

Global Regulation: Quorum Sensing

See Reference List and Chapter 13 pg. 587-594

Regulatory mechanism in which local cell density controls gene expression

- **Quorum:**
- **Also known as autoinduction:**
- **Members of the same species communicate by releasing and up-taking a diffusible molecule**

Processes regulated by quorum sensing:

- **Bioluminescence- *Vibrio fischeri***
- **Virulence factors, biofilm formation, extracellular enzyme secretion, antibiotic synthesis, etc.**

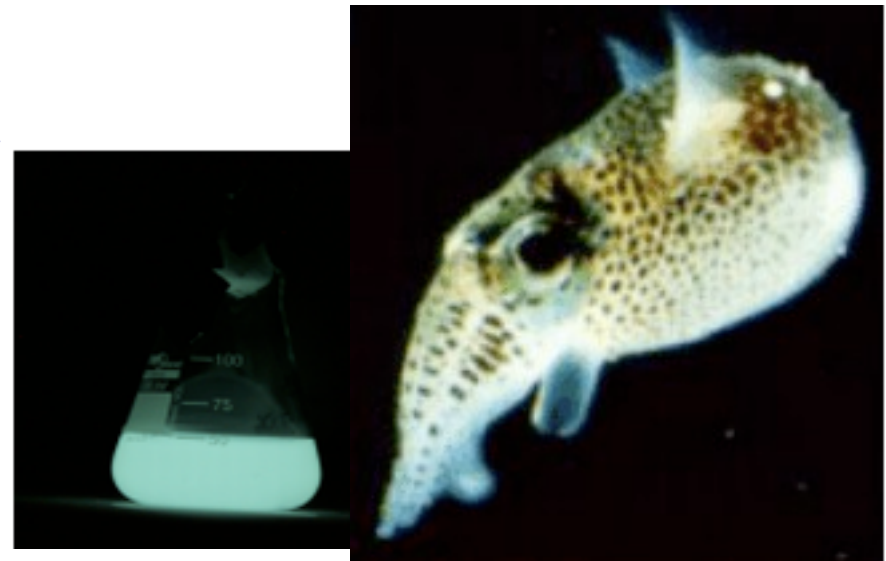
Bioluminescence

Squid that contains a light organ colonized by *Vibrio fischeri*

- Uses light organ in a protective manner to camouflage itself from predators by ventrally projecting light
 - Mimics moonlight so that a shadow is not cast
- Newly hatched squids are colonized by *V. fischeri* in less than one day

V. fischeri production of light

- Luciferase:



Population density-based control of luciferase production

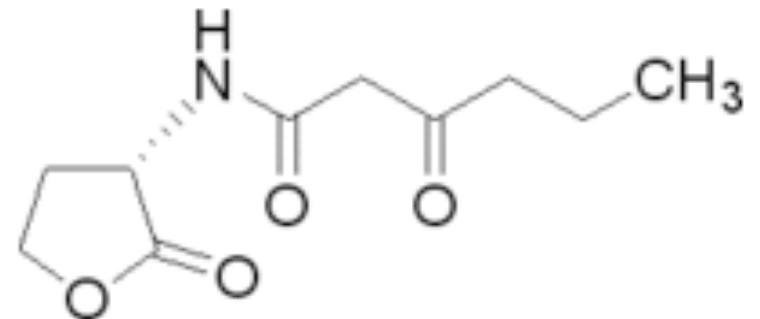
Population density is monitored by:

- *V. fischeri* produce a diffusible autoinducer molecule that accumulates in the surrounding environment

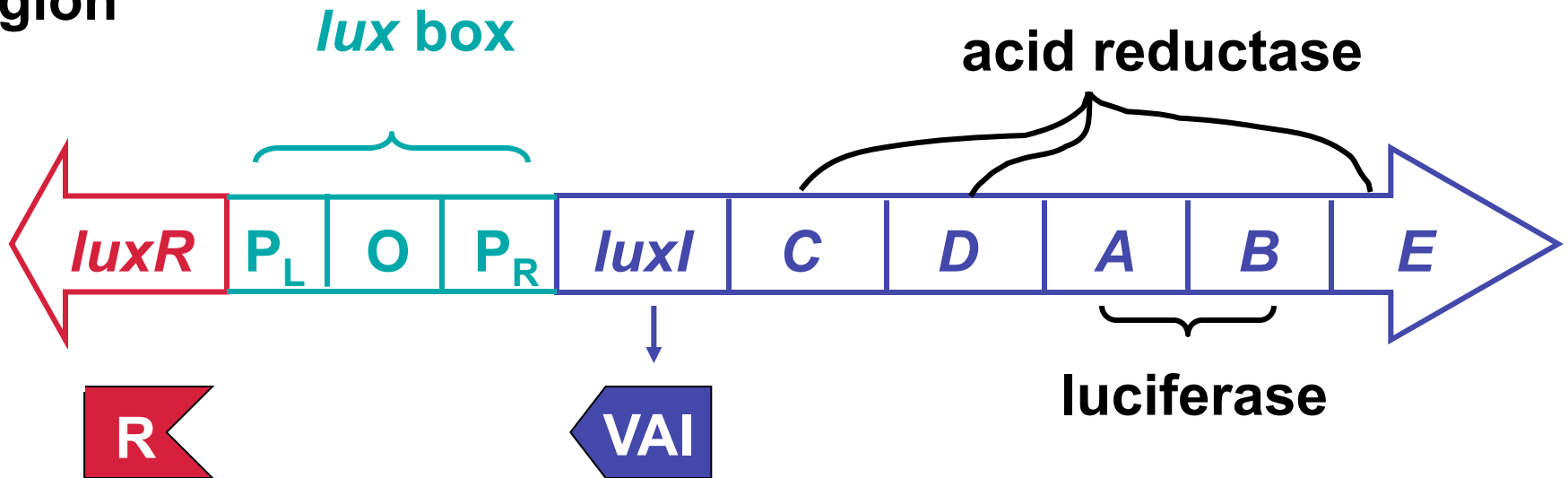
➤ VAI: 3-oxohexanoyl-homoserine lactone

↳ bacterial cell membrane is permeable to VAI, so the autoinducer accumulates in the growth medium or light organ

↳



Two *lux* operons are controlled by the same regulatory region



luxI operon:

- low level transcription when low cell density
- activated by:

➤ *LuxI*: VAI synthase

➤ *LuxCDABE*: structural genes products involved in luciferase production

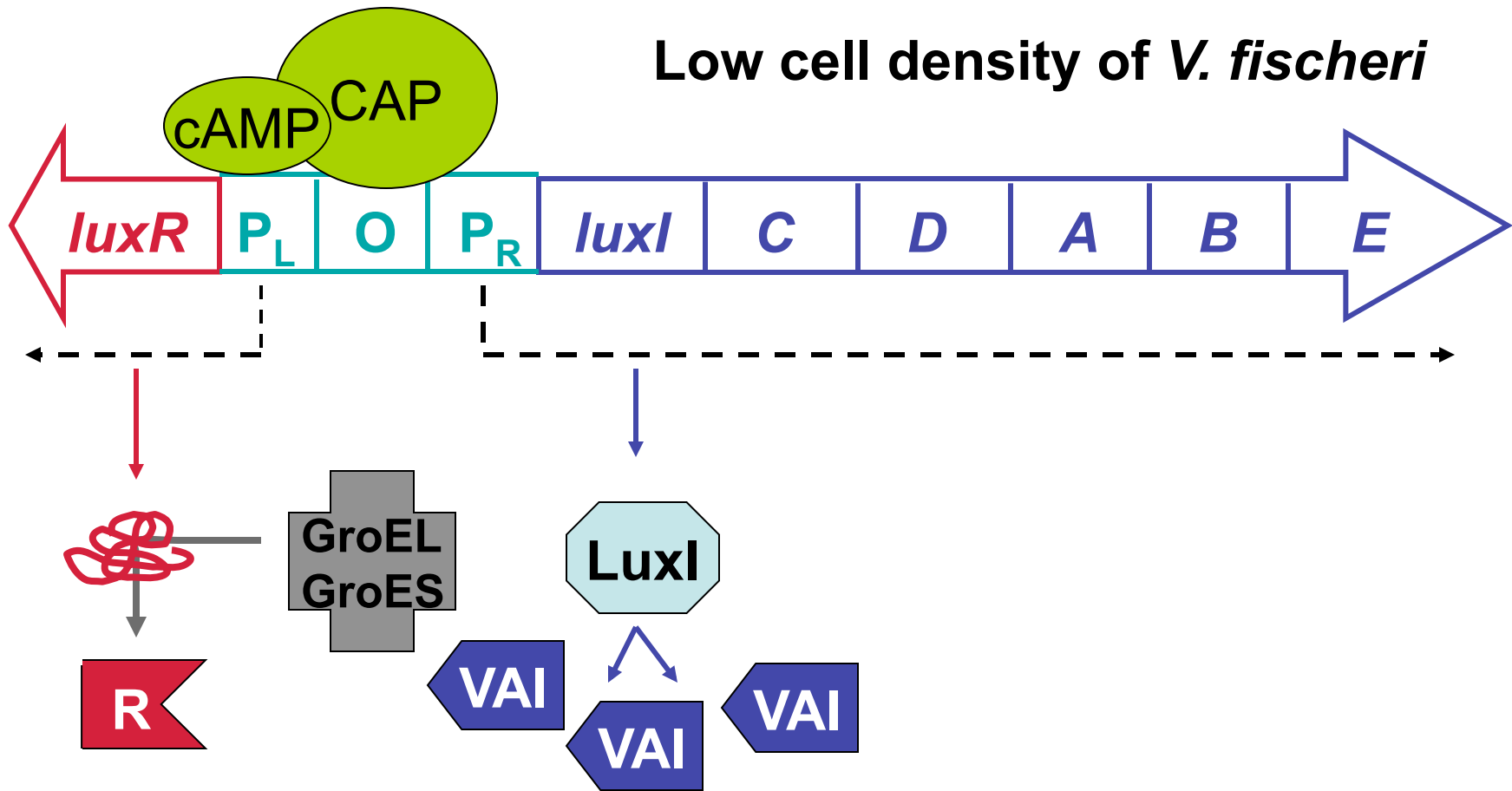
luxR:

- activated by: 1) cAMP-CAP; 2) low levels of LuxR-AI
- repressed by:

➤ **LuxR: Activates transcription from P_R when sufficient VAI present**

↳ **protein folded into active conformation by GroEL and GroES proteins (stress proteins)**

***lux* box- regulatory region that controls txn from P_L and P_R and contains DNA-binding sites for:**

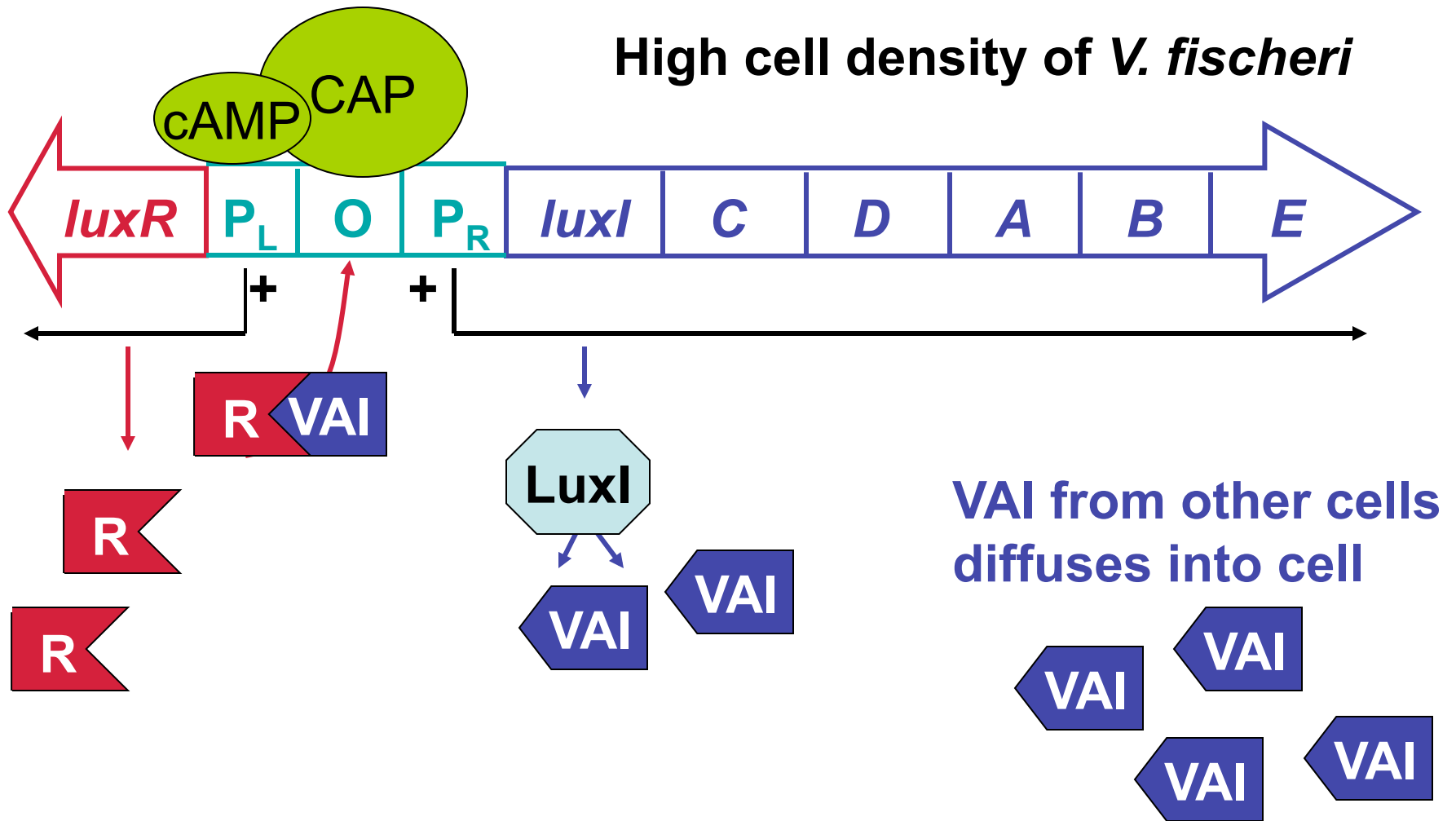


1) Basal level transcription of *luxICDABE*



2) If glucose absent, cAMP-CAP activates txn of P_L

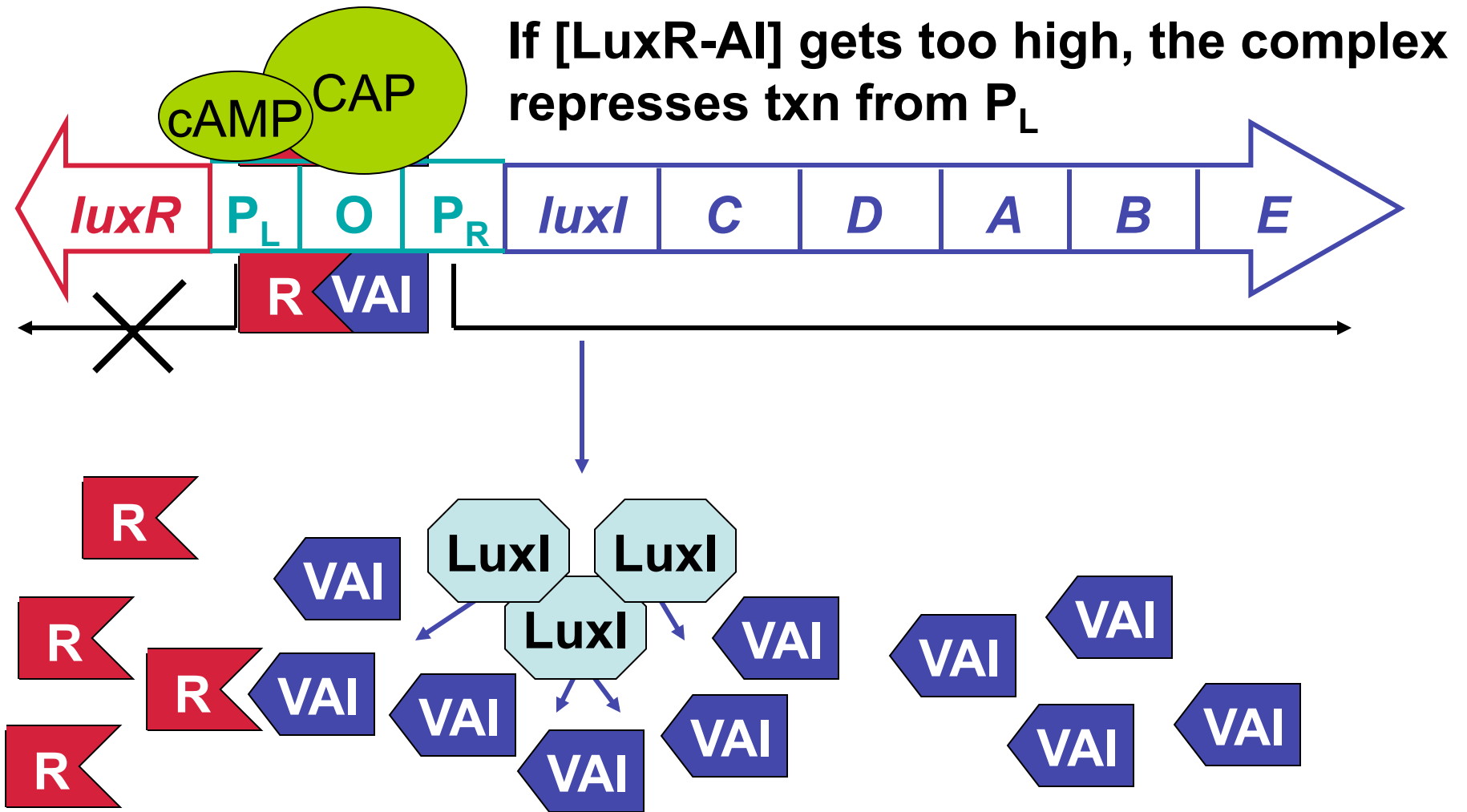
High cell density of *V. fischeri*



1) As cell density increases, so does [VAI]



2) LuxR-AI binding to *lux* box increases txn from P_L and P_R



Cell needs to be able control the level of LuxR produced, or quorum sensing activation cannot be turned off

Factors besides cell density that affect bioluminescence

- **Catabolite repression:**

- **Glucose needs to be absent, which would likely be the case inside a high density culture**

- **Presence of iron: represses txn from P_L**

- **Iron should be absent inside the squid light organ**

- **Presence of GroELS proteins: fold **LuxR** into an active enzyme**



Summary

Interspecies Quorum Sensing?

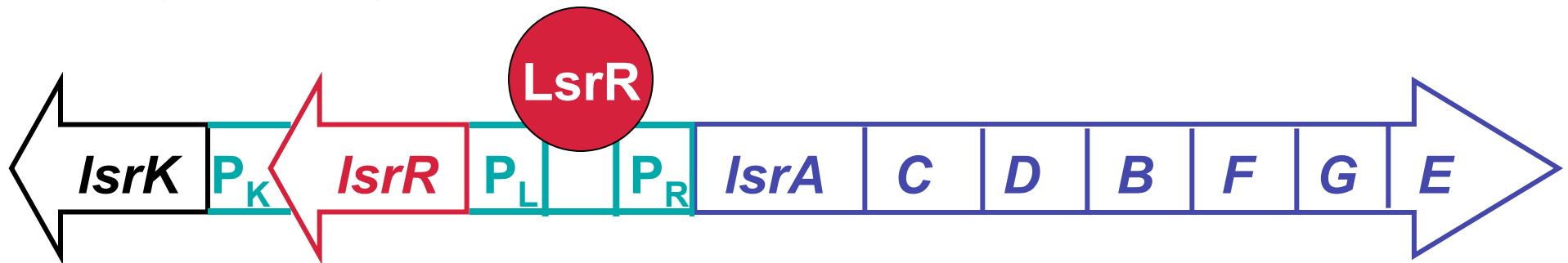
Different types of bacteria can respond to a special signal molecule produced by other types of bacteria

Autoinducer molecule AI-2:

- Produced by a number of different types of bacteria during exponential phase
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- Phosphorylated AI-2 has been shown to activate:
 - Virulence factors
 - Motility
 - Biofilm production
 - Antibiotic production

Since AI-2 is not diffusible, the cell must regulate its import

lsr genes regulate:



- **LsrR**: repressor of transcription from P_R
 - Inducer molecule is phosphorylated AI-2
- P_R : induced by cAMP-CAP
- **LsrACDB**: involved in import of AI-2
- **LsrFG**: involved in degradation of AI-2
- **LsrK**: kinase that phosphorylates AI-2



Sequence of events following AI-2 production

1) AI-2 is synthesized by the LuxS enzyme and exported out of the cell

➤ *luxS* gene is not linked to the *lsr* genes

2) If cAMP-CAP is present, transcription from P_R is partially activated

3) Expression of *lsrACBD* produces a transporter for up-take of AI-2

4) Once AI-2 enters cell it can be phosphorylated by LsrK



5) Phosphorylated AI-2 inactivates LsrR so that increased expression from P_R occurs

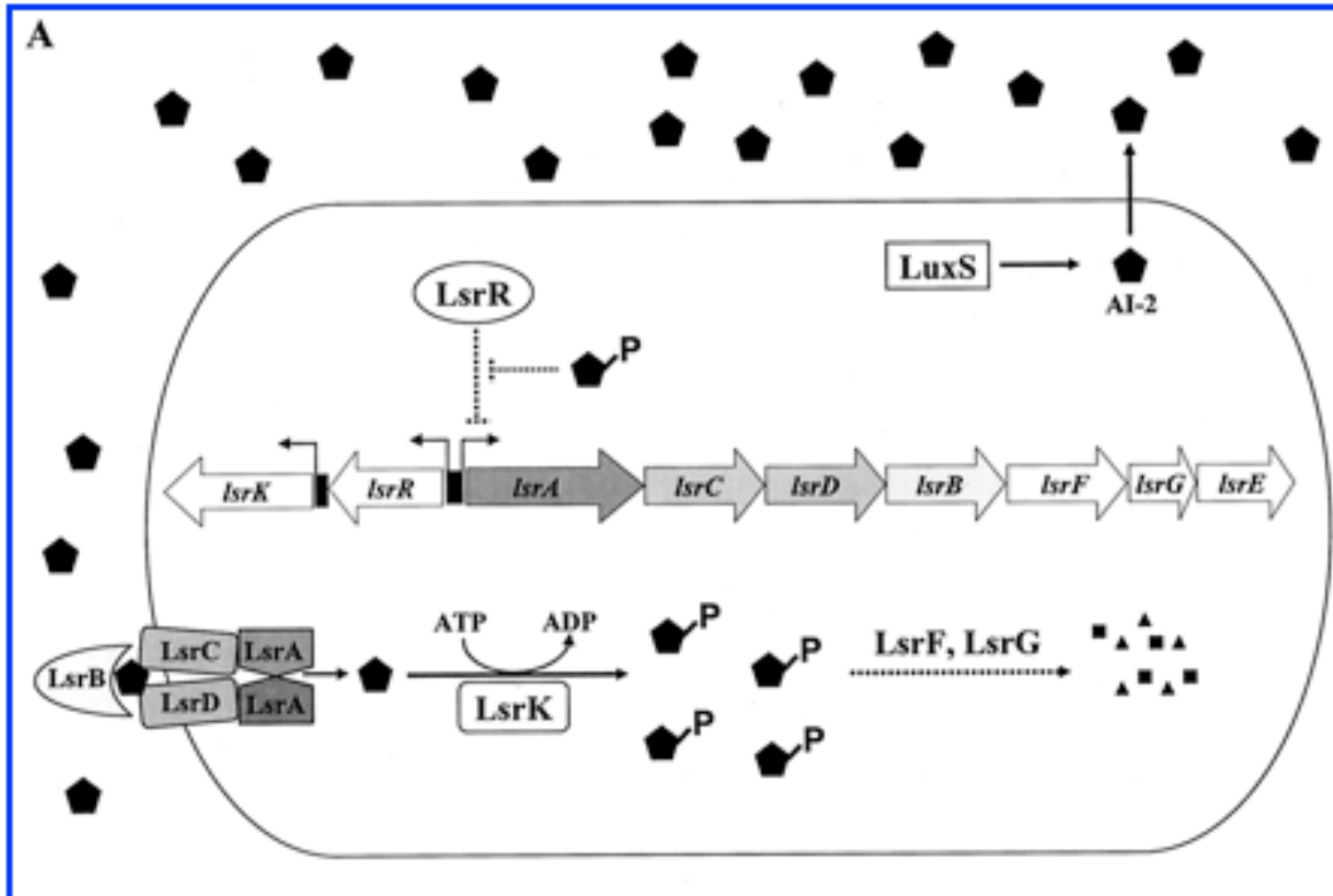
6) Increased expression from P_R leads to increased import of AI-2

7) Degradation of phosphorylated AI-2 by LsrFG keeps levels of the inducer in check

Phosphorylated AI-2 is involved in activating regulons involved in biofilm formation, virulence factors, motility, etc.

****Amount of intracellular phosphorylated AI-2 is regulated by:**

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- **Uptake by LsrACBD**
- **LsrK (regulated by numerous mechanisms)**



**Model of AI-2 uptake and regulation proposed by:
Xavier and Bassler, 2005. J. Bacteriol. 187: 238-248**