# Modelling trafficking of proteins within the mammalian cell using Bio-PEPA

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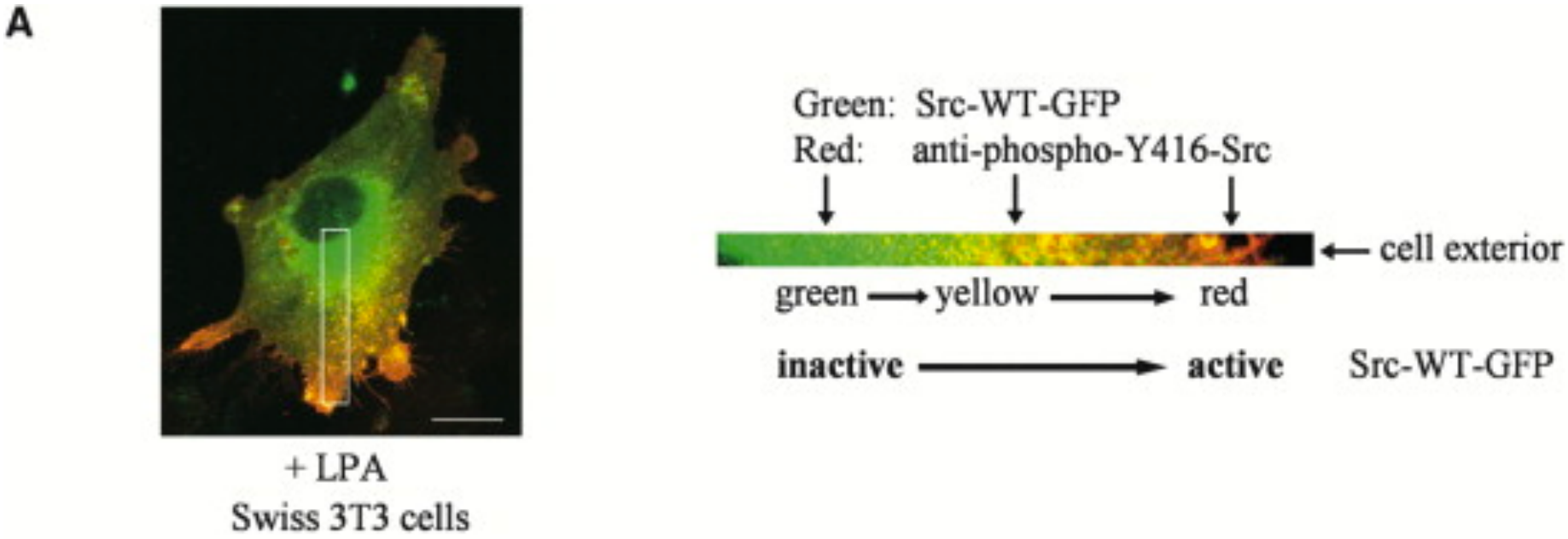
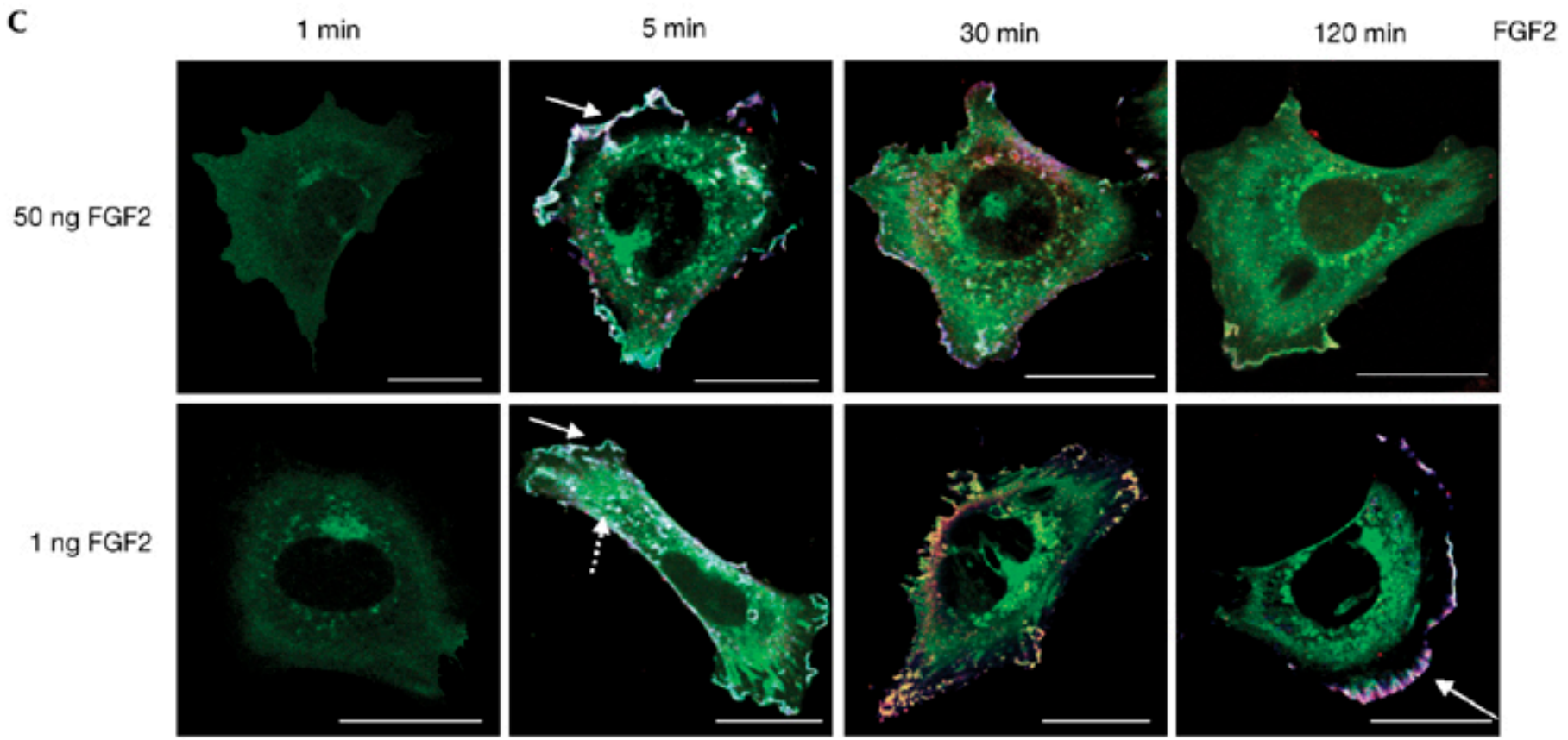
4 October 2012

# Src response to FGF, activation and relocation

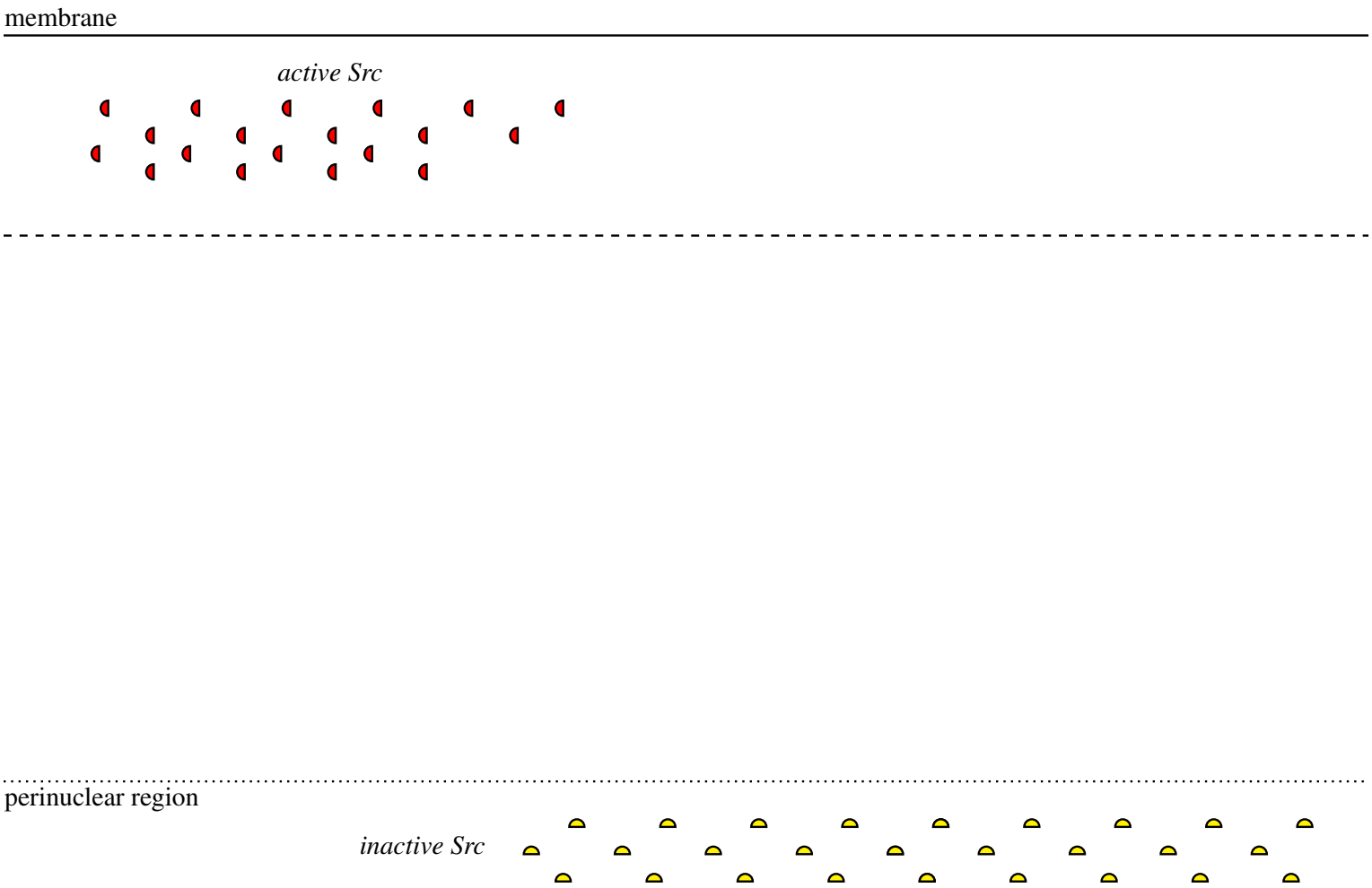


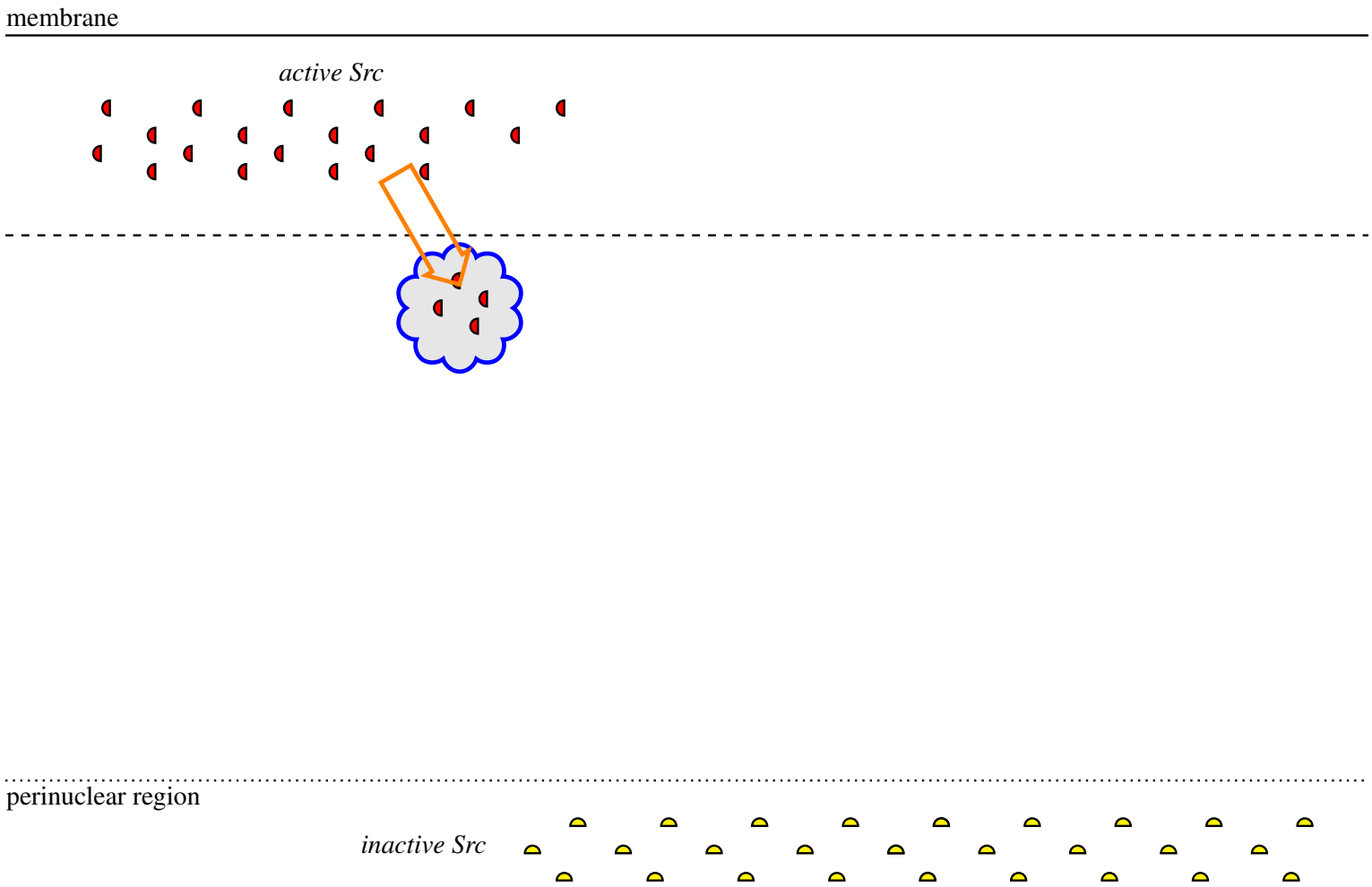

(Sandilands *et al*, Dev. Cell 7, 2004)

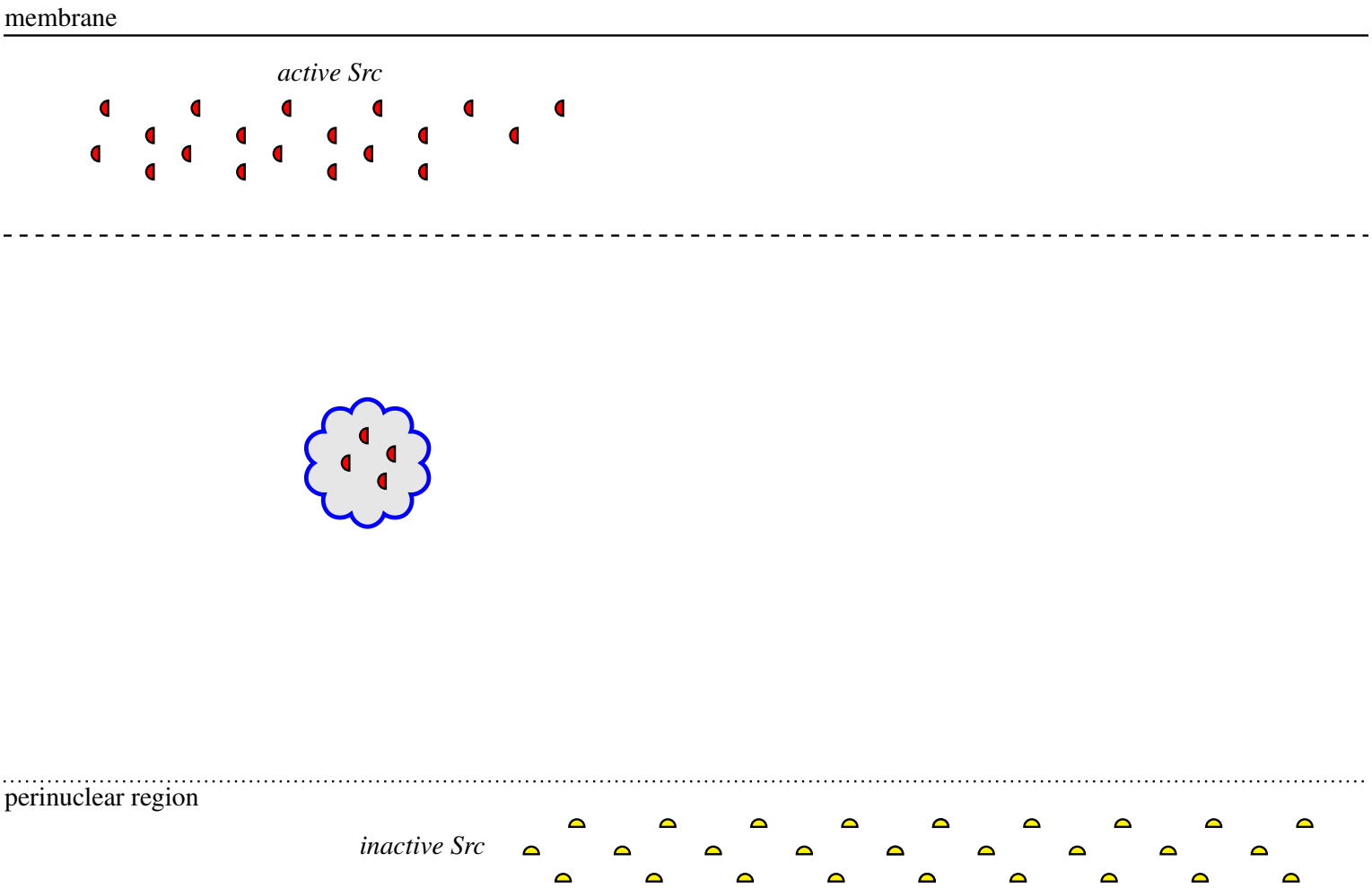
# Src response to FGF, activation and relocation

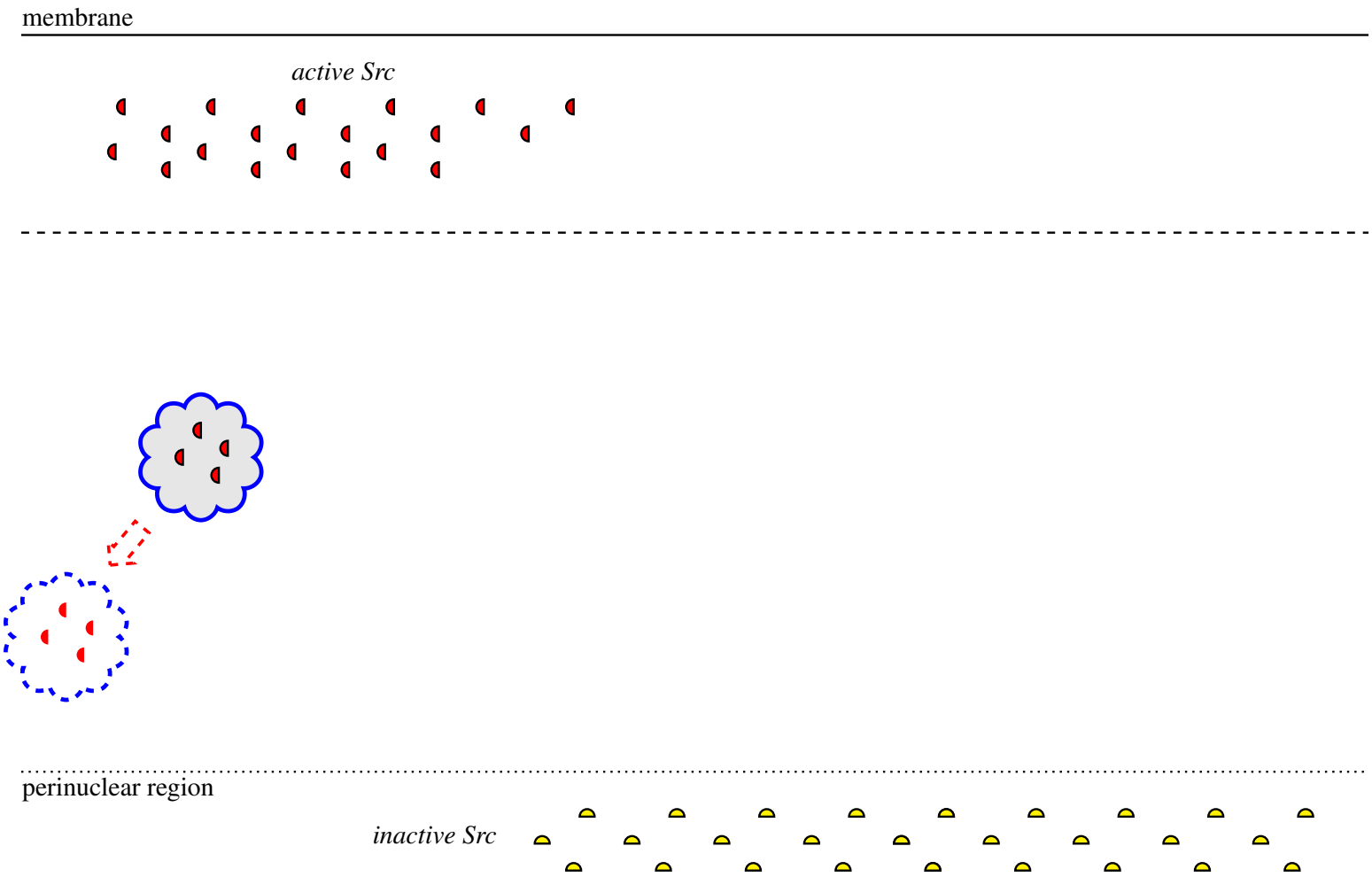


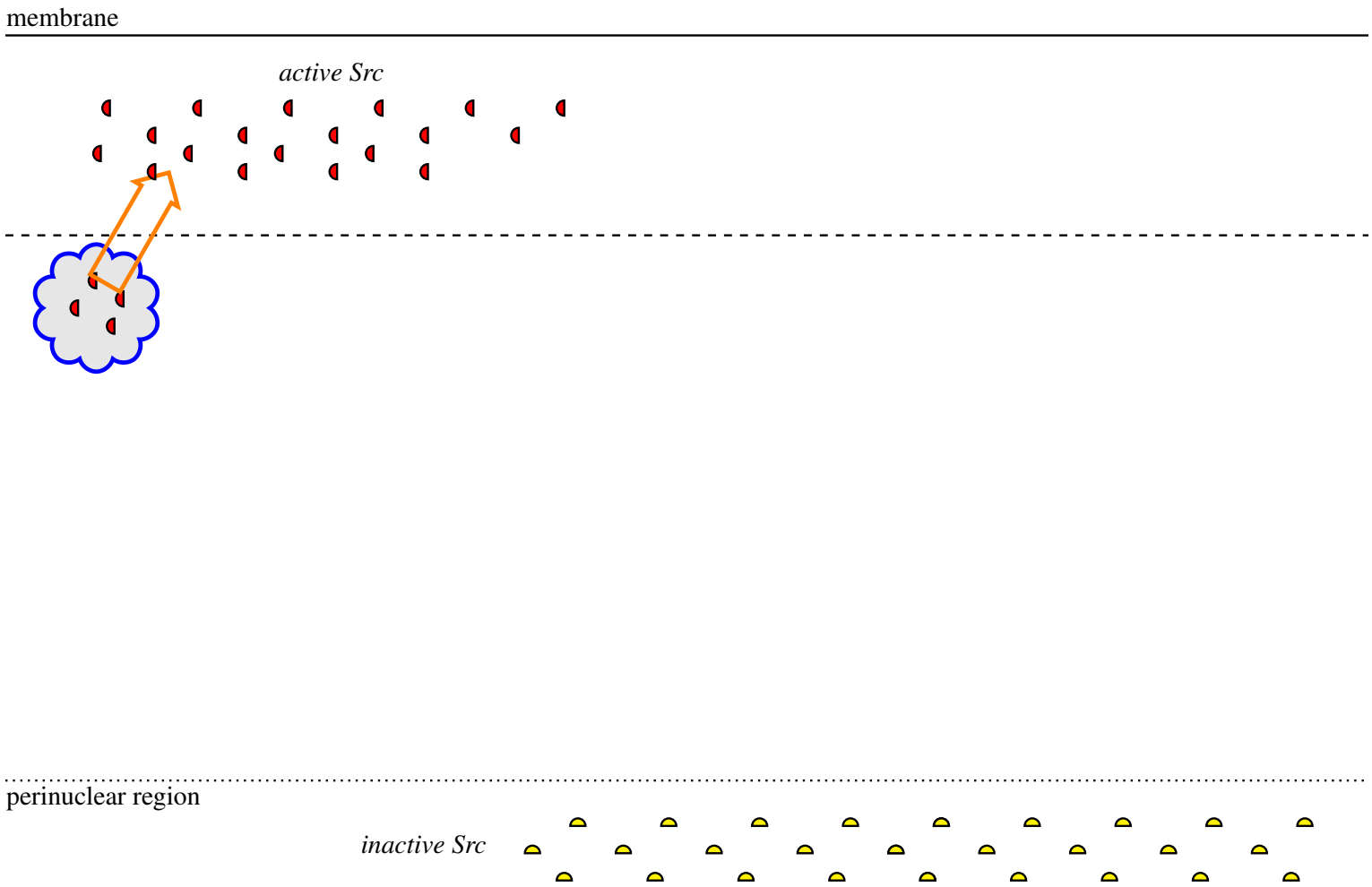

(Sandilands *et al*, EMBO Reports 8, 2007)

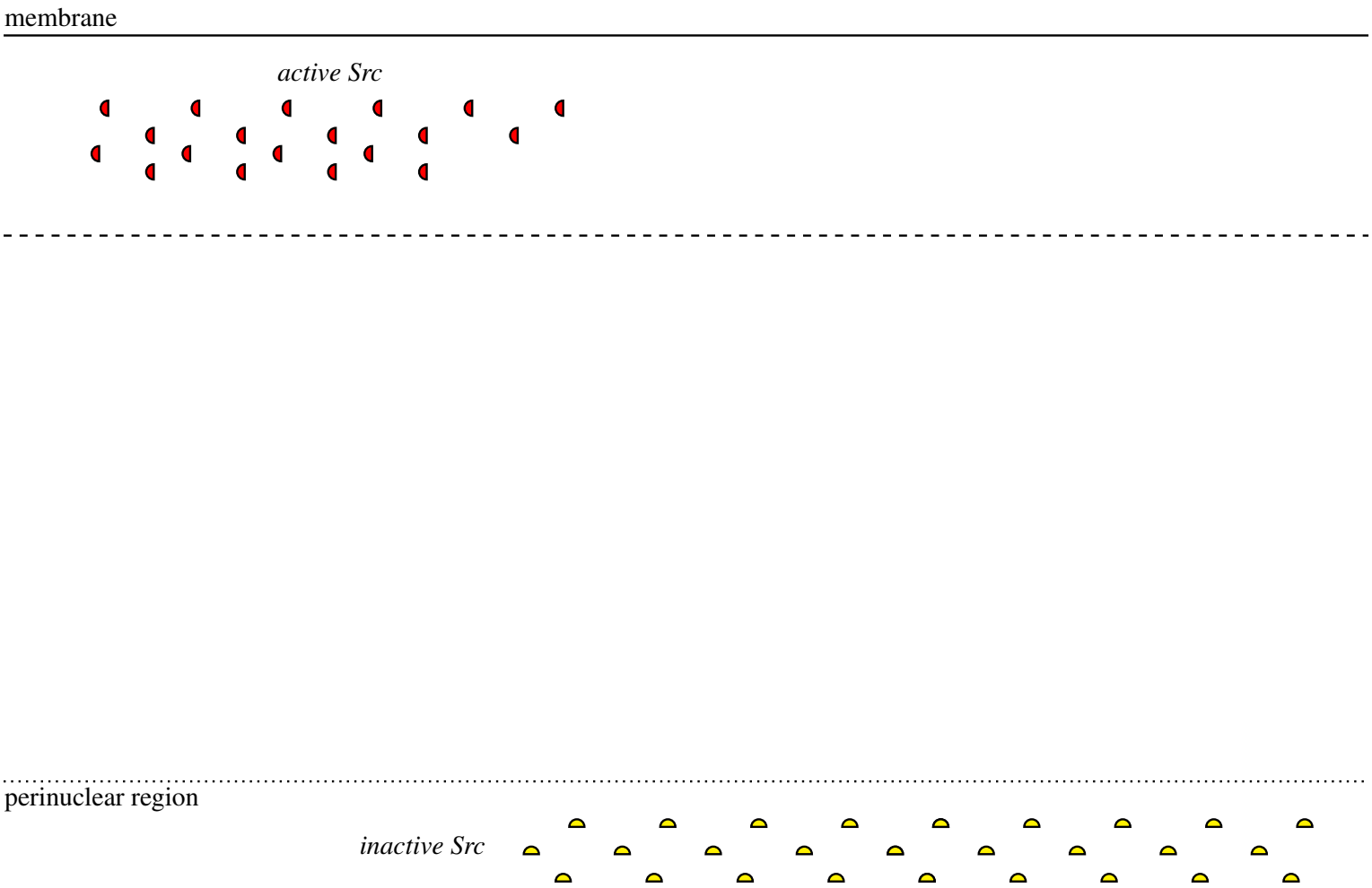

membrane
active Src
perinuclear region
inactive Src

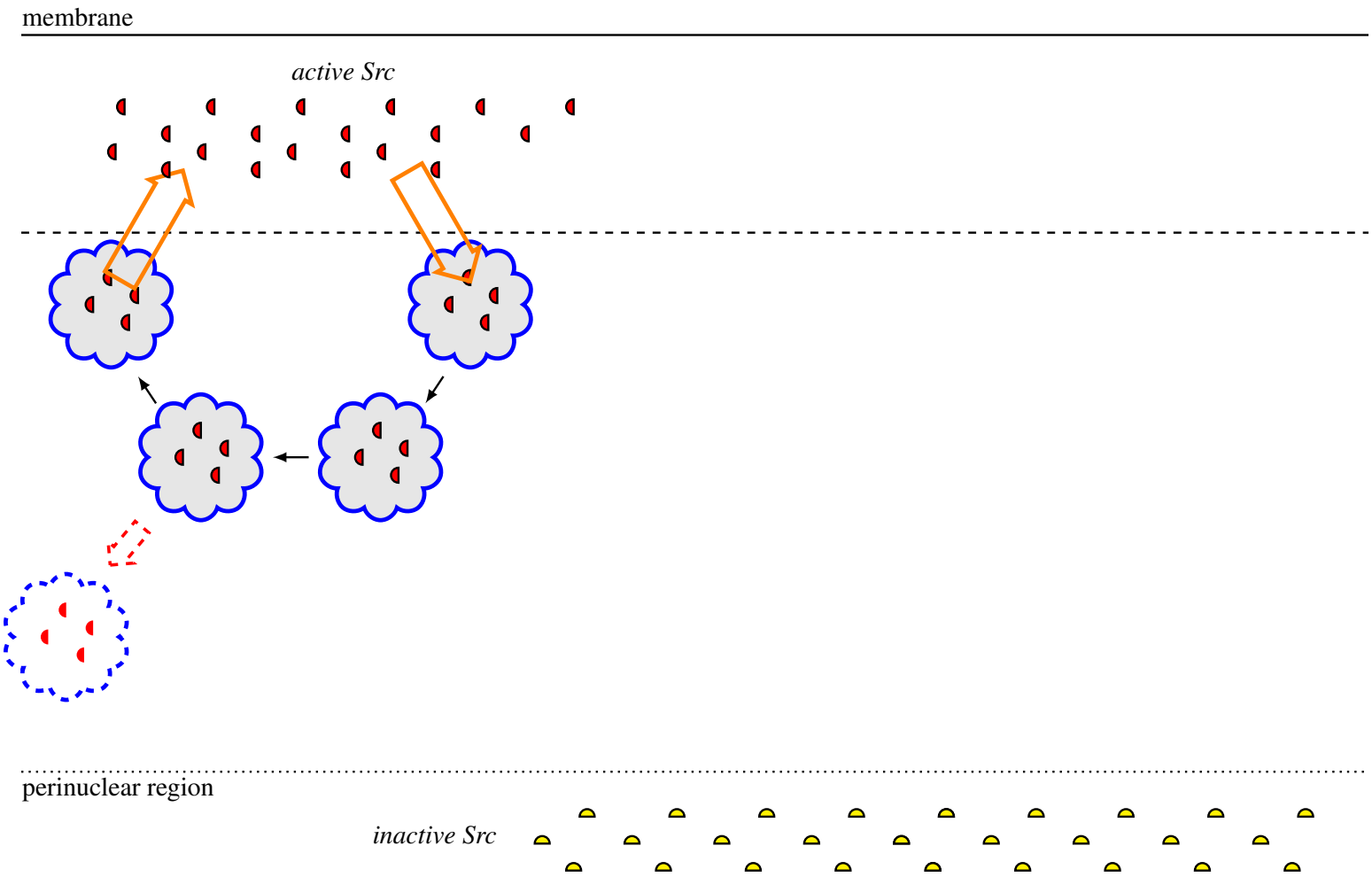

membrane
active Src
perinuclear region
inactive Src

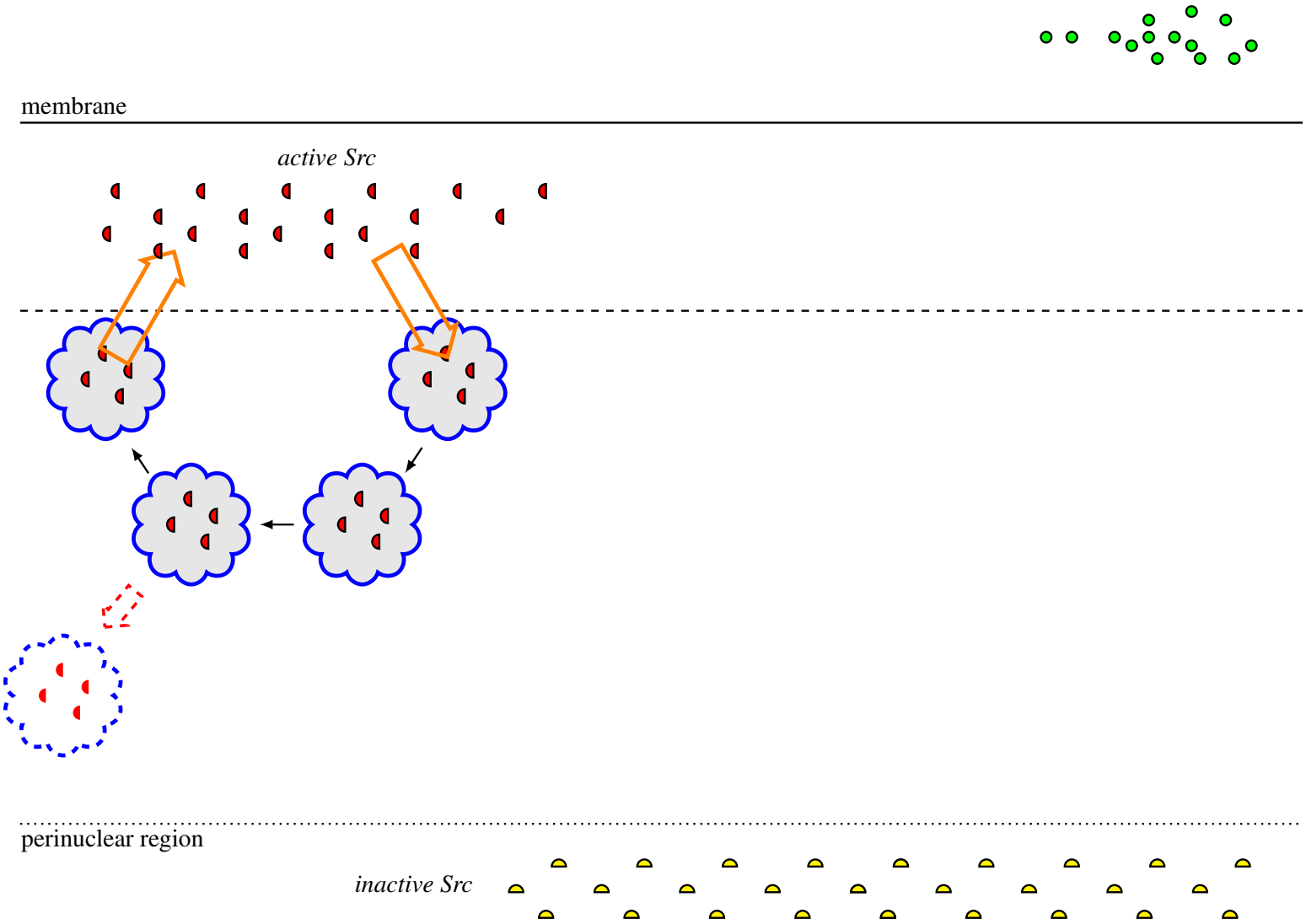

membrane
active Src
perinuclear region
inactive Src

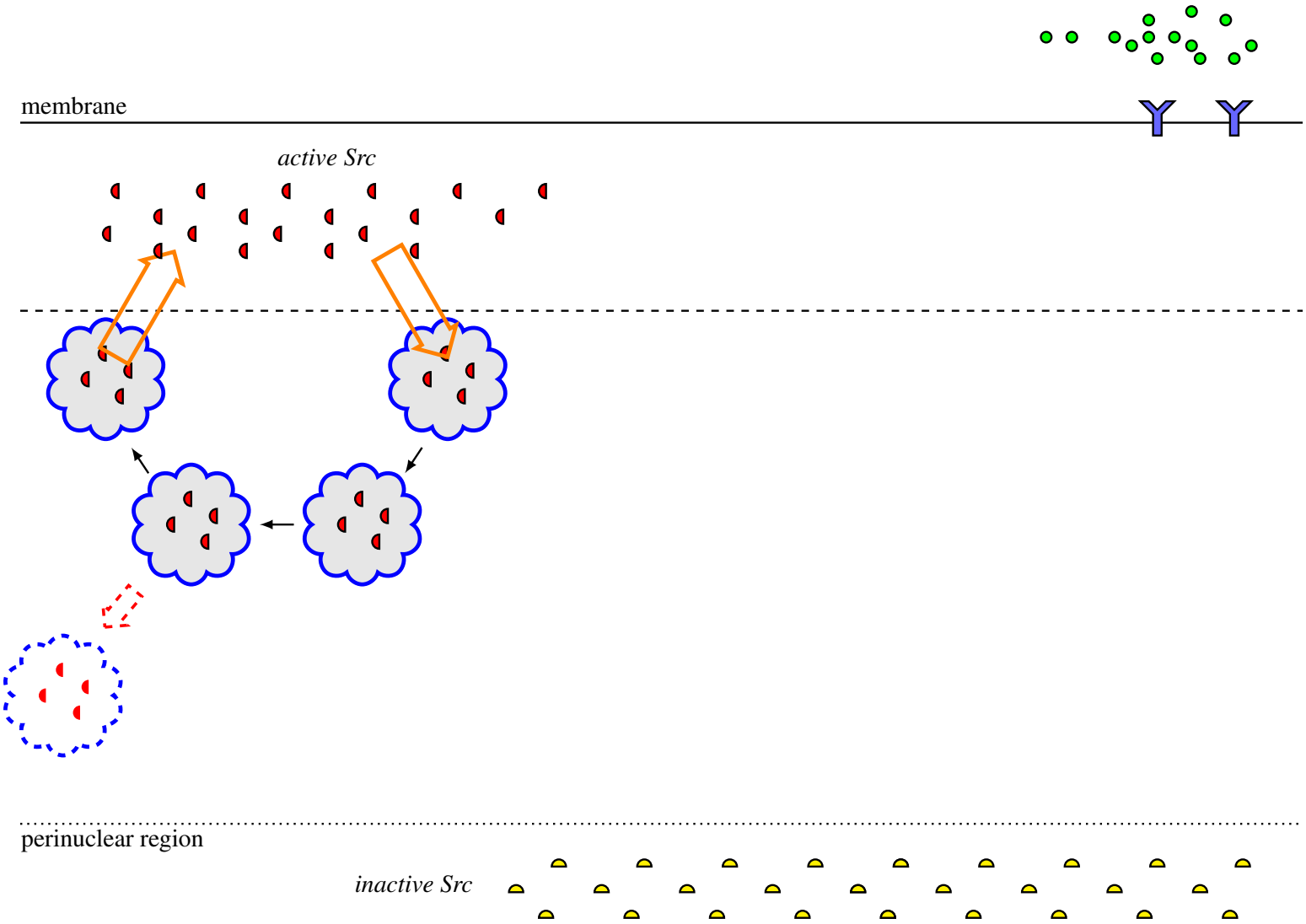

membrane
active Src
perinuclear region
inactive Src

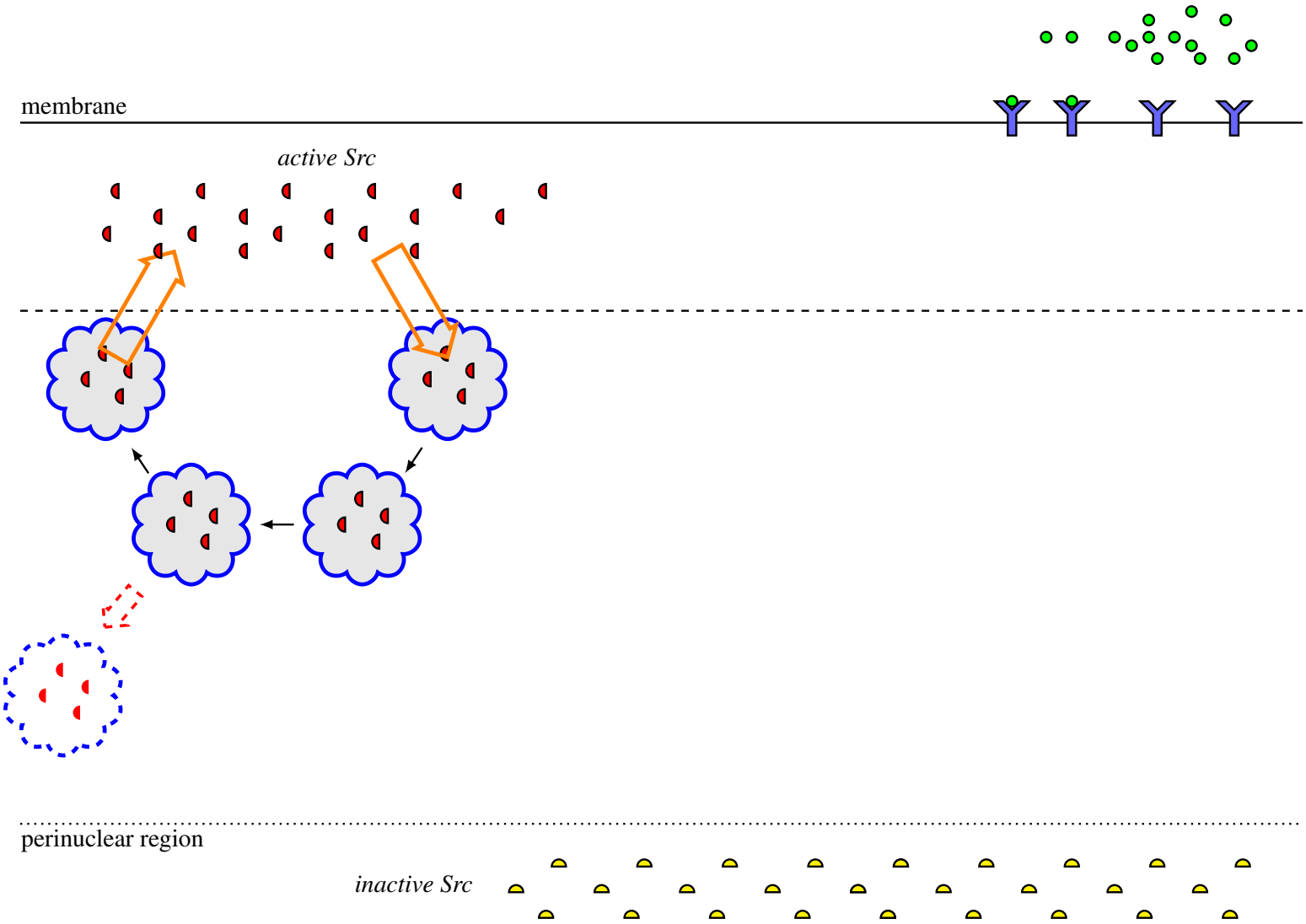

membrane
active Src
perinuclear region
inactive Src

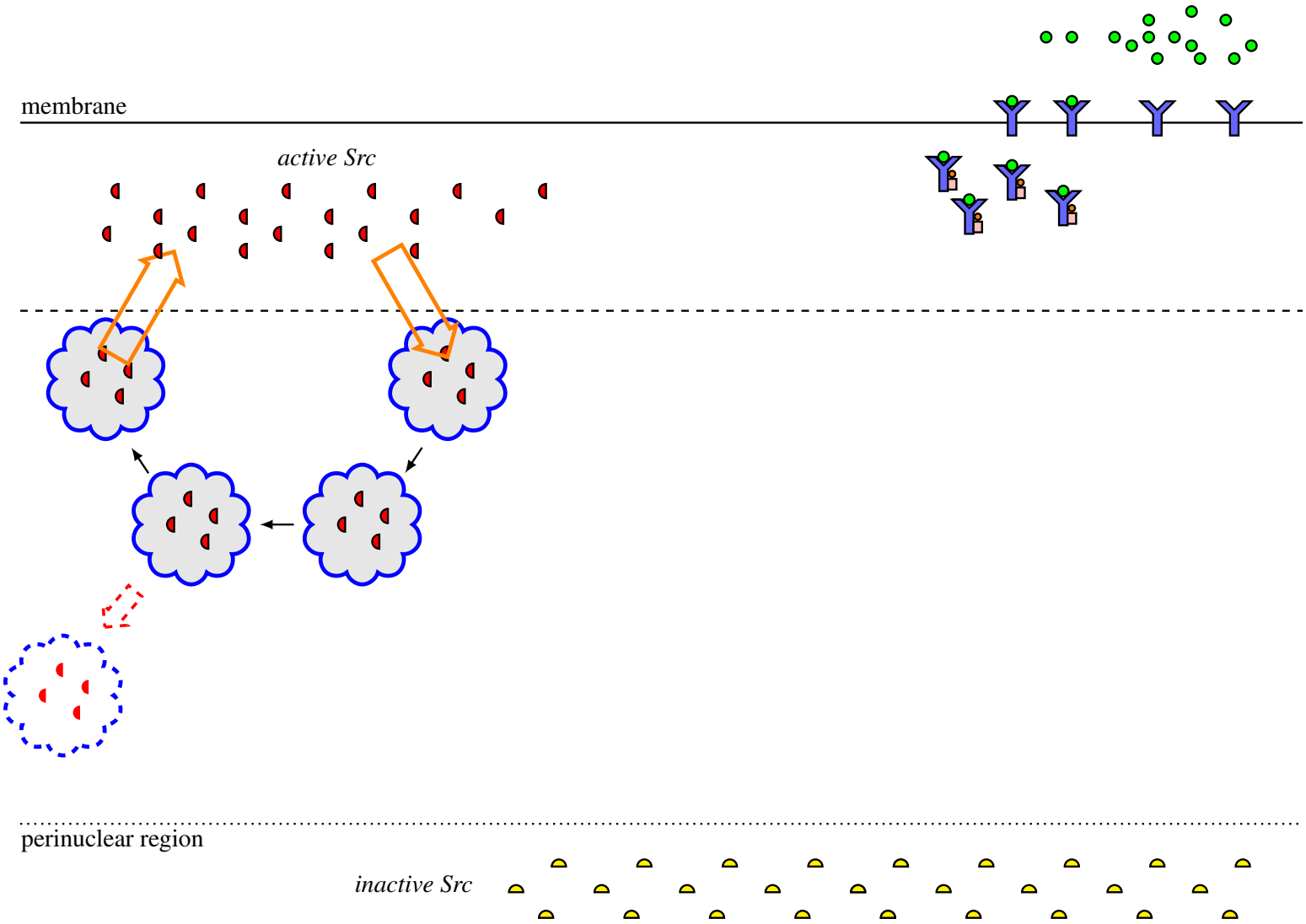

membrane
active Src
perinuclear region
inactive Src

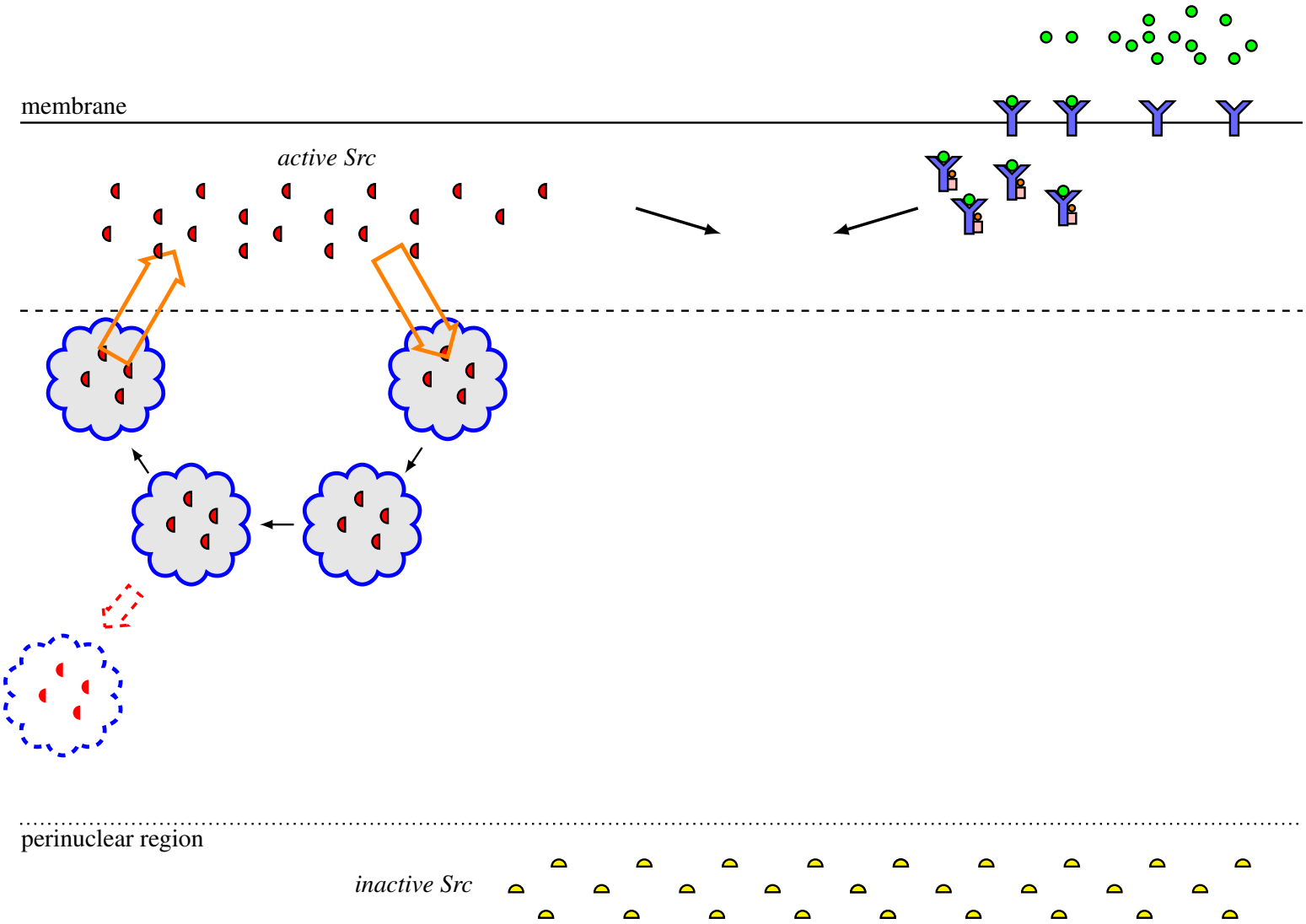

membrane
active Src
perinuclear region
inactive Src

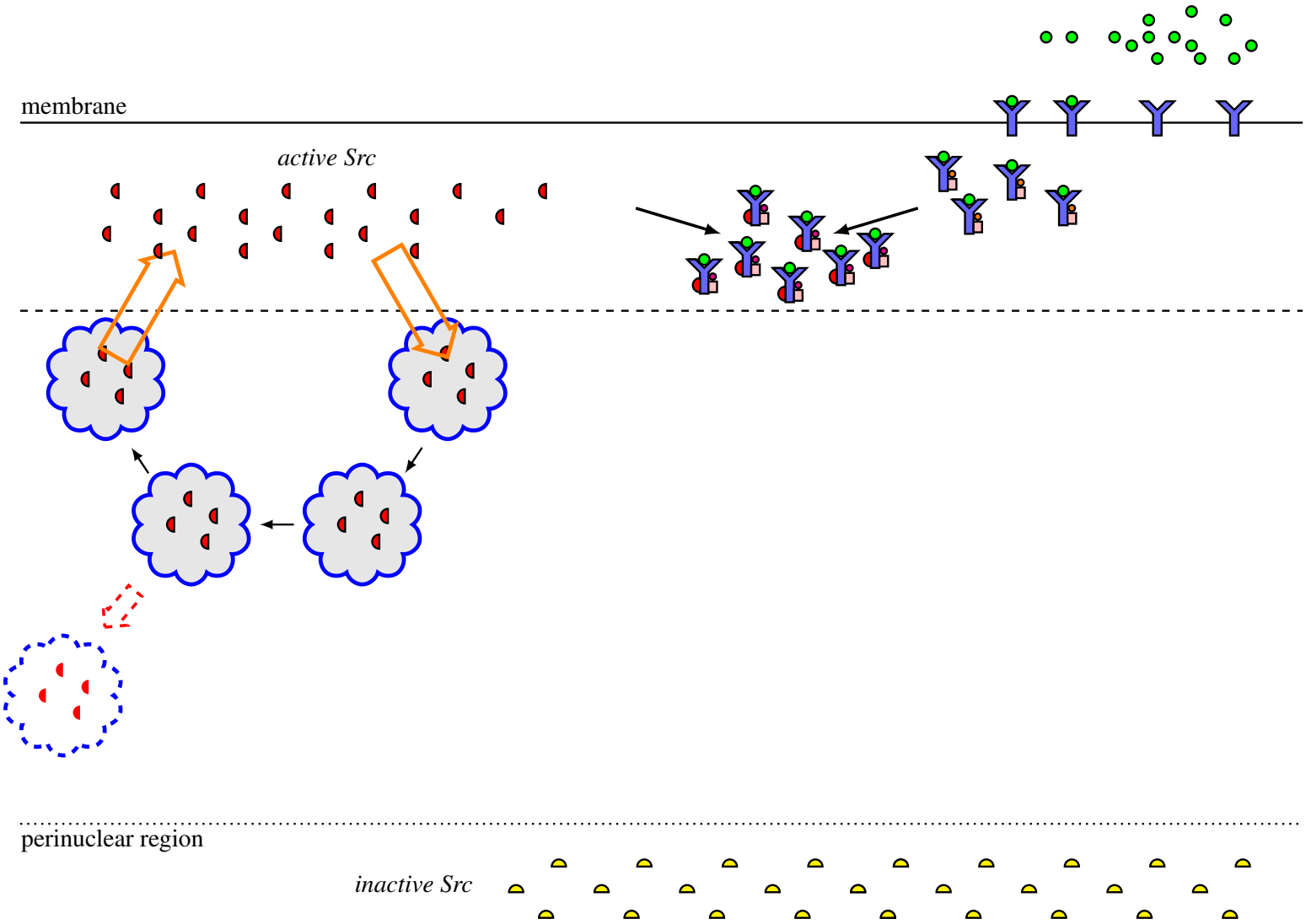

membrane
active Src
perinuclear region
inactive Src

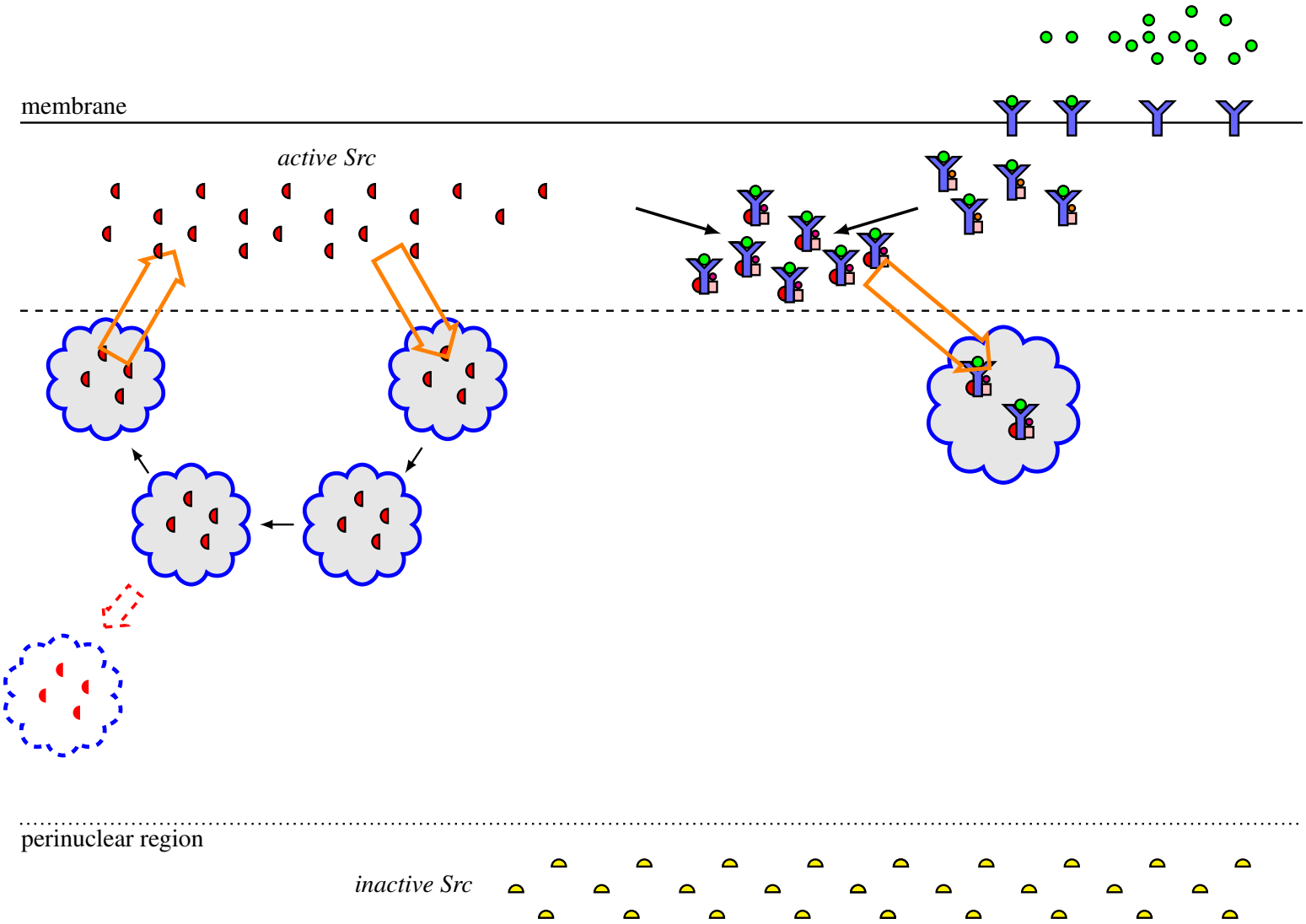

membrane
active Src
perinuclear region
inactive Src

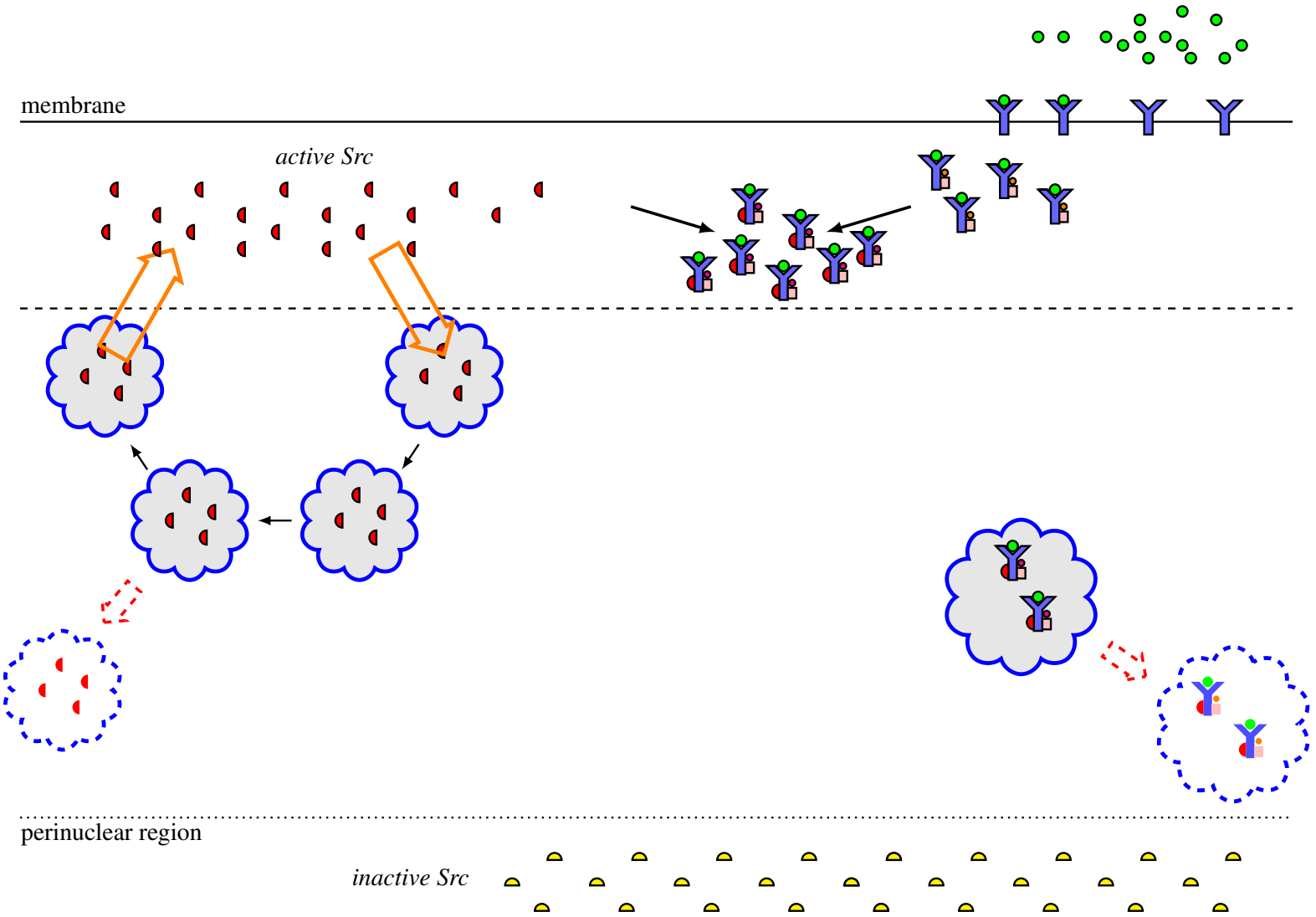

membrane
active Src
perinuclear region
inactive Src

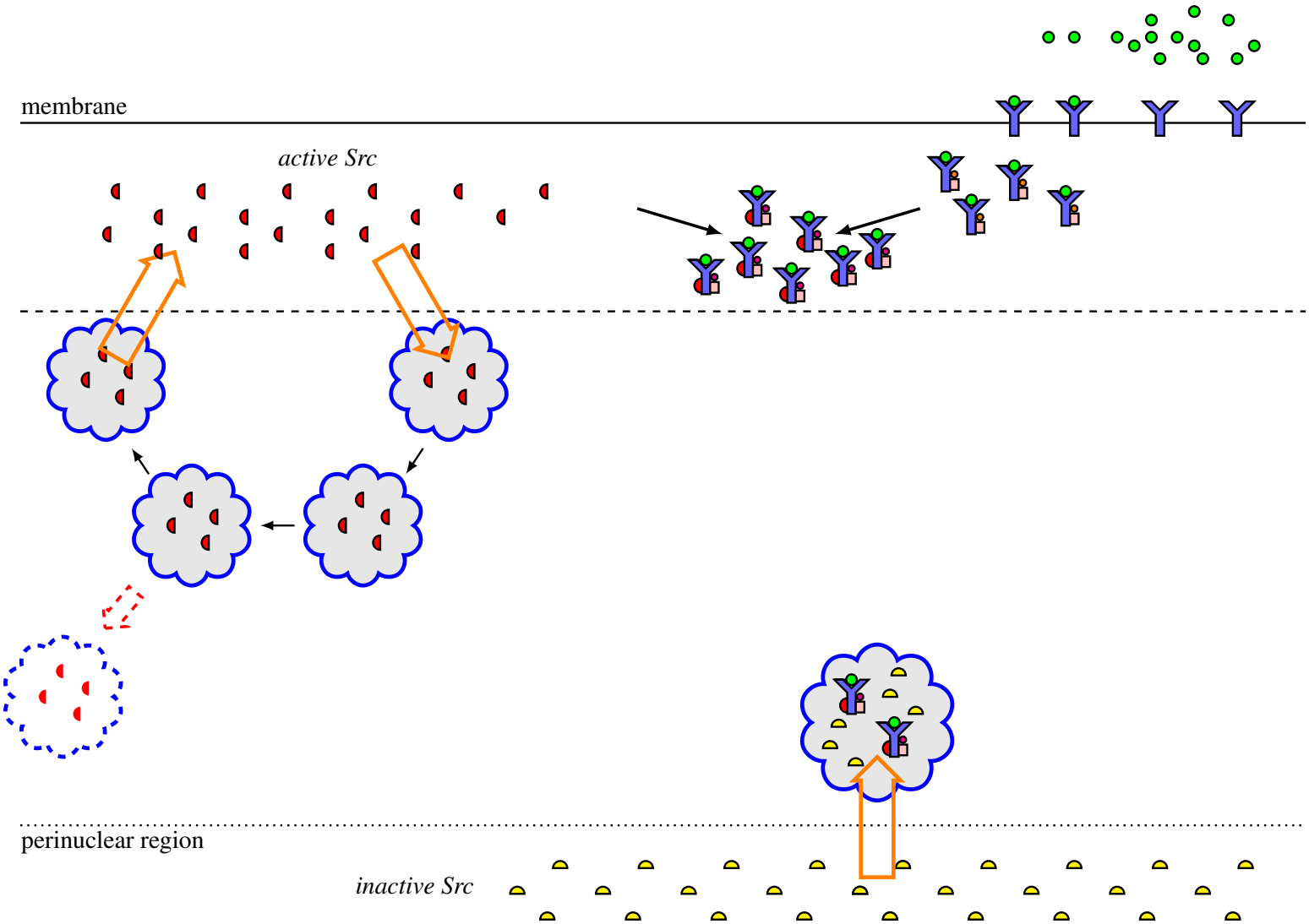

membrane
active Src
perinuclear region
inactive Src

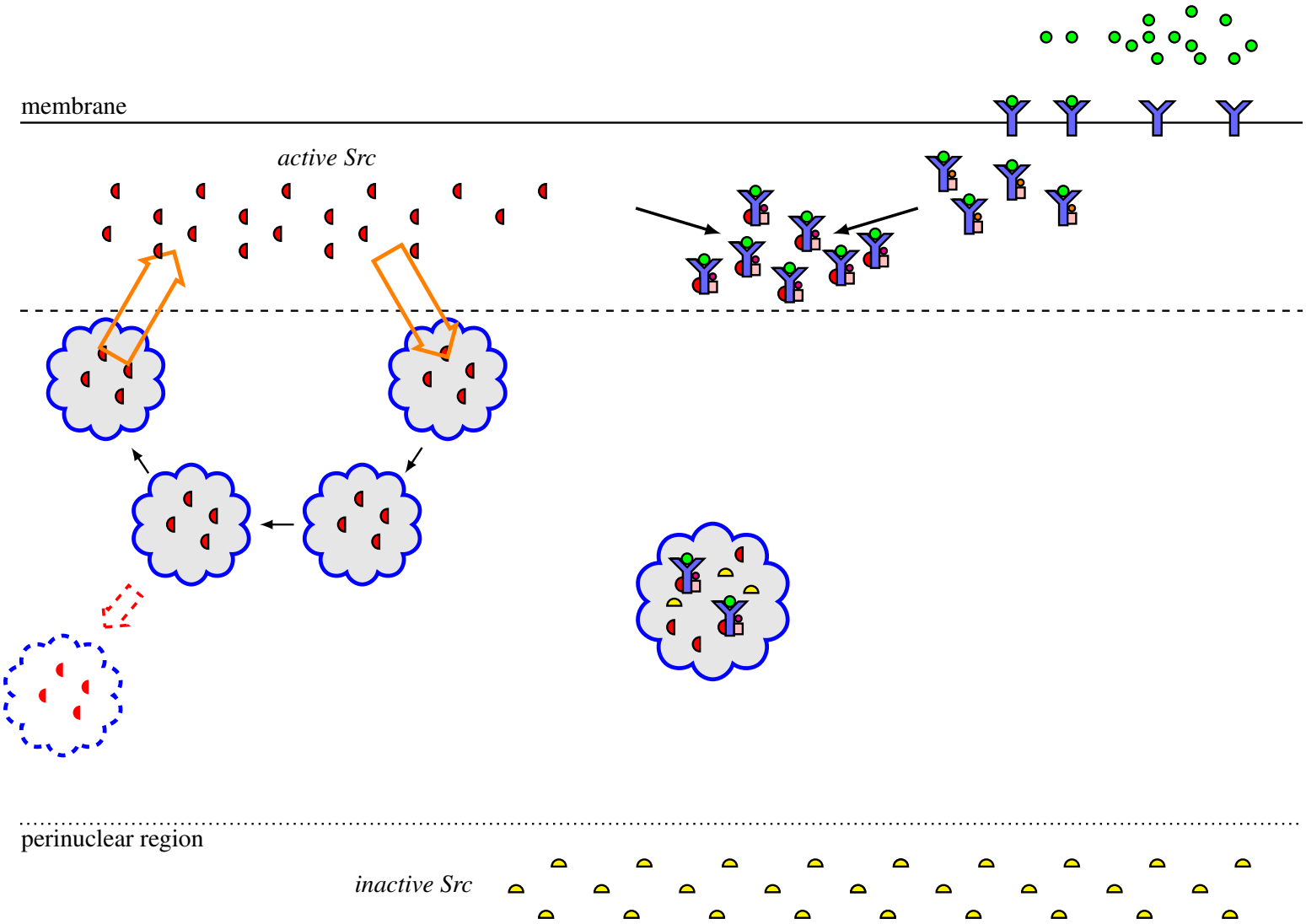

membrane
active Src
perinuclear region
inactive Src

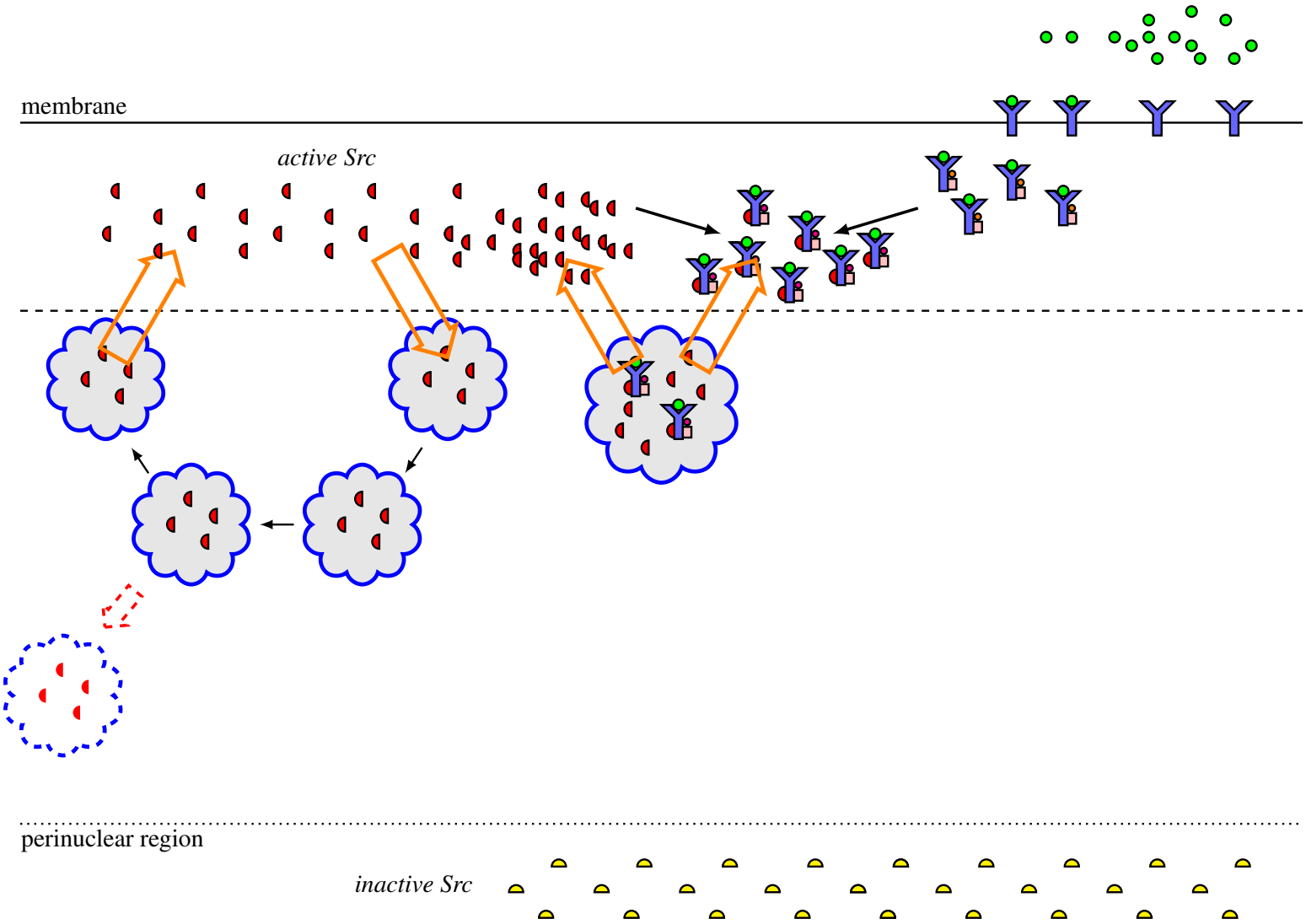

membrane
active Src
perinuclear region
inactive Src

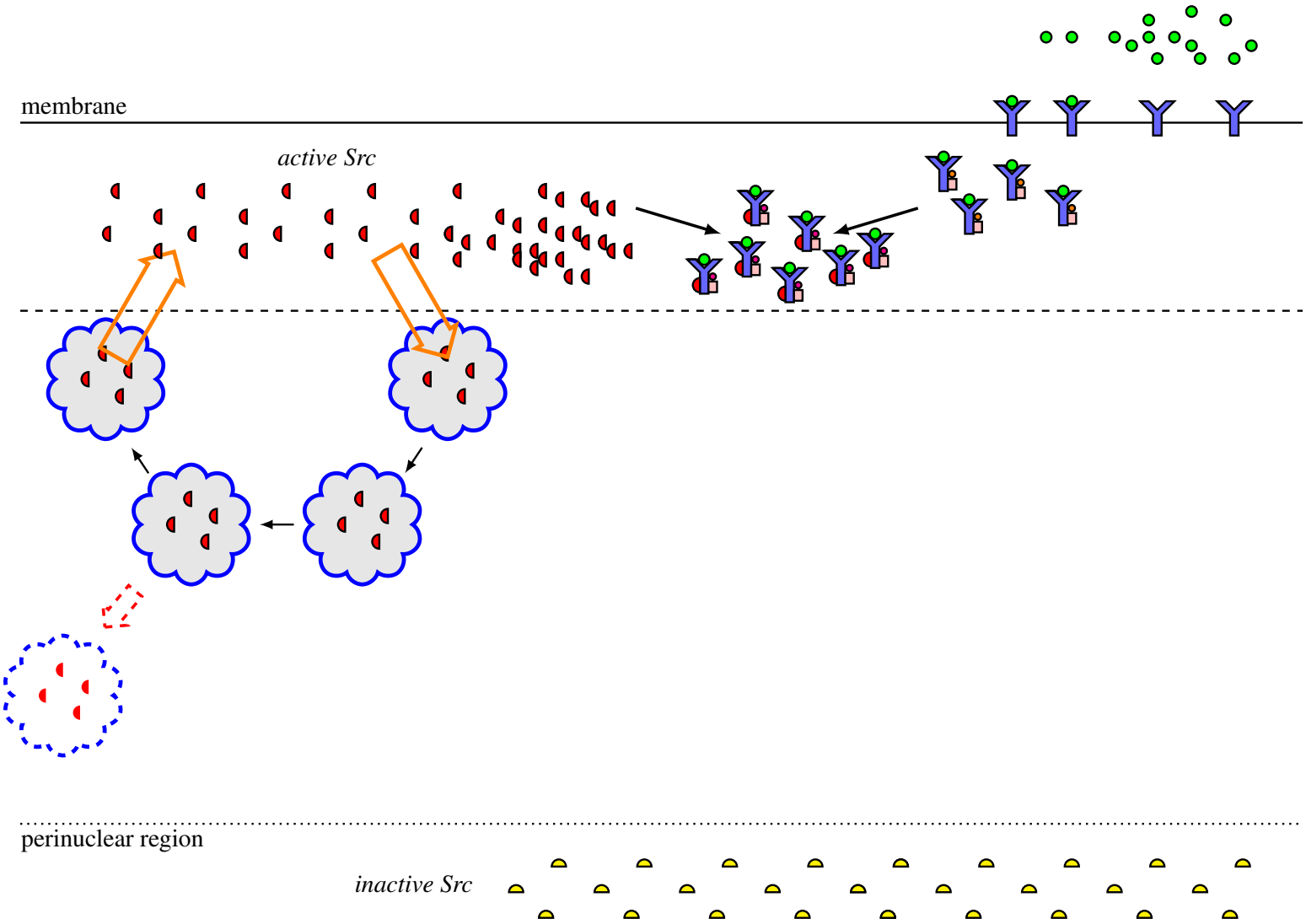

membrane
active Src
perinuclear region
inactive Src

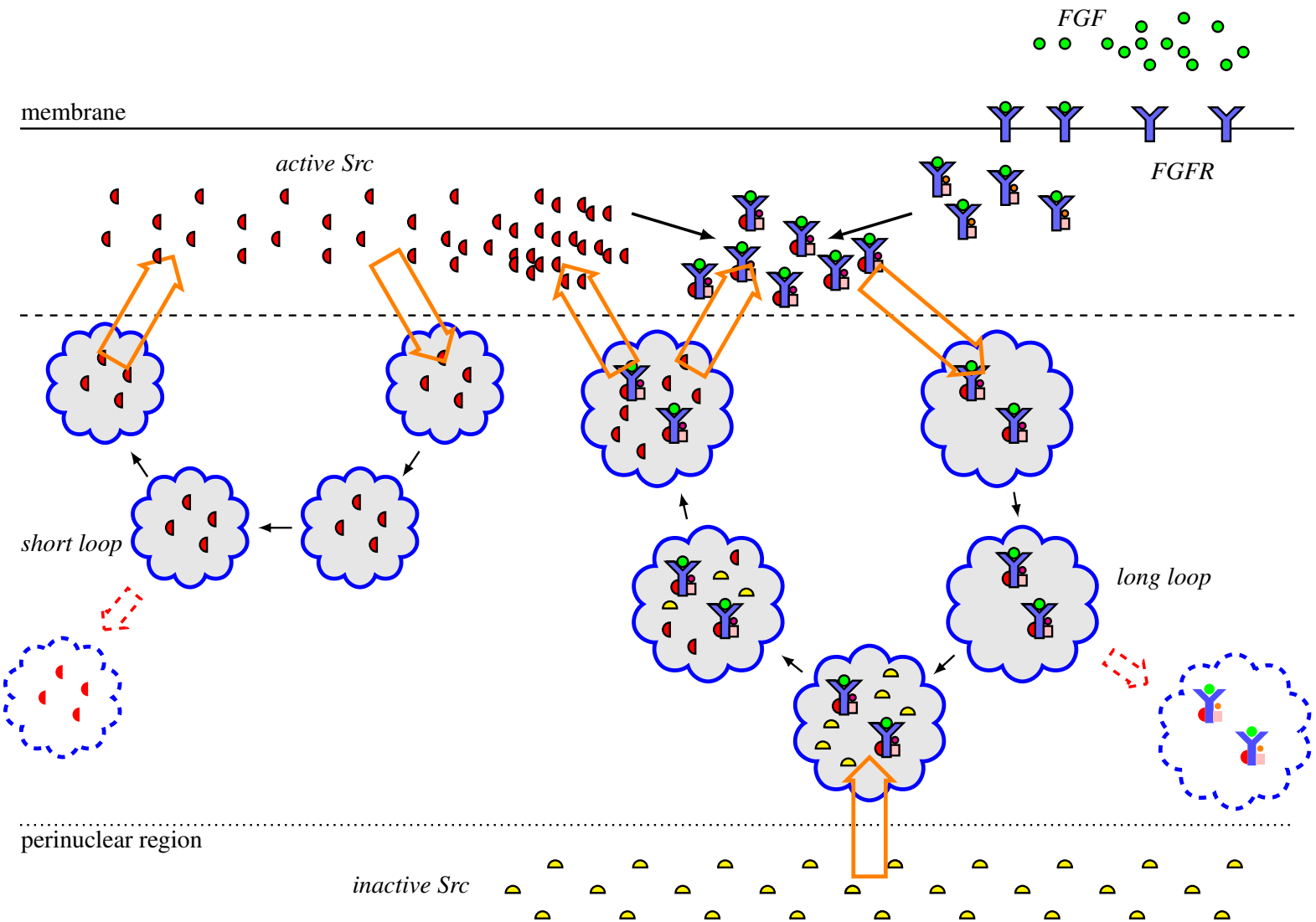

membrane
active Src
perinuclear region
inactive Src


membrane
active Src
perinuclear region
inactive Src


membrane
active Src
perinuclear region
inactive Src


membrane
active Src
perinuclear region
inactive Src


membrane
active Src
perinuclear region
inactive Src


FGF
membrane
active Src
FGFR
short loop
long loop
perinuclear region
inactive Src

# The challenges

- identification of recycling loops: number and type
- data is very limited
- qualitative
  - gradient of inactive versus active, activation within endosomes
  - endosome movement is directional along microtubules
- quantitative
  - estimates of endosome speeds and length of recycling loops
  - timing from FGF stimulation experiment

# Bio-PEPA, a stochastic process algebra

- species: reactions, stoichiometry, roles $\mathrm{op}_i \in \{\downarrow, \uparrow, \oplus, \ominus, \odot\}$

$$C \stackrel{def}{=} (\alpha_1, \kappa_1)\ \mathrm{op}_1\ C\ +\ \ldots\ +\ (\alpha_n, \kappa_n)\ \mathrm{op}_n\ C$$

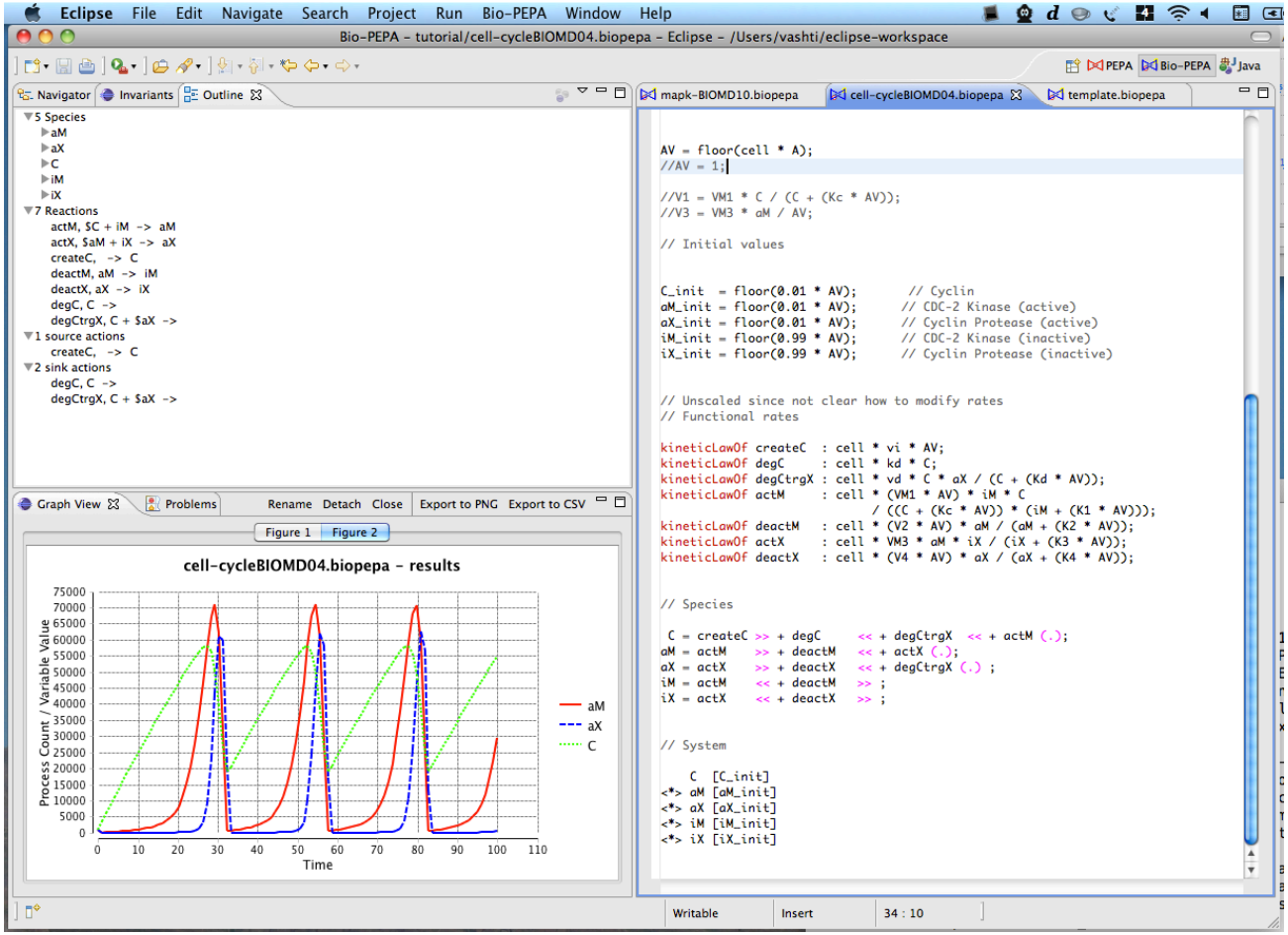
- model: quantities of species, interaction between species

$$P \stackrel{def}{=} C@(x_1) \underset{*}{\bowtie} \ldots \underset{*}{\bowtie} C(x_p)$$

- definition of behavioural semantics
- use of stoichiometry in model

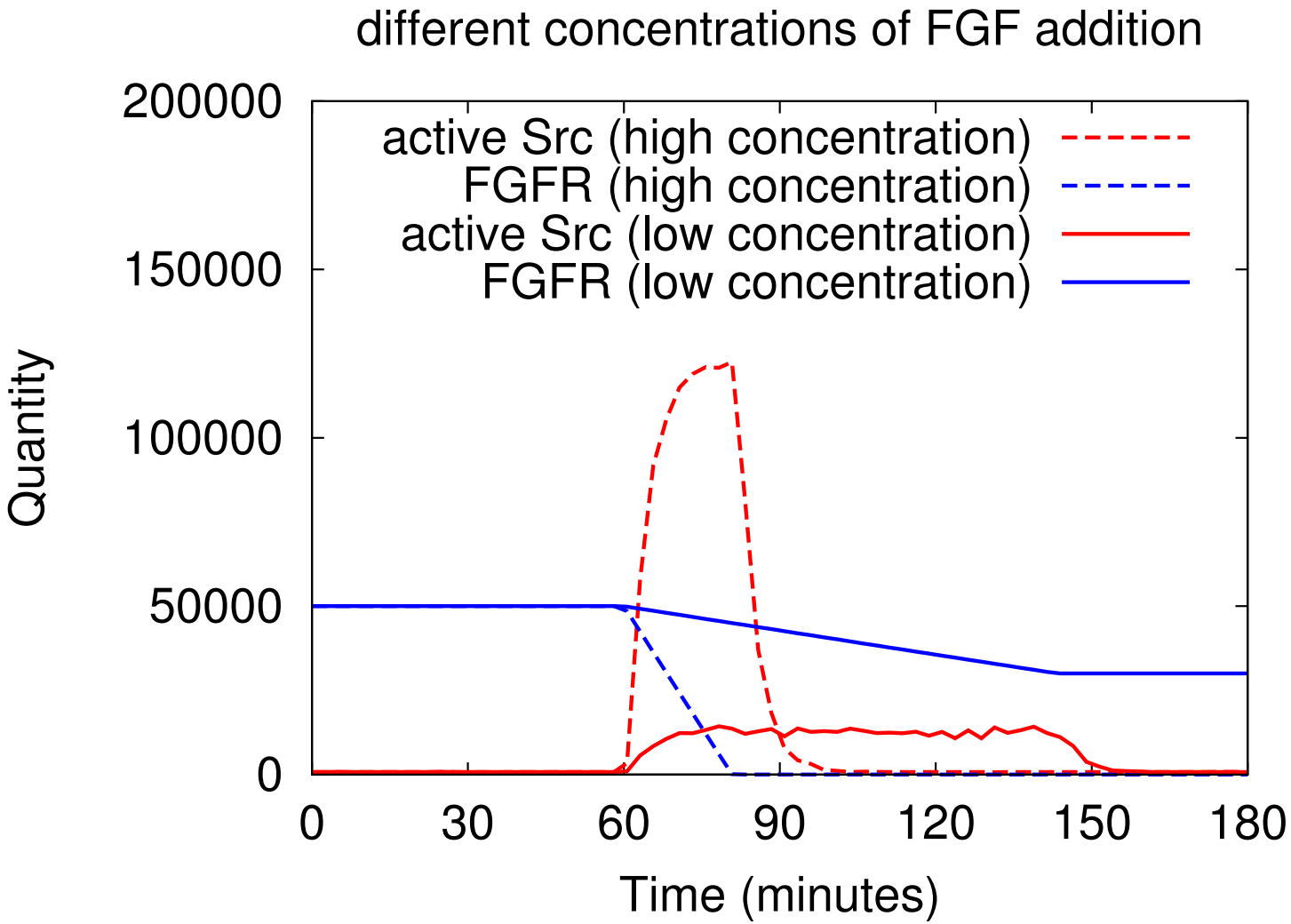
```
activeSrc   =   ... + (into_endosome,150) << activeSrc + ...
Endosome    =   ... + (into_endosome,1)   >> Endosome  + ...

into_endosome:  150 activeSrc -> Endosome
```

# Bio-PEPA Eclipse Plug-in




available for download at `www.biopepa.org`

# The results


different concentrations of FGF addition
active Src (high concentration)
FGFR (high concentration)
active Src (low concentration)
FGFR (low concentration)
Quantity
200000
150000
100000
50000
0
0
30
60
90
120
150
180
Time (minutes)

# Acknowledgements

**PEPA Group**
School of Informatics
University of Edinburgh
Jane Hillston

**Cancer Research UK**
Edinburgh
Margaret Frame
Emma Sandilands

**SynthSys/CSBE**
University of Edinburgh

**EPSRC**
**BBSRC**