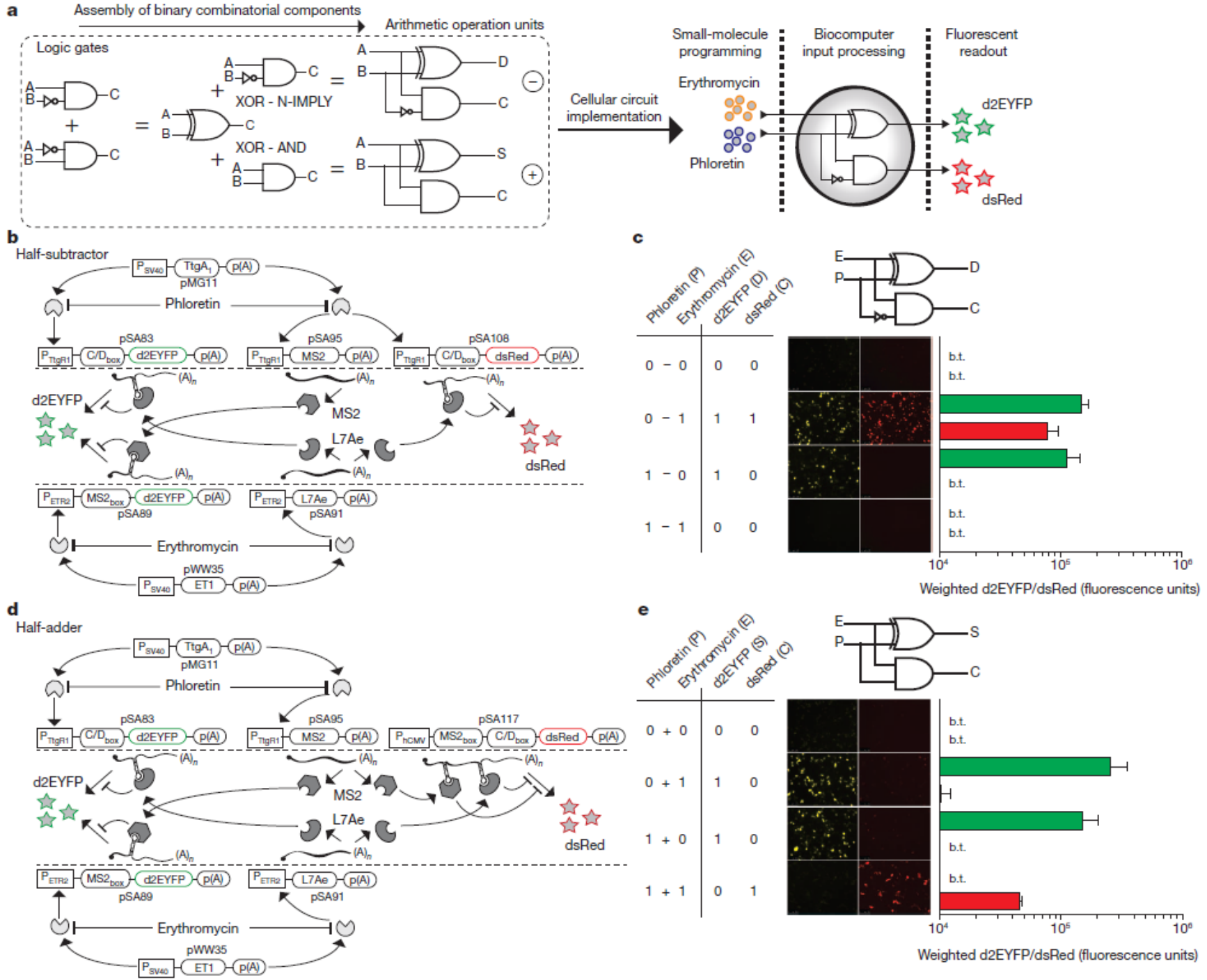


- L7Ae bind RNA C/D box
  - Archaeal ribosomal protein L7Ae
- MS2 bind RNA MS2box
  - Bacteriophage MS2 coat protein



IMPLEMENT OF BINARY OPERATION

HALF-SUBTRACTOR
HALF-ADDER


a
Assembly of binary combinatorial components
Arithmetic operation units
Logic gates
XOR - N-IMPLY
XOR - AND
Cellular circuit implementation
Small-molecule programming
Biocomputer input processing
Fluorescent readout
Erythromycin
Phloretin
d2EYFP
dsRed
b
Half-subtractor
pMG11
pSA83
pSA95
pSA108
d2EYFP
MS2
L7Ae
dsRed
pSA89
pSA91
pWW35
c
Phloretin (P)
Erythromycin (E)
d2EYFP (D)
dsRed (C)
0 – 0 0 0
0 – 1 1 1
1 – 0 1 0
1 – 1 0 0
b.t.
Weighted d2EYFP/dsRed (fluorescence units)
d
Half-adder
pSA117
e
d2EYFP (S)
0 + 0 0 0
0 + 1 1 0
1 + 0 1 0
1 + 1 0 1
Weighted d2EYFP/dsRed (fluorescence units)

SUMMARY

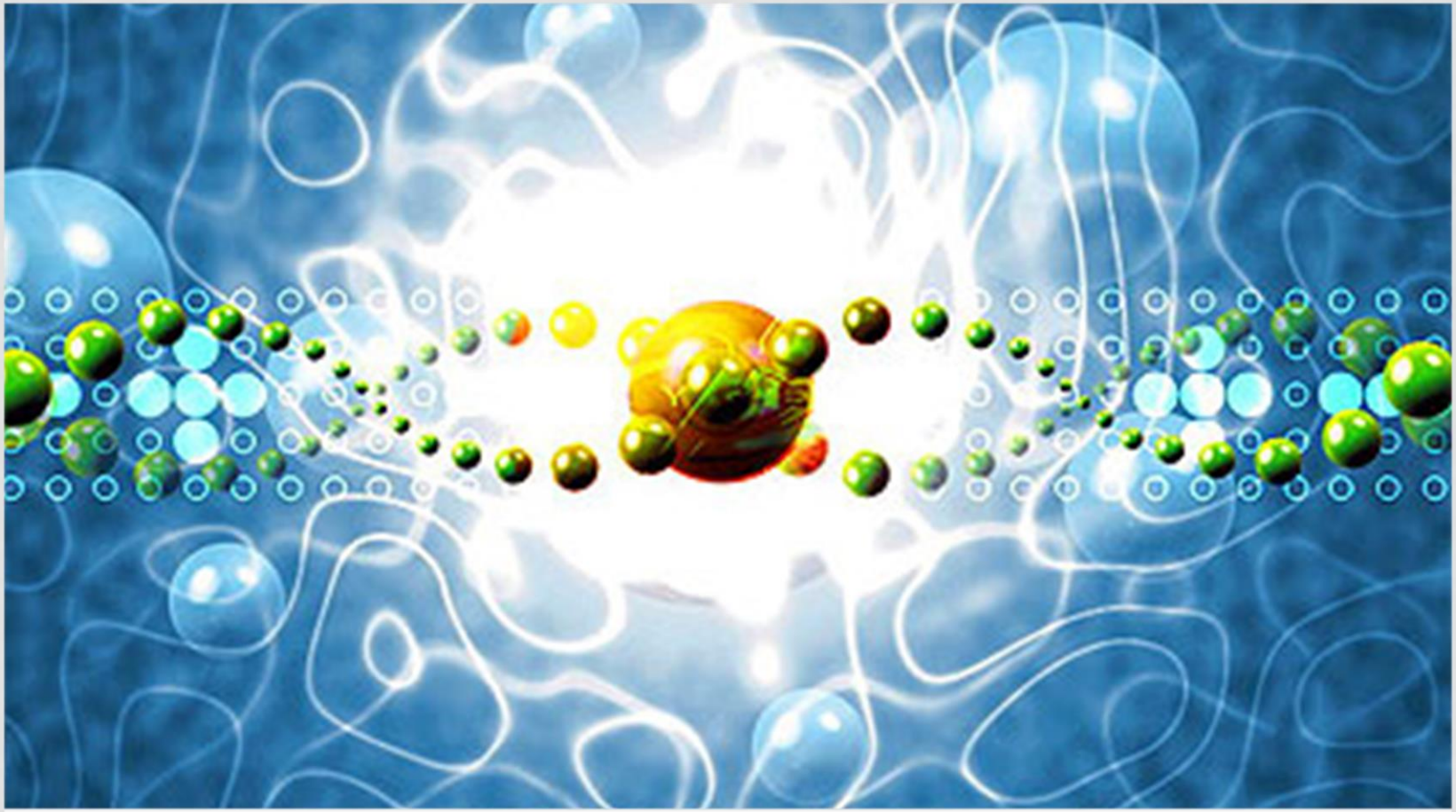
- Increase parallel processing power
  - With any physiological trigger
- Genetically programmed to execute encoded activities
- Scalable to tissue structures
- Straightforward to interface
  - With host metabolism to achieve therapeutic impact

SUMMARY

- Functional isolation from the cellular metabolism
- Complex multi-bit processing devices engineered in single bacterial or yeast cells
- Multicellular assemblies
- This paper:
  - Complex XOR, half-adder and half subtractor
  - Precision, robustness and predictability
  - Complex human-machine interfaces
    - Diagnostic information
    - Therapeutic interventions

PROBLEMS

- Input and removal of signal molecular
- Detection of Signals
- Multiple singals
- Living Cell



THANKS