

Image: Growth factor stimulated human breast cancer cells stained for actin (blue), nuclei (green) and the Golgi apparatus (purple). Courtesy of Torsten Witmann. Used with permission.

**Anonymous
students
MK & NM**

Tech Spec Review **oncoCURES**

DESIGN

LOGISTICS

ISSUES

oncoCURES

Tech Spec Review

The “What?”

- added cells mark cancer in metastasis
- lights up near tumors

The “Why?”

- main cause of death
- possibility of killing tumor cells

The “How?”

- use dual signaling to indicate metastasis
- signals production of light
- shows tumor cells moving

SYSTEM OVERVIEW

DESIGN

LOGISTICS

ISSUES

DEVICE-LEVEL DIAGRAM:

PATIENT T-CELL CHASSIS

“DEBRIS”

MMP-1

MMP
SENSOR

C1+ PRODUCTS

“AND”

SIGNAL
PRODUCER

LIGHT
PRODUCER

LIGHT

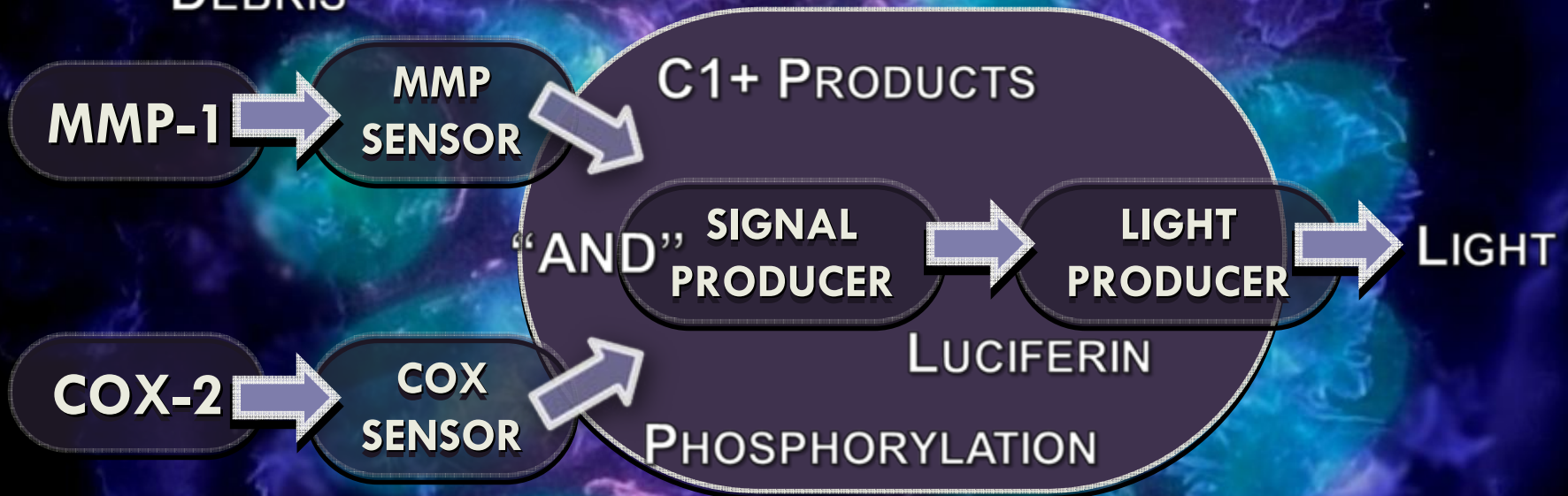
COX-2

COX
SENSOR

LUCIFERIN

PHOSPHORYLATION

PROSTANOIDS



SYSTEM OVERVIEW

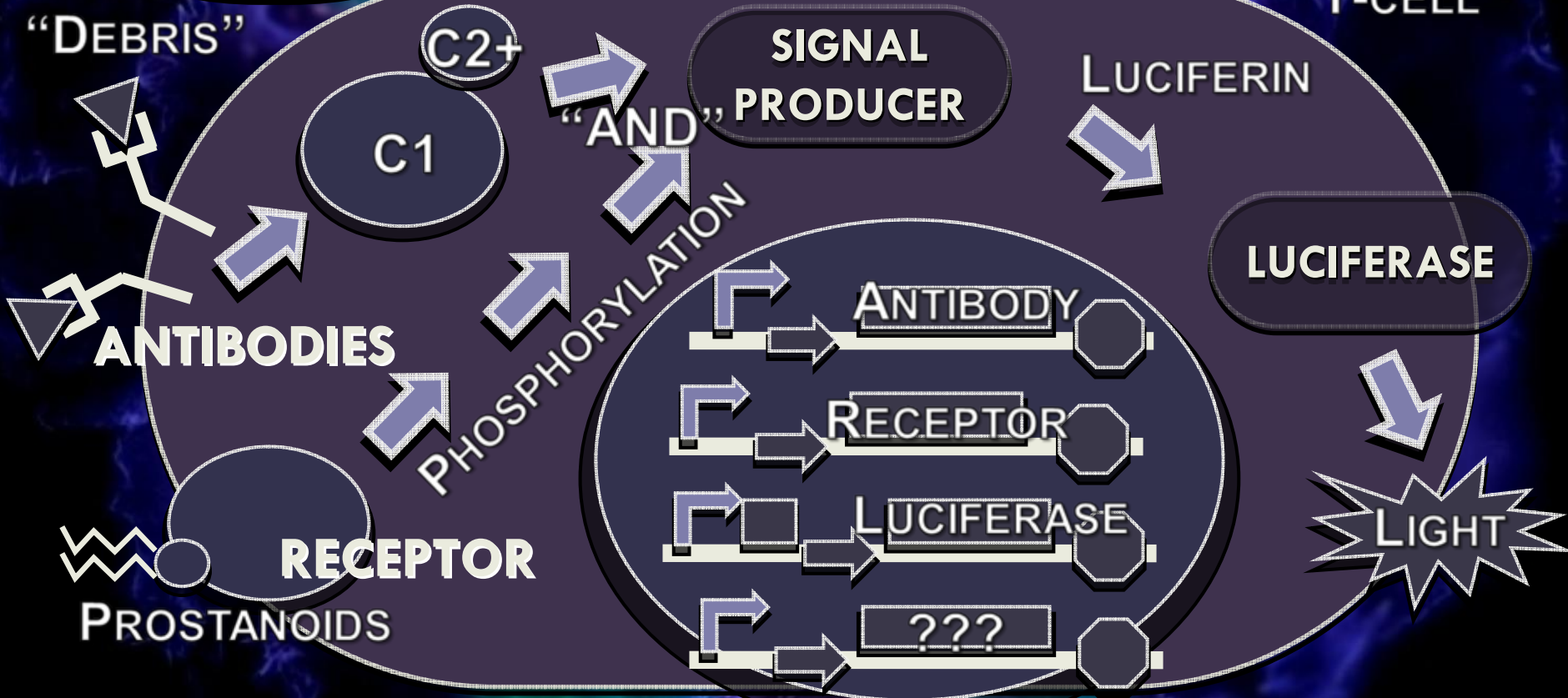
DESIGN

LOGISTICS

ISSUES

PARTS-LEVEL DIAGRAM:

T-CELL



MMP SENSOR

DESIGN

LOGISTICS

ISSUES

MMP-1

“DEBRIS”

MMP
SENSOR

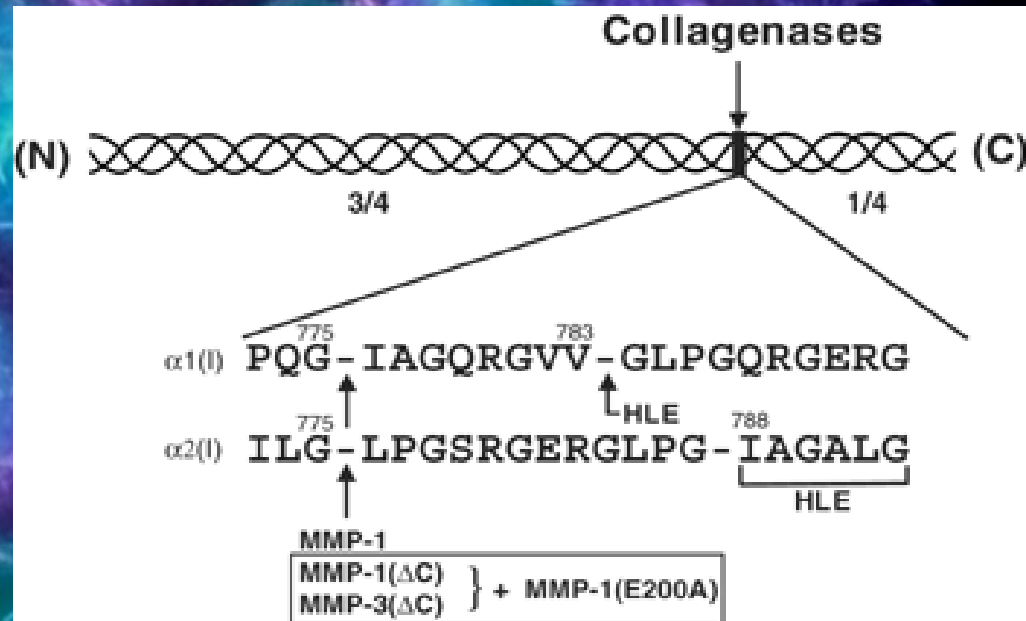
C1+ PRODUCTS

“DEBRIS”

MMP-1



Courtesy of RCSB.org



Source: Chung, L., et al. "Collagenase unwinds triple-helical collagen prior to peptide bond hydrolysis." *The EMBO Journal* 23 (2004): 3020-3030. Courtesy of Hideaki Nagase. Used with permission.

MMP SENSOR

DESIGN

LOGISTICS

ISSUES

MMP-1

“DEBRIS”

MMP
SENSOR

C1+ PRODUCTS

PARTS:

- GENE REGULATION
- ANTIBODIES, C1

FUNCTION:

- STRONG PROMOTER, GENE, TERMINATOR
- SURFACE ANTIBODIES BIND MMP PRODUCTS
- DETECT MMP-1 ENZYME IN AREA (METASTASIS)

MCMV

ANTIBODY

BBA_J63002

MMP SENSOR

DESIGN

LOGISTICS

ISSUES

MMP-1

“DEBRIS”

MMP
SENSOR

C1+ PRODUCTS

COLLAGEN “DEBRIS”

HYDROLYSIS

C1

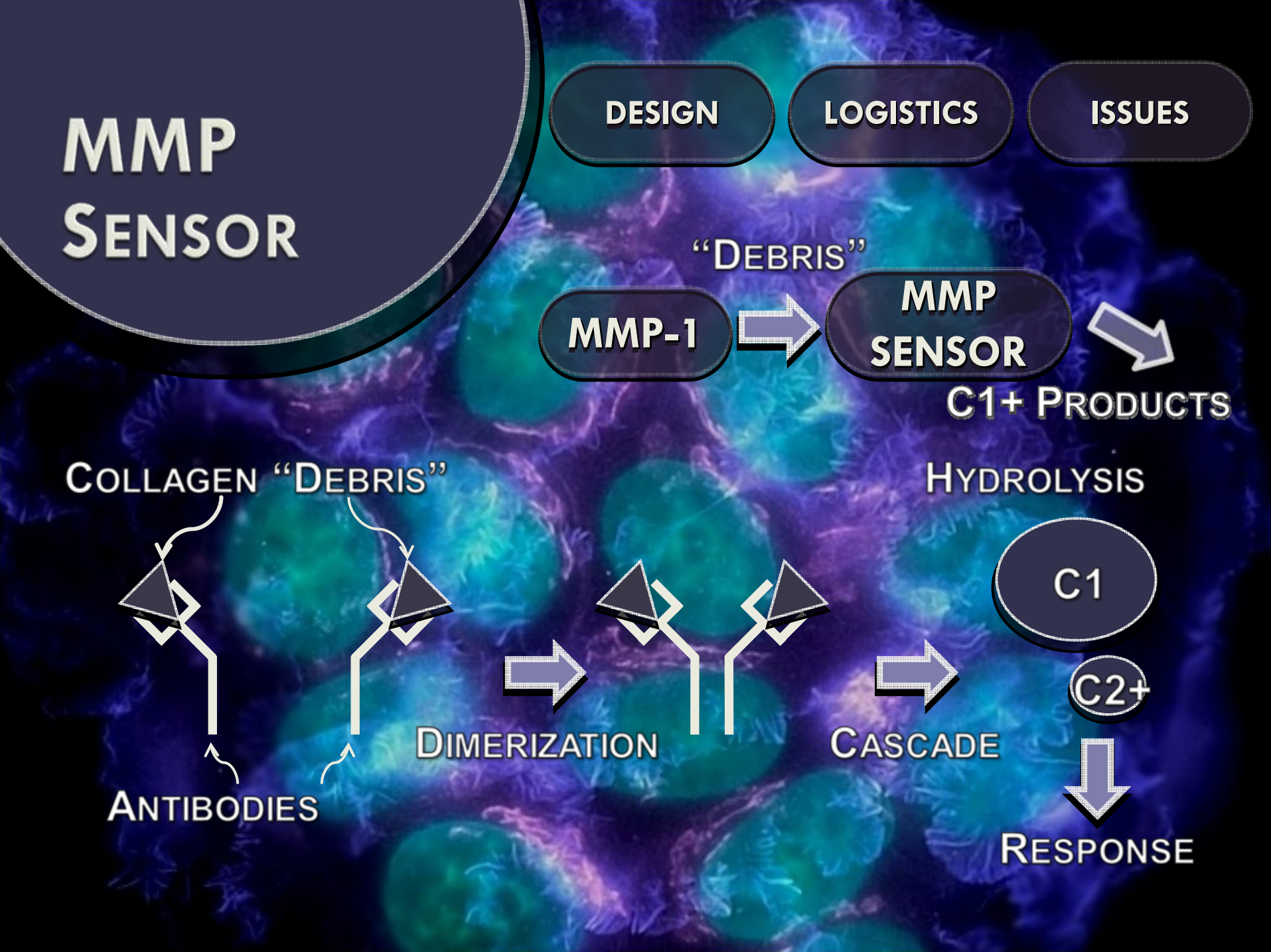
C2+

DIMERIZATION

CASCADE

RESPONSE

ANTIBODIES



COX SENSOR

DESIGN

LOGISTICS

ISSUES

COX-2



PHOSPHORYLATION
COX
SENSOR



PROSTANOIDS

Image removed due to copyright restrictions.

COX SENSOR

DESIGN

LOGISTICS

ISSUES

COX-2



COX
SENSOR



PHOSPHORYLATION

PROSTANOIDS

PARTS:

- GENE REGULATION
- RECEPTOR

FUNCTION:

- STRONG PROMOTER, GENE, TERMINATOR
- RECEPTORS BIND COX PRODUCTS
- DETECT COX-2 ENZYME IN AREA (METASTASIS)

MCMV



RECEPTOR

BBA_J63002

SIGNAL PRODUCER

DESIGN

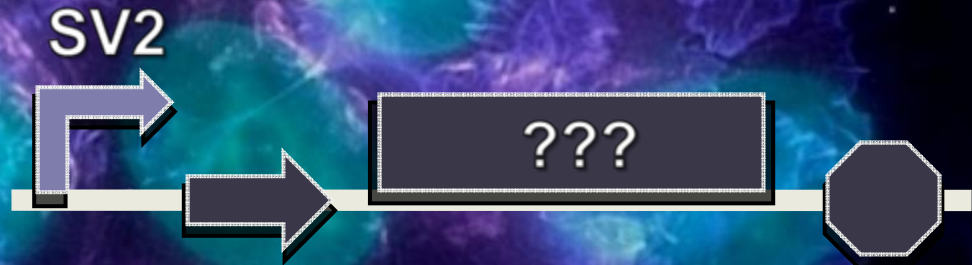
LOGISTICS

ISSUES



PARTS:

- GENE REGULATION
- BLACK BOX



BBA_J63002

FUNCTION:

- MODERATELY STRONG PROMOTER, TERMINATOR, GENE?
- MAKES LUCIFERIN FOR LUCIFERASE
- “AND” GATE ENSURES TUMOR PROXIMITY

LIGHT PRODUCER

DESIGN

LOGISTICS

ISSUES

LUCIFERIN



LIGHT PRODUCER



LIGHT

$\text{LUCIFERIN} + \text{ATP} \rightarrow \text{LUCIFERYL ADENYLATE} + \text{ADP}$

$\text{LUCIFERYL ADENYLATE} + \text{O}_2 \rightarrow \text{OXYLUCIFERIN} + \text{AMP} + \text{LIGHT}$

SUBSTRATES:

- ATP PRESENT
- O_2 AFFECTED BY TUMOR, INVERTER?
- LUCIFERIN FROM SIGNAL PRODUCER

Image removed due to copyright restrictions.
Photo of a glowing insect.

LIGHT PRODUCER

DESIGN

LOGISTICS

ISSUES

LUCIFERIN

LIGHT PRODUCER

LIGHT

PARTS:

- GENE REGULATION
- LUCIFERASE

H2CMV



SV40

LUCIFERASE



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FUNCTION:

- STRONGER PROMOTER, ENHANCER, GENE, TERMINATOR
- EXCESSIVE PRODUCTION OF LIGHT
- HIGHLIGHTS TROUBLED AREAS

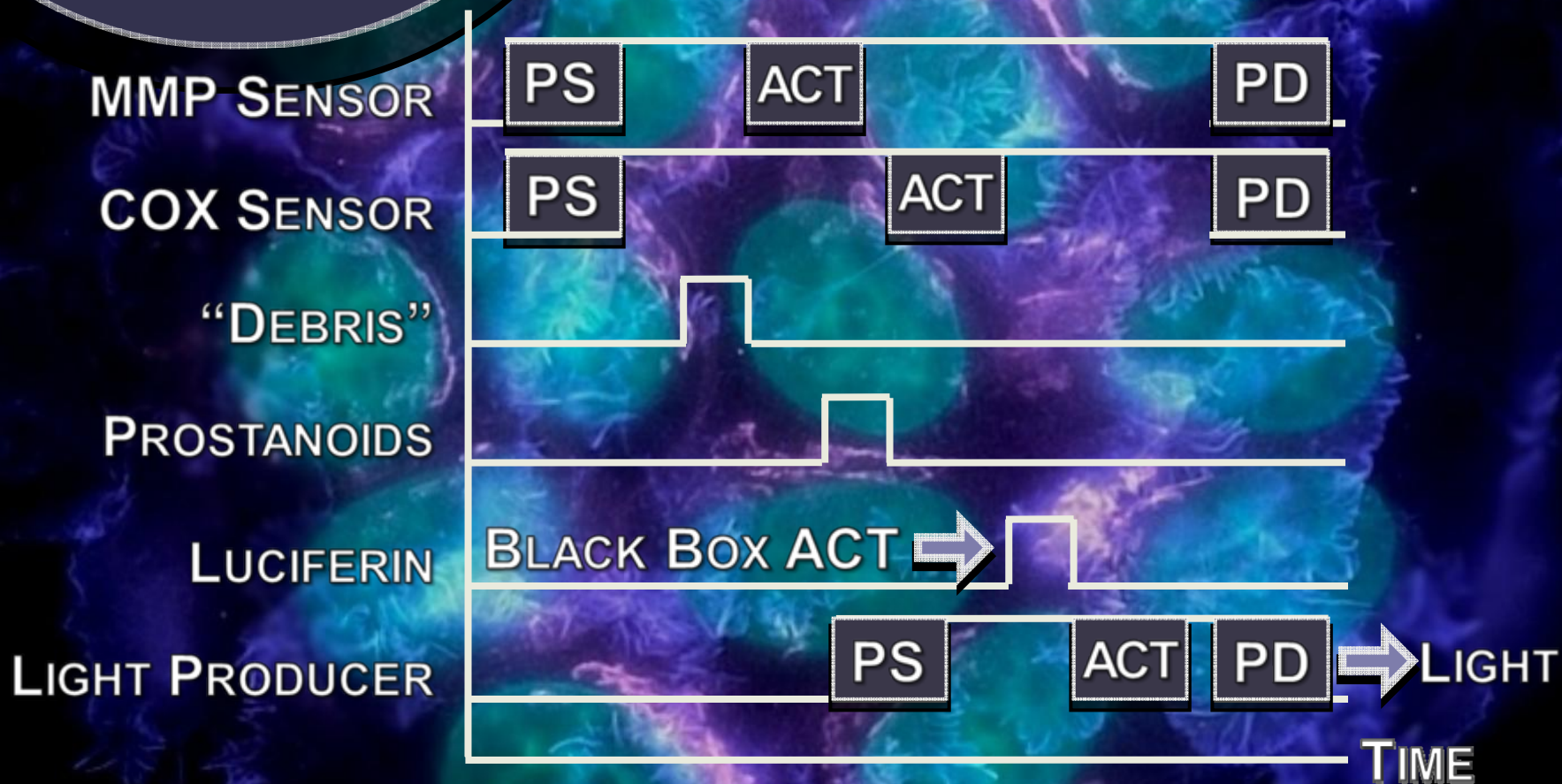
TIMING DIAGRAM

DESIGN

LOGISTICS

ISSUES

PS = SYNTHESIS ACT = ACTIVATION
PD = DEGRADATION



MAKING IT WORK

DESIGN

LOGISTICS

ISSUES

TESTING:

- MEMBRANE PRESENCE, CELL FREEZE-FRACTURE
- EXTRACELLULAR BINDING

DEBUGGING:

- REPORTERS USING INTERMEDIATES
- IN VITRO, BBA_I13522, GFP FOR DEVICE PRODUCTION
- LUCIFERIN REACTION

Image removed due to copyright restrictions.

Diagram with caption “freeze-fracture splits membrane.”

QUESTIONS

DESIGN

LOGISTICS

ISSUES

BUILDABLE?

- USED IN OTHER RESEARCH
- IMITATES DEVELOPING MEDICAL TREATMENTS

COST?

- PRODUCTION OF ANTIBODIES, RECEPTOR EVOLUTION, ETC.

TIME?

- EXPERIMENTATION AND TESTING
- SEVERAL PARTS TO DEVELOP

QUESTIONS

DESIGN

LOGISTICS

ISSUES

SAFETY?

- POSSIBLE TRIGGERING AT WRONG TIMES
- FOREIGN BODY, MUST BE TEMPORARY

SECURITY?

- ABUSE OF TECHNOLOGY IN HUMANS
- TAKING ADVANTAGE OF EXCEPTION TO IMMUNE RESPONSE

BENEFITS

DESIGN

LOGISTICS

ISSUES

IMPACT:

- DETECT BEGINNING OF METASTASIS
- UNDERSTAND CAUSES
- PATTERN IN MOVEMENT
- SENSE OF TIMING FOR DIAGNOSIS

Image removed due to copyright restrictions. Artist's rendering of breast cancer metastasis at <http://www.topcancernews.com/news/2073/breast-cancer-metastasis-could-be-predicted.html>



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Tech Spec Review

Final Decision?

- several uncertainties
- however, experimentation leads to insight on workings of metastasis
- worth exploring

YES!

WORKS CITED

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20.020 Introduction to Biological Engineering Design
Spring 2009

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