Qee cruzi

A cell-free diagnostic for congential Chagas disease

UNIVERSITY OF OXFORD
DEPARTMENT OF BIOCHEMISTRY UNIVERSITY OF OXFORD
DEPARTMENT OF ENGINEERING SCIENCE
University of Oxford MEDICAL SCIENCES DIVISION
Department of Zoology
PEMBROKE COLLEGE OXFORD
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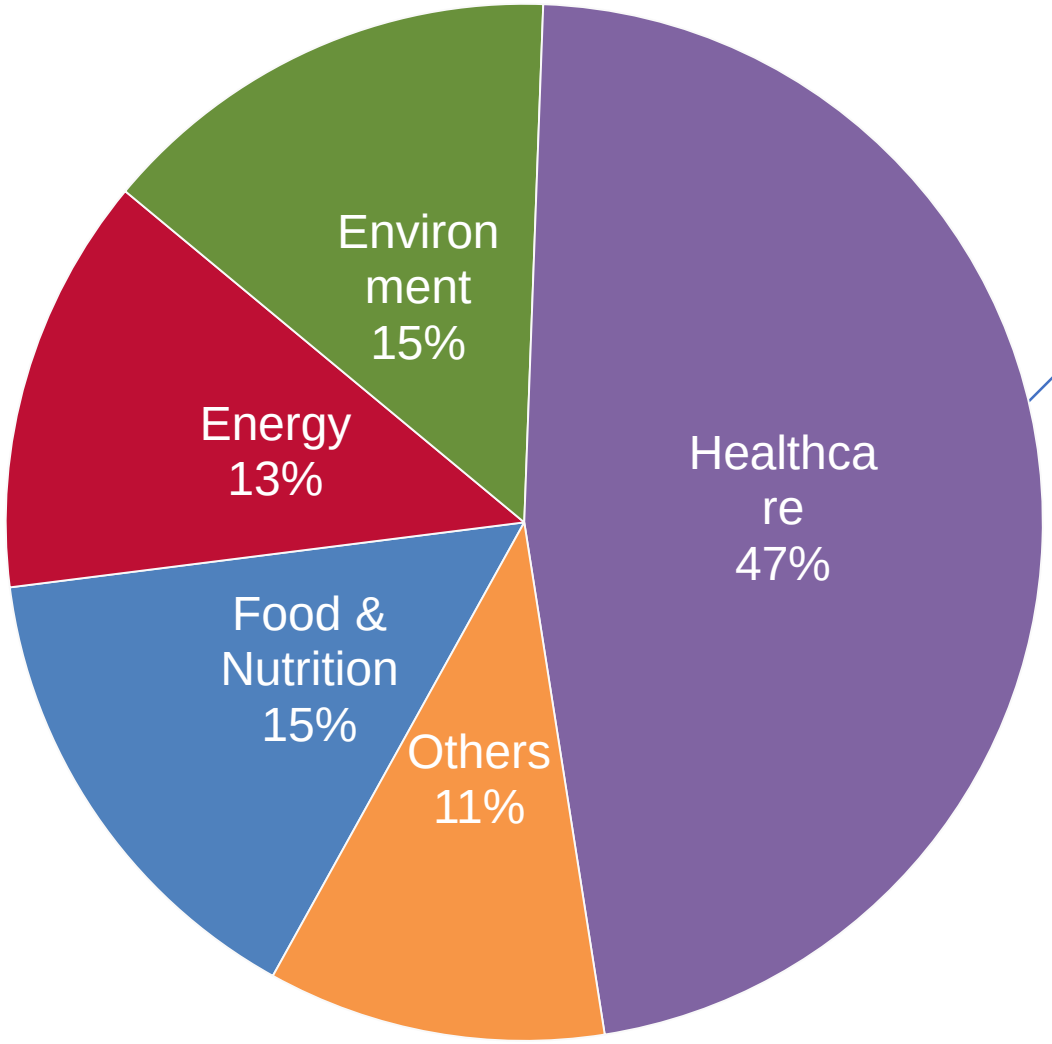
Survey of Public Showed Preference for Healthcare



Diagnostic

Chagas Disease – Our Real World Problem

6-8 mil
people infected

$627.5 mil
annual healthcare costs

21 endemic countries

95% not adequately treated or diagnosed

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"Chagas disease, caused by the protozoan *Trypanosoma cruzi*, is responsible for a greater disease burden than any other parasitic disease in the New World"

WHO

Limitations in Diagnostics

Immunocompromised

Coinfection with HIV

Infants

Variable efficiency

Evolution of surface antigens

Differences between strains

Investigating the Feasibility of Our Diagnostics

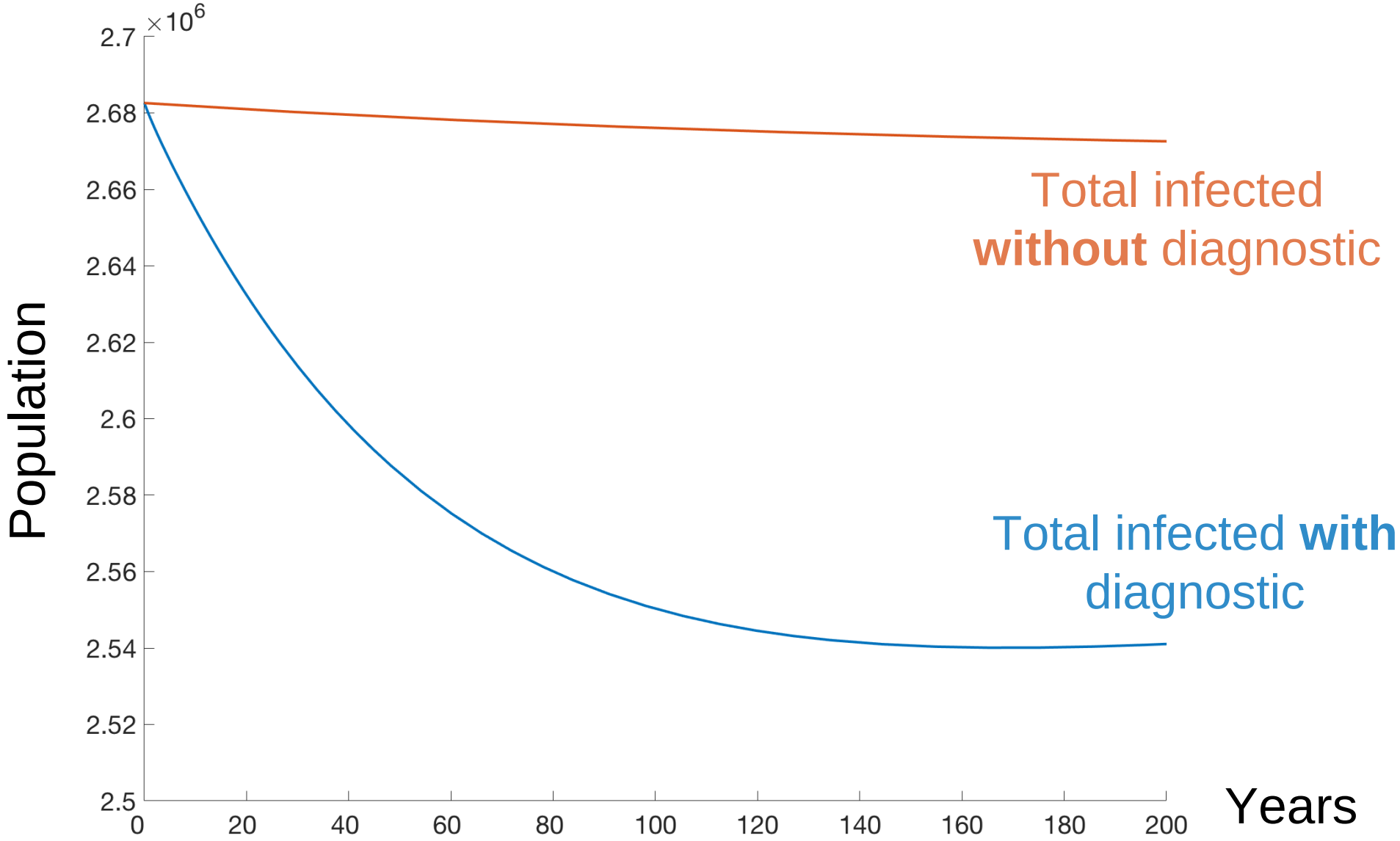
Would screening all infants impact epidemiology?

Would our diagnostic be a viable investment?

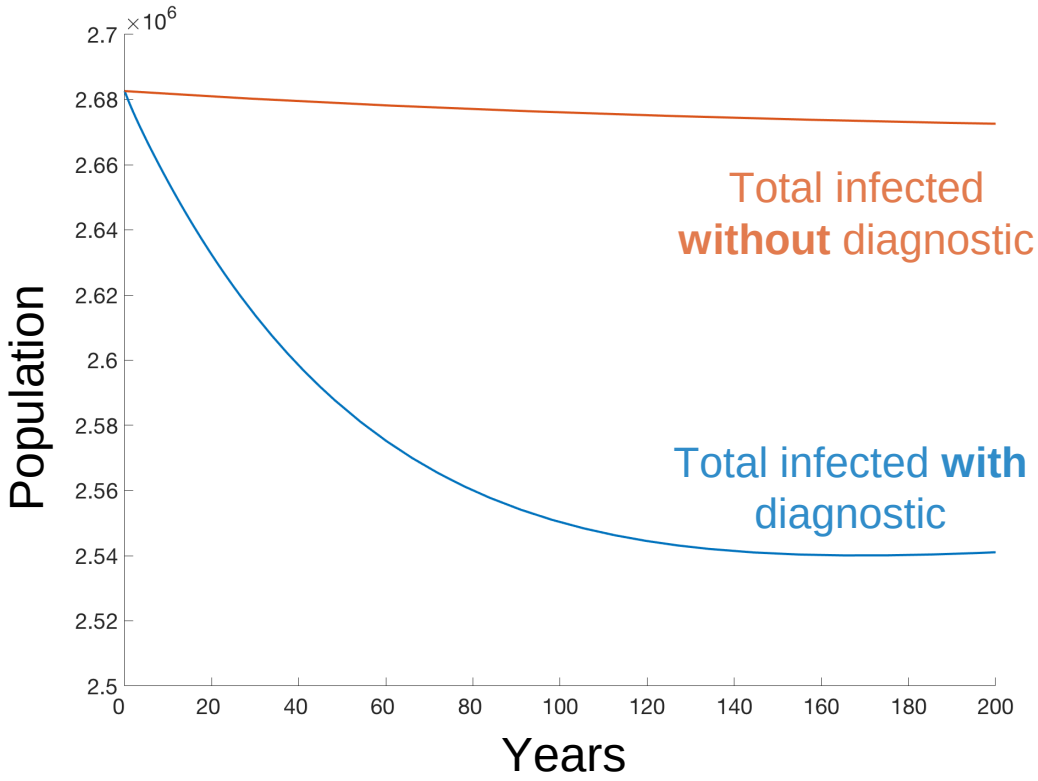
Can our project make a real difference?

Prof Yves Carlier, expert in Infectious Diseases (Université Libre de Bruxelles)
Provided us with useful insights into Chagas disease throughout our project

Epidemiological Model Shows a Congenital Chagas Diagnostic is Viable



Epidemiological Model Shows a Congenital Chagas Diagnostic is Viable



>130,000 fewer infected individuals

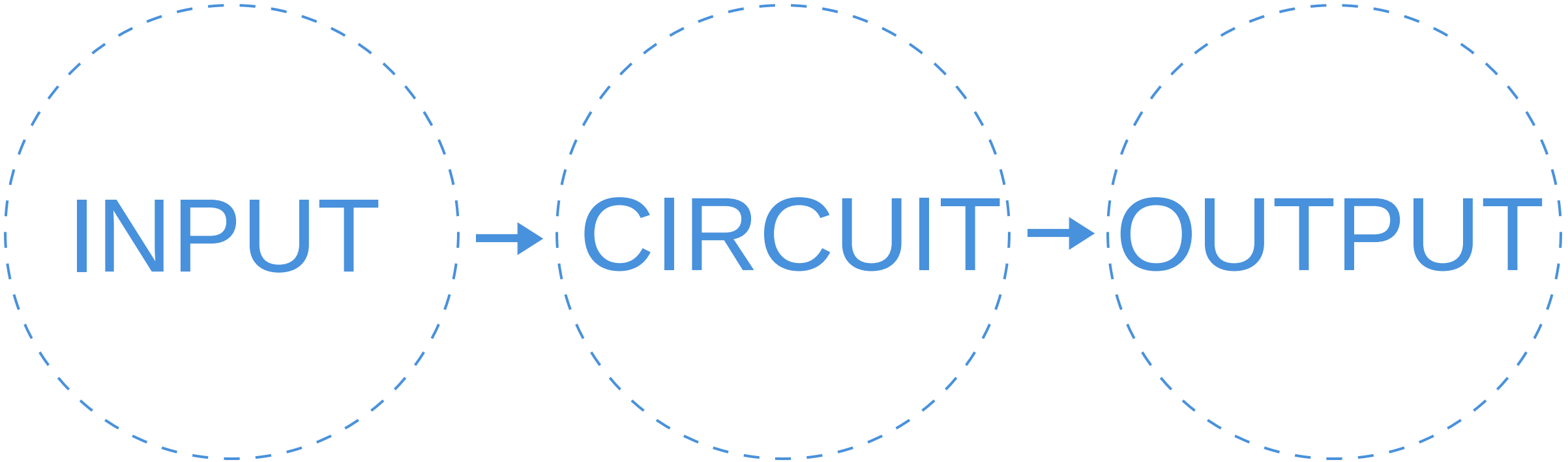
$61 mil in healthcare costs saved annually

37,000 DALYs per year eliminated

Prof Mike Bonsall, Professor of Mathematical Biology (University of Oxford)

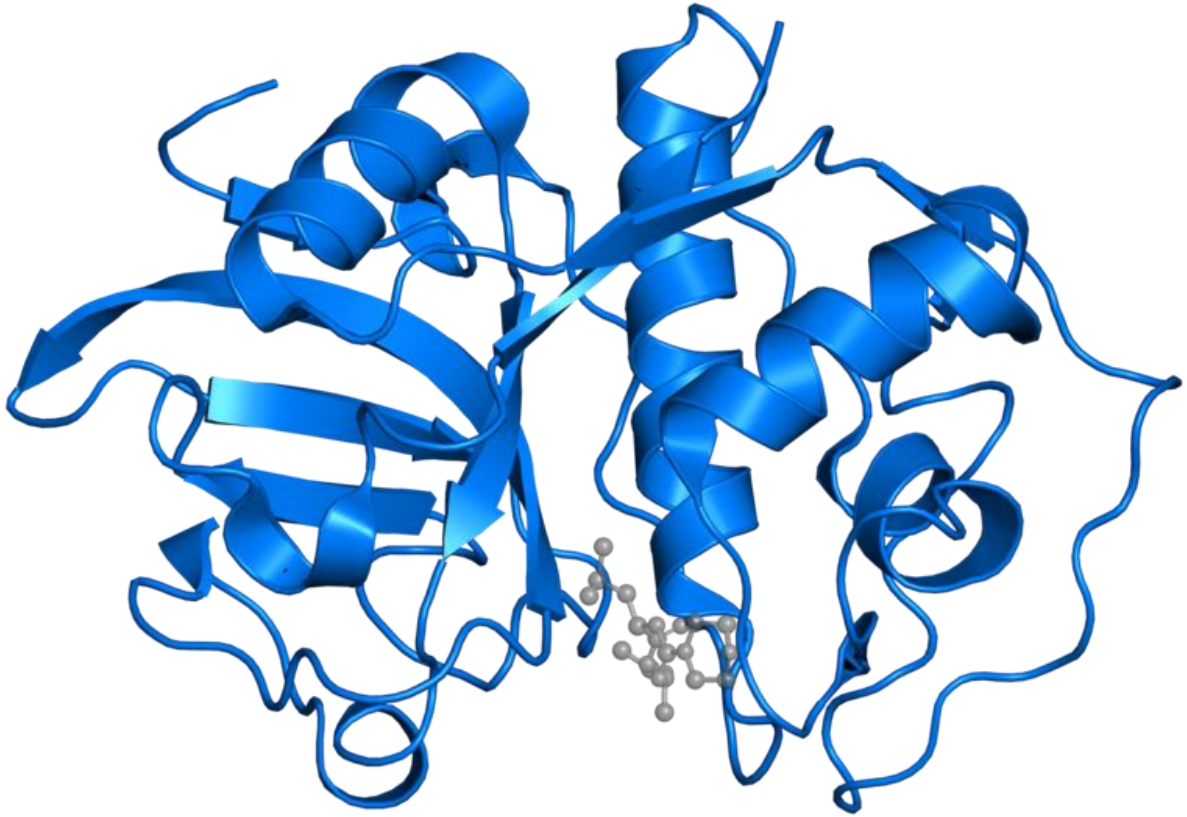
Helped us gain a better understanding of the principles of disease modelling, and equipped us with the skills to create our own epidemiological model for Chagas disease

Canonical Diagnostic Circuitry



Protease Detection is an Ideal Opportunity for a Platform Diagnostic

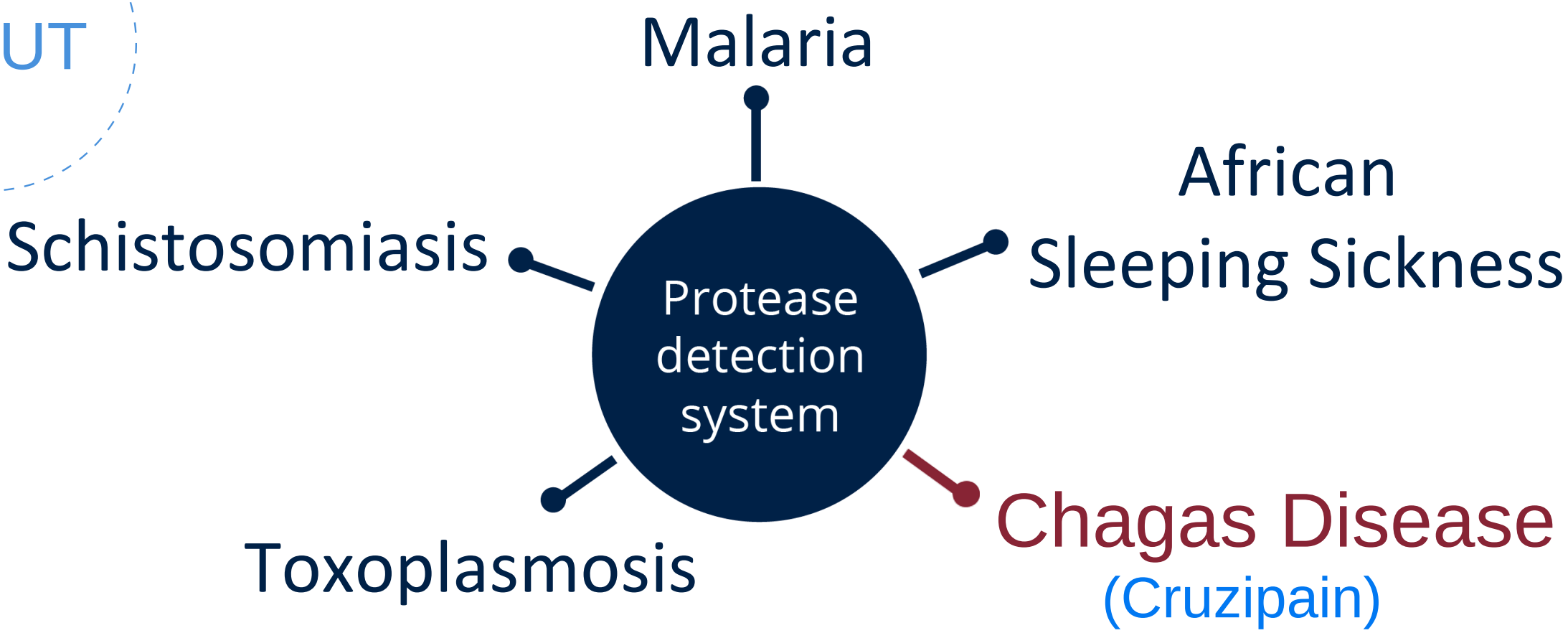
INPUT



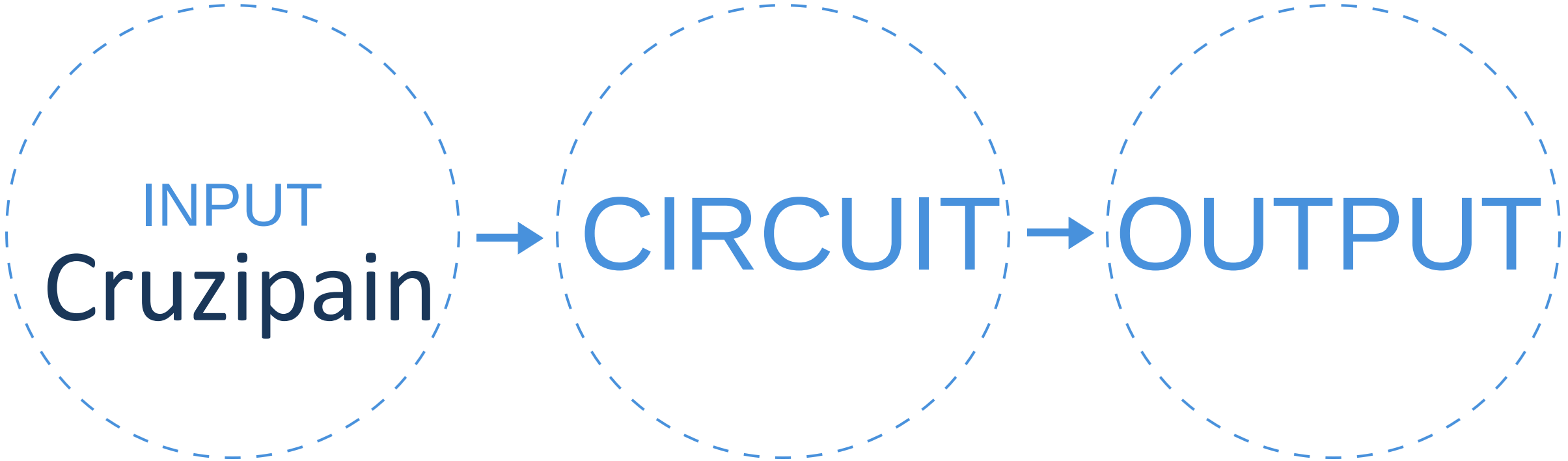
Cruzipain

Protease Detection is an Ideal Opportunity for a Platform Diagnostic

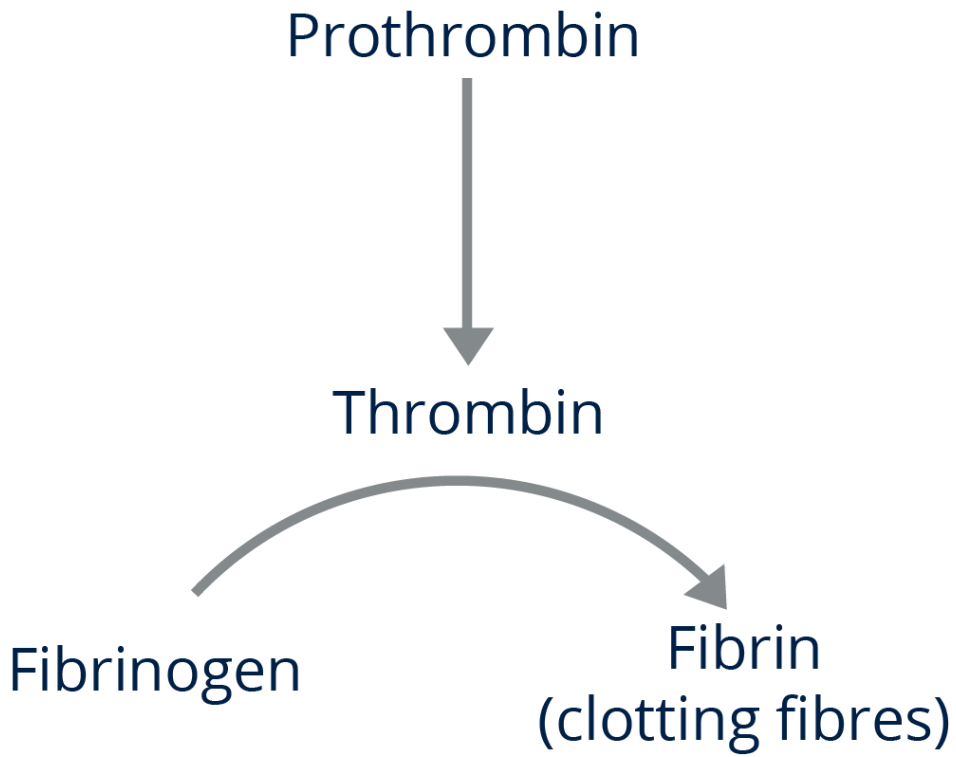
INPUT

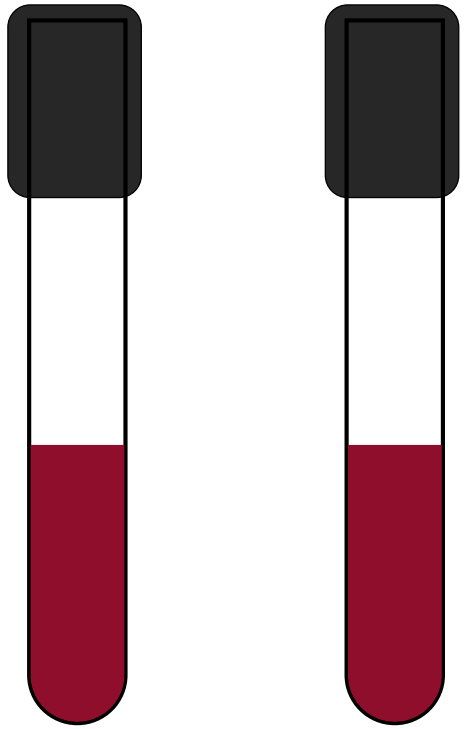


Canonical Diagnostic Circuitry



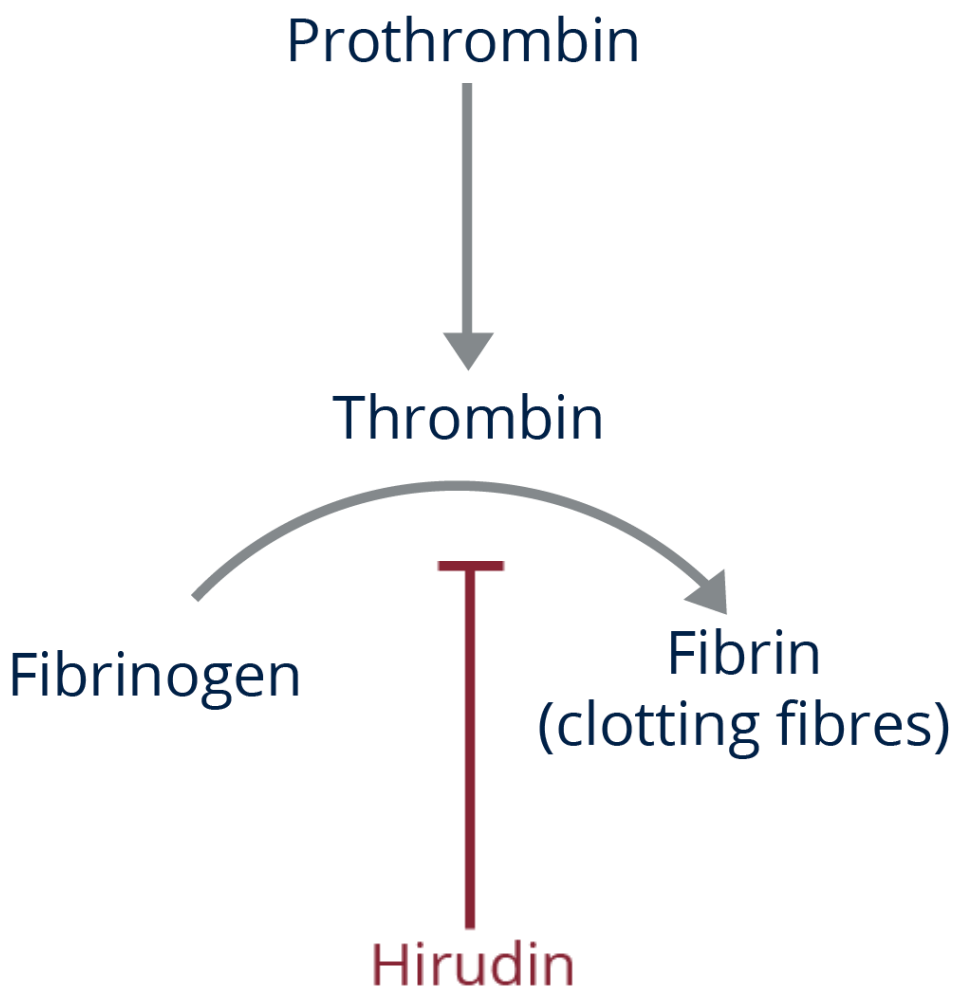
Blood Clotting Assay is Most Appropriate for our Diagnostic



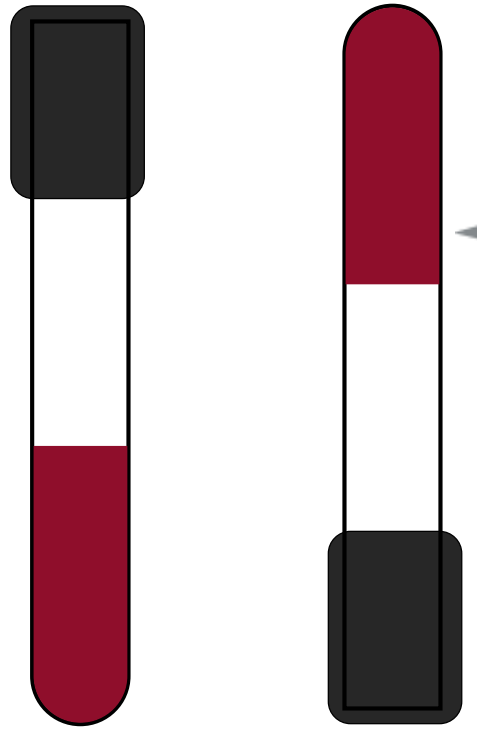


OUTPUT

Blood Clotting Assay is Most Appropriate for our Diagnostic



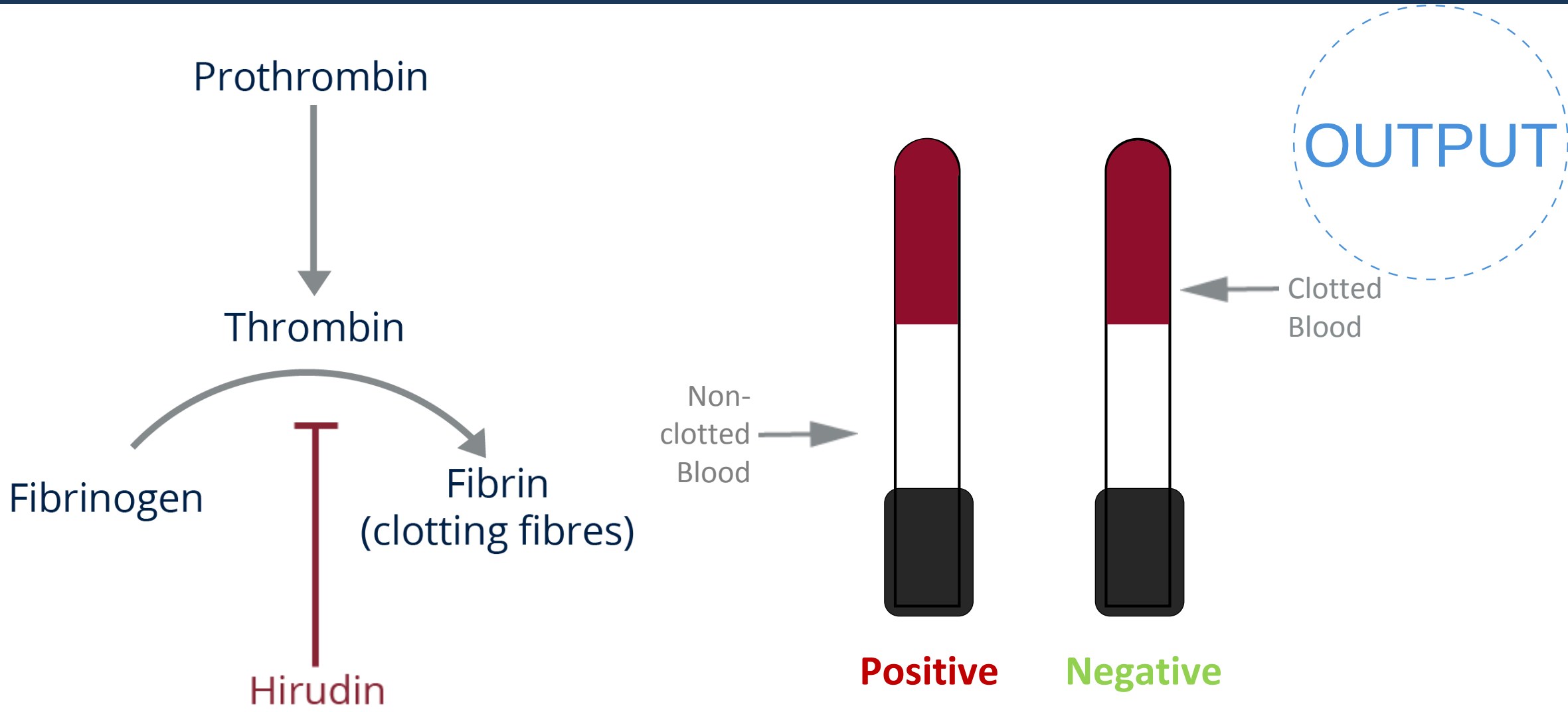
OUTPUT



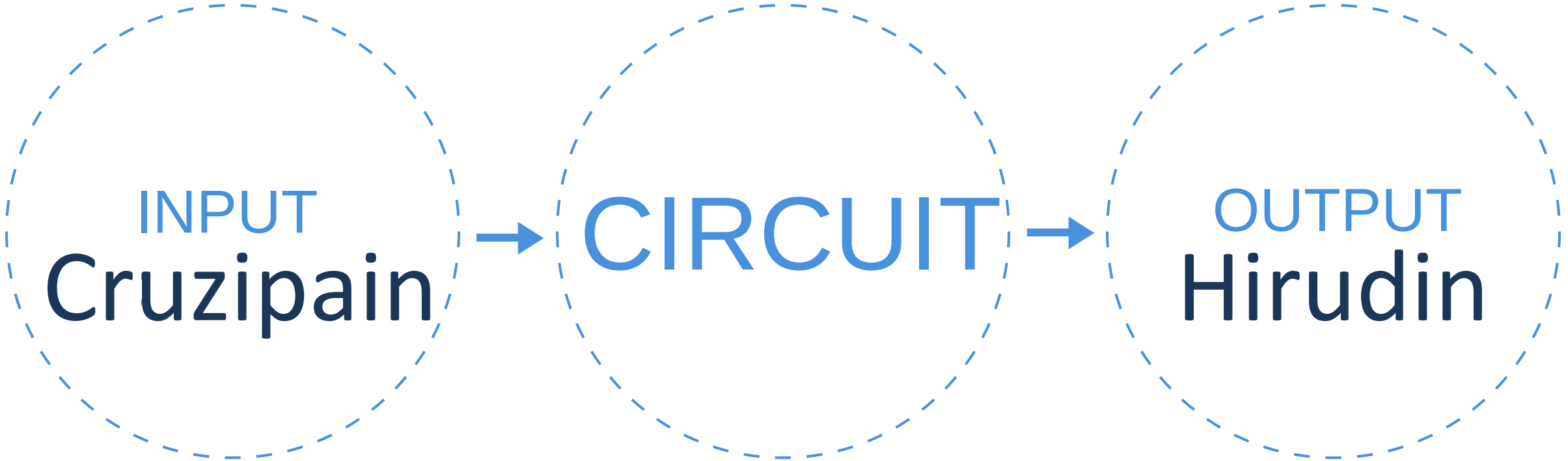
Clotted Blood

Negative

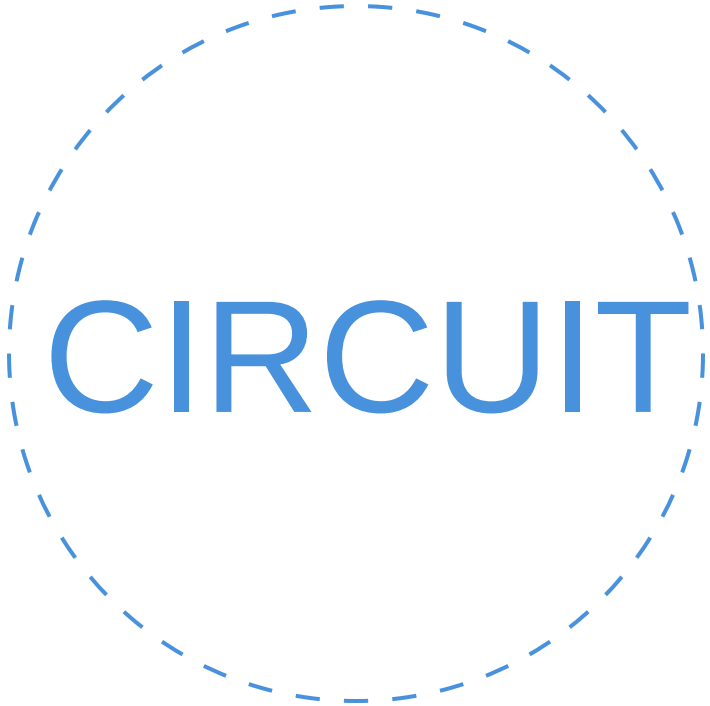
Blood Clotting Assay is Most Appropriate for our Diagnostic



Canonical Diagnostic Circuitry



Canonical Diagnostic Circuitry



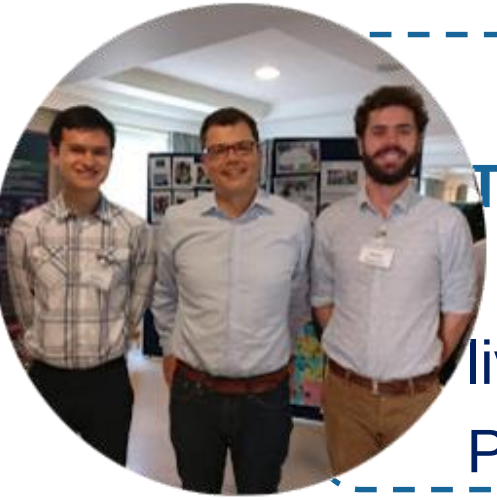
Cell-free Overcomes Conventional Synbio Problems

CIRCUIT

Lower risk of contamination

No need for impractical cell culture

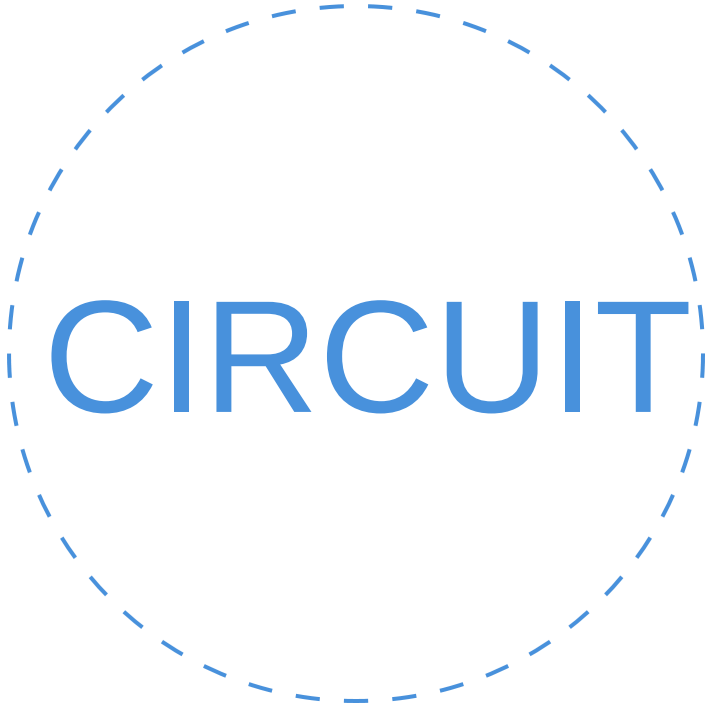
Freeze-dried powder eliminates need for cold chain



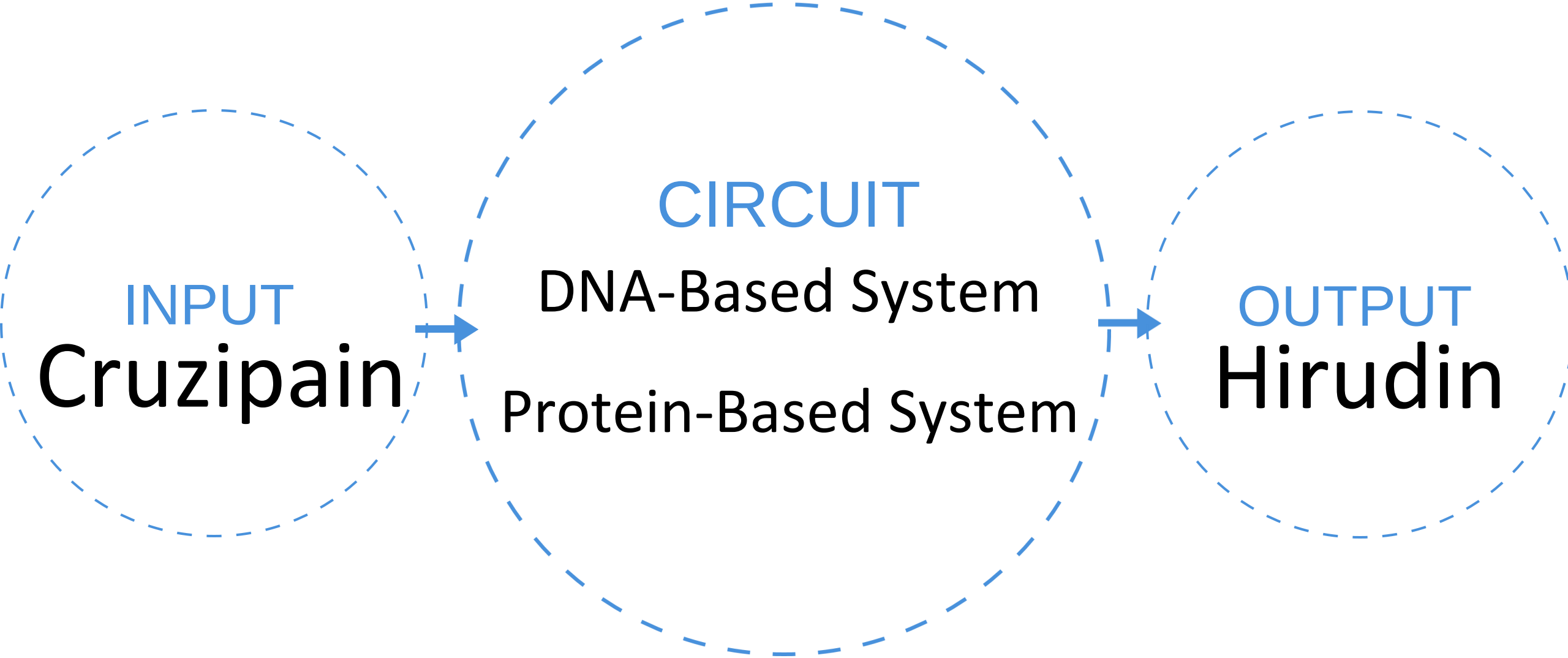
Prof Keith Pardee, pioneer in cell-free technologies (University of Toronto)

"[Freeze-dried cell-free] systems … could alleviate both the restrictions of live-cell biosynthesis and cold-chain distribution requirements" – Keith Pardee

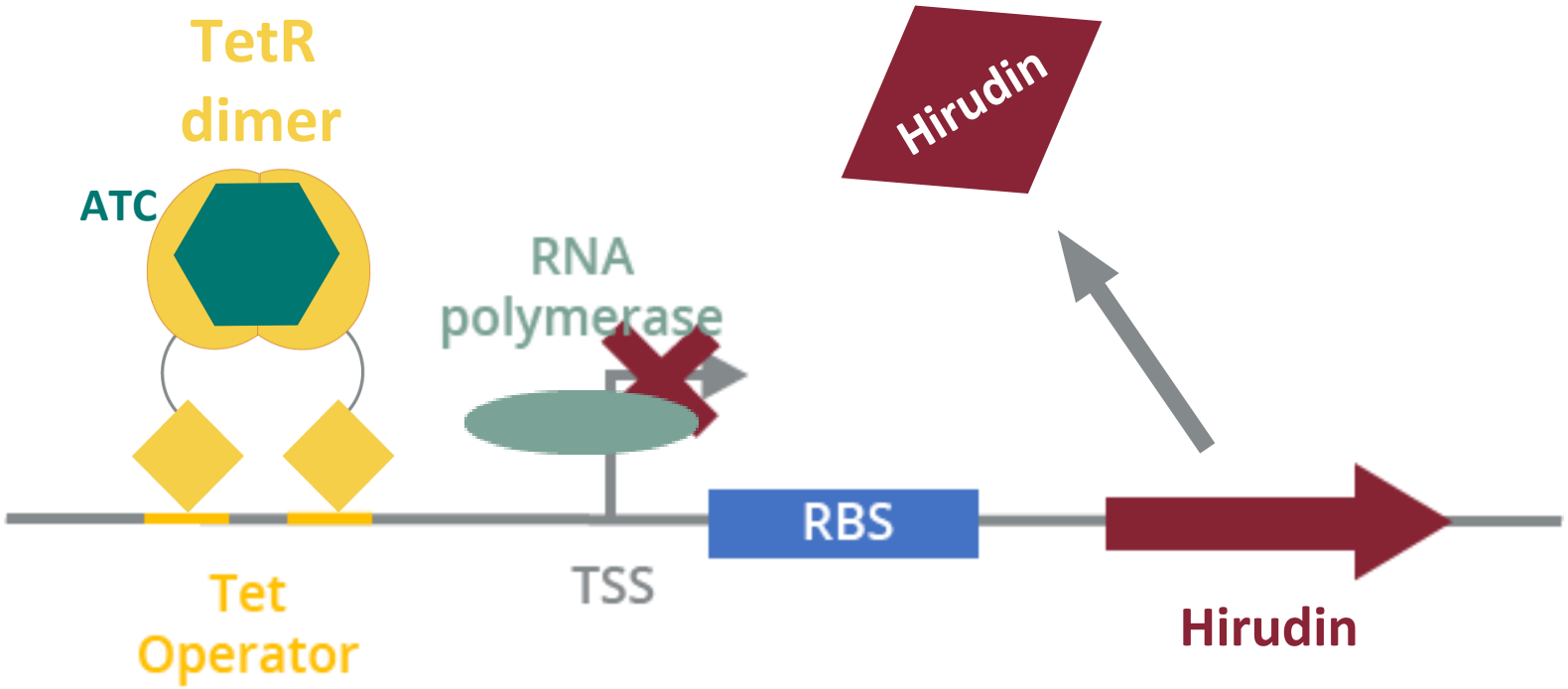
Canonical Diagnostic Circuitry



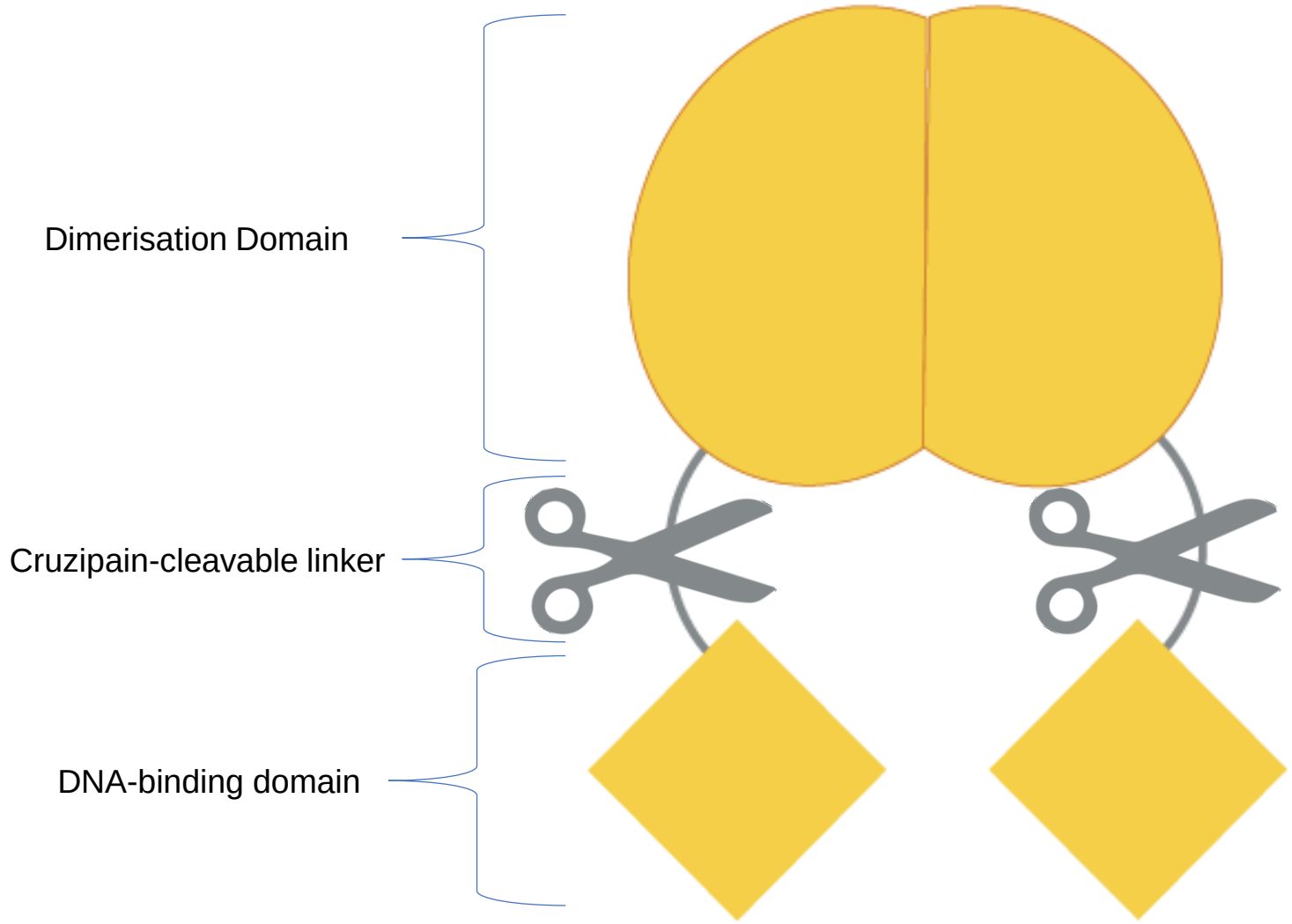
We Propose Two Novel Cell-Free Protease Detection Systems



Redesigned System Produced TEV Protease for Amplification



Initial Design Produced Hirudin Directly



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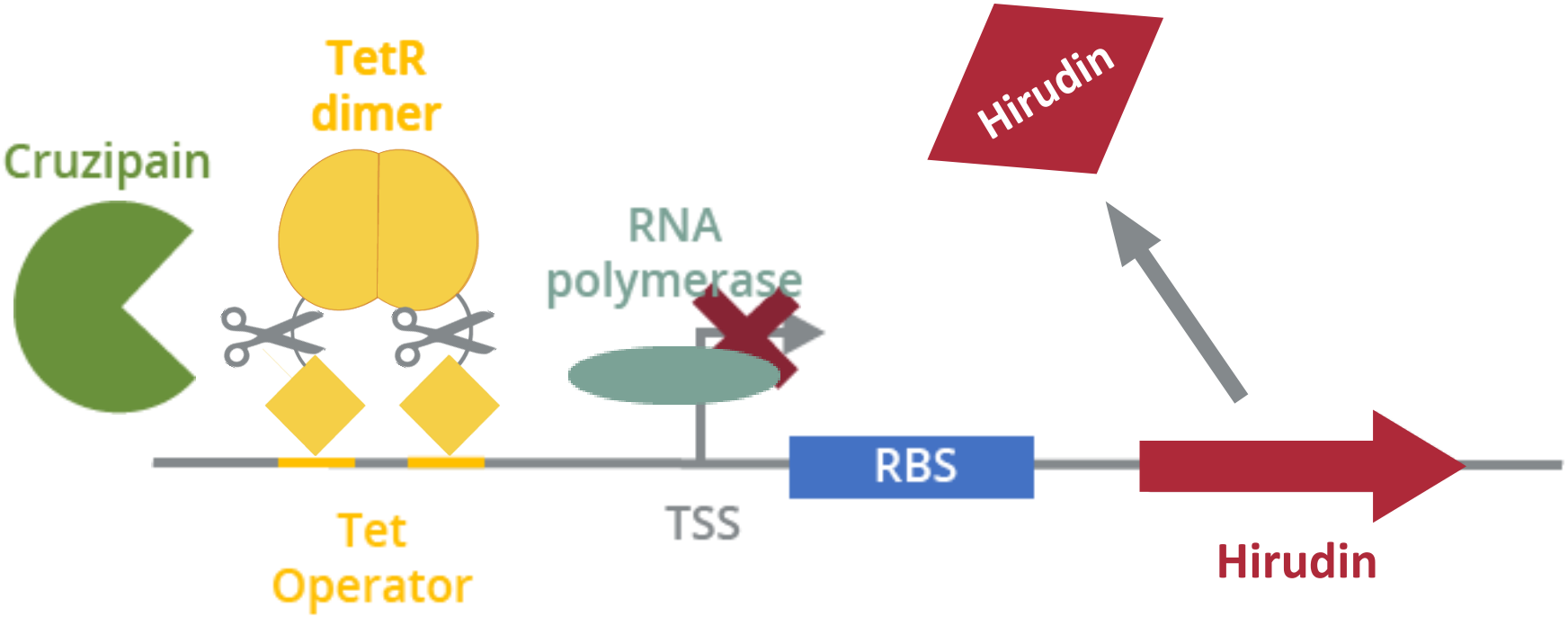
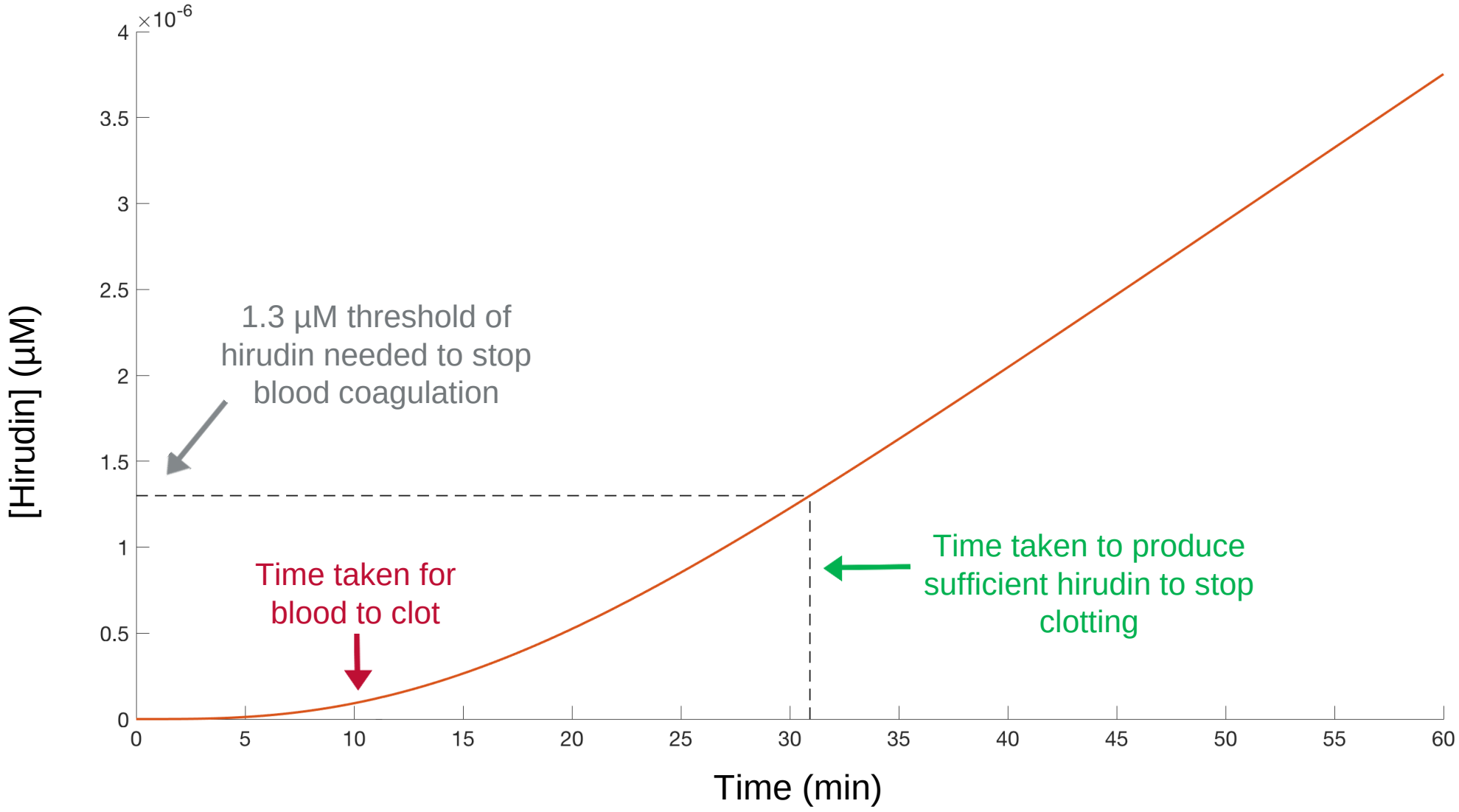


Transcription and Translation of Hirudin is Insufficient to Prevent Blood Coagulation



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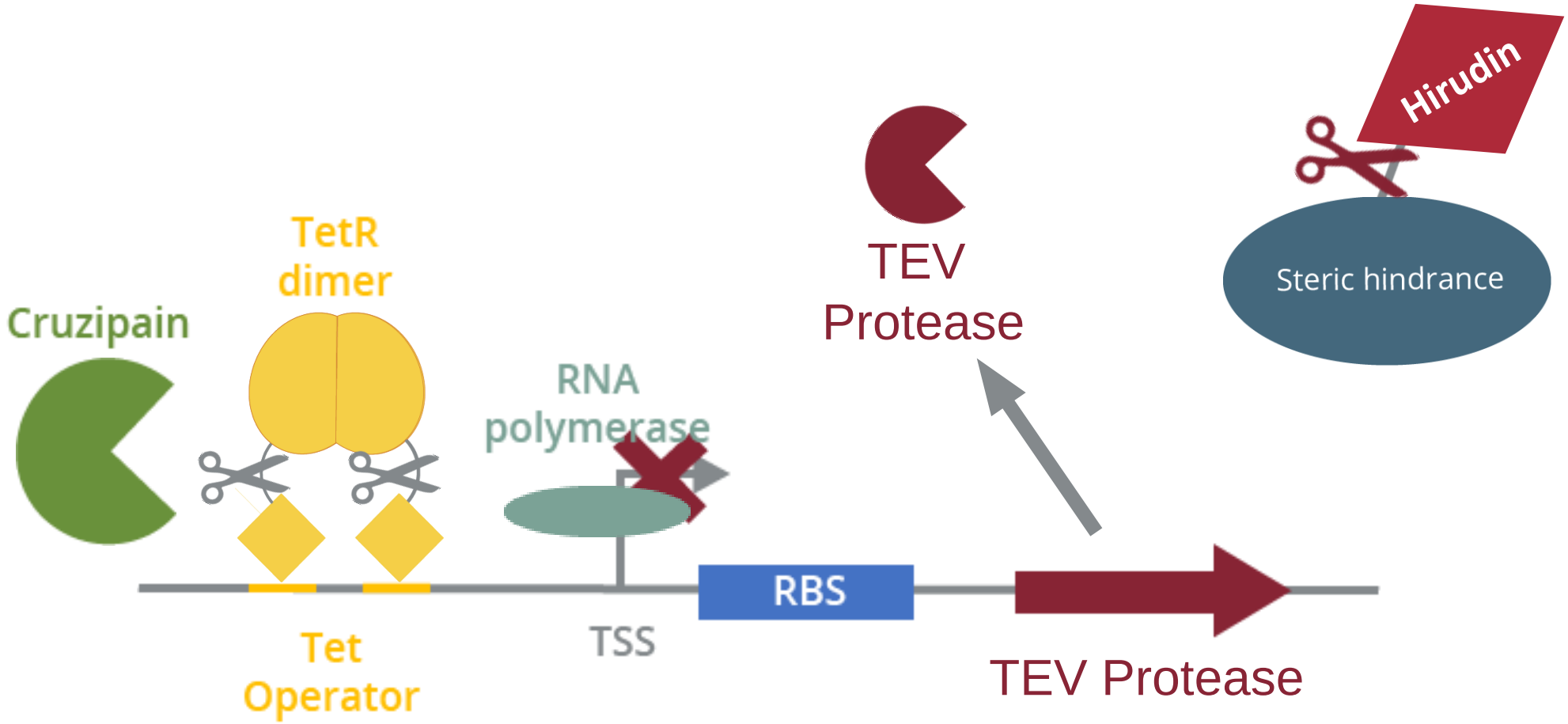
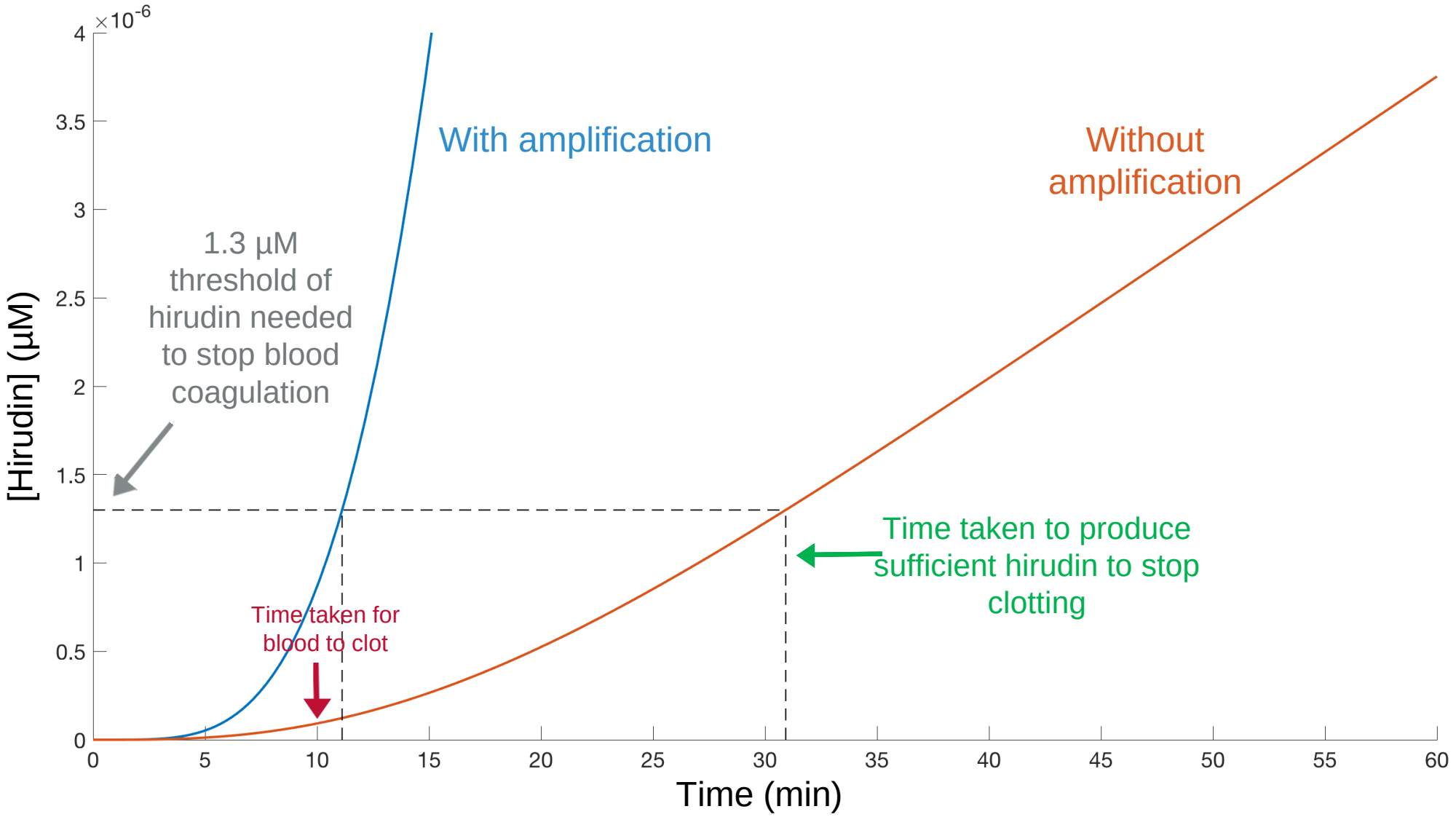
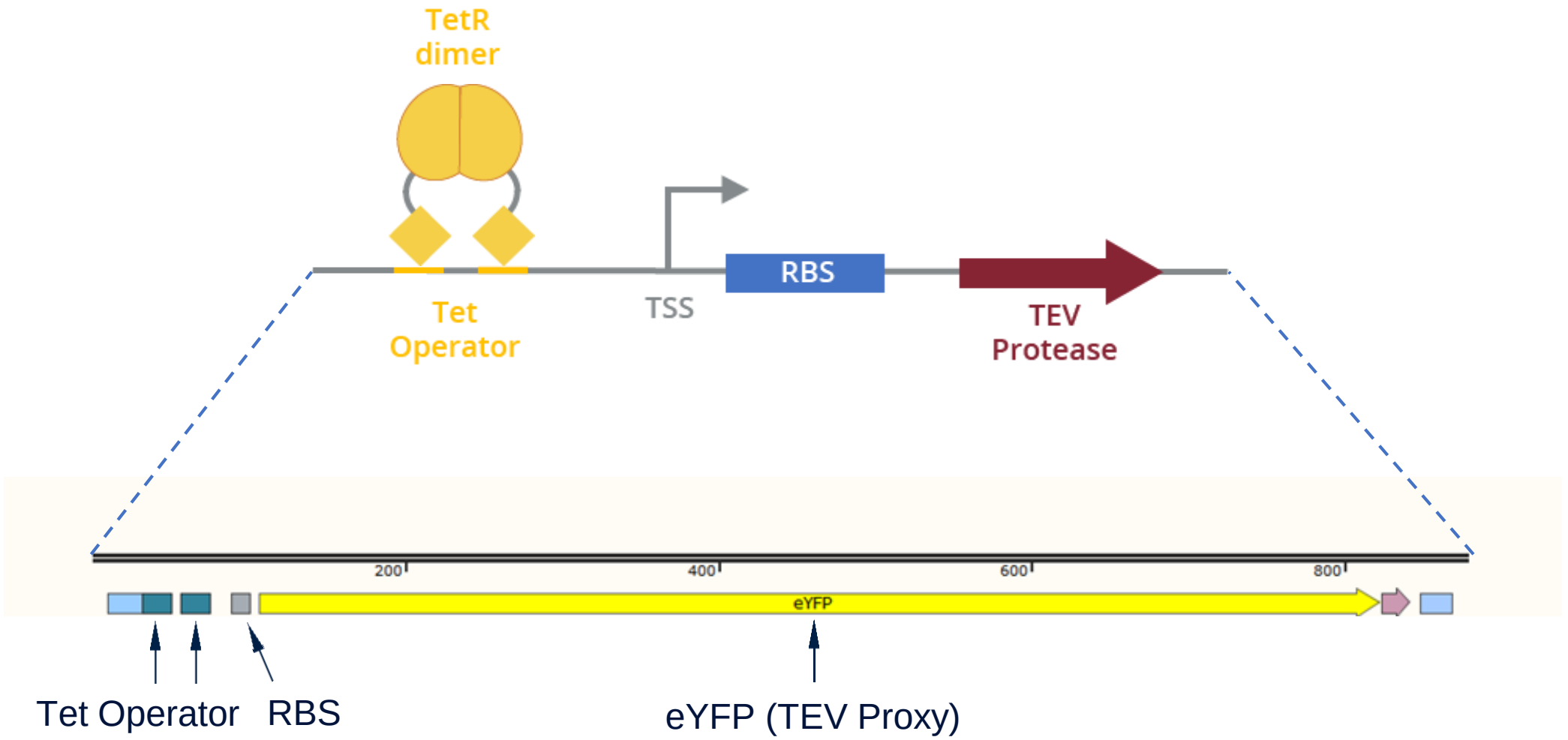


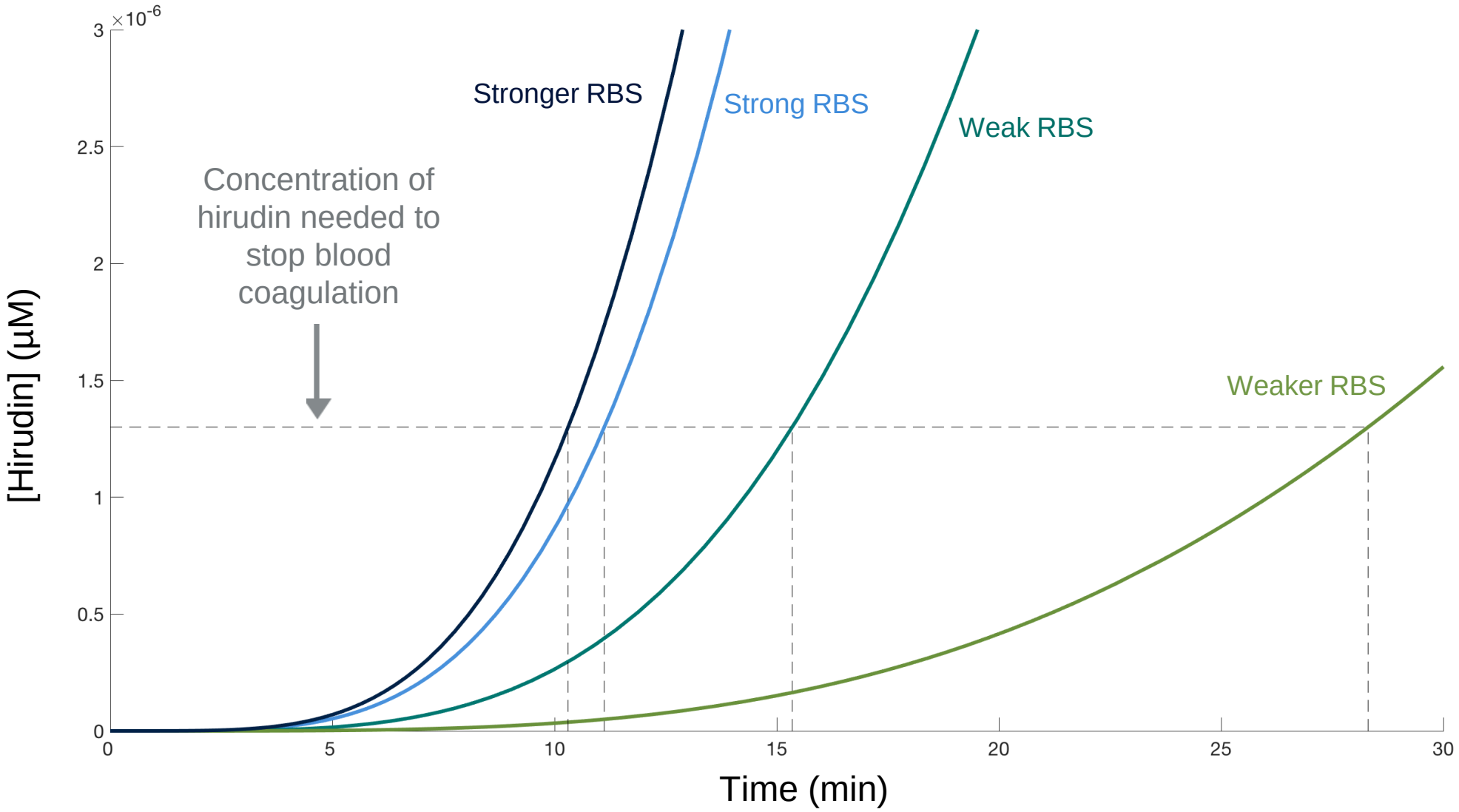
Modified Model Showed Amplification Increased Hirudin Production



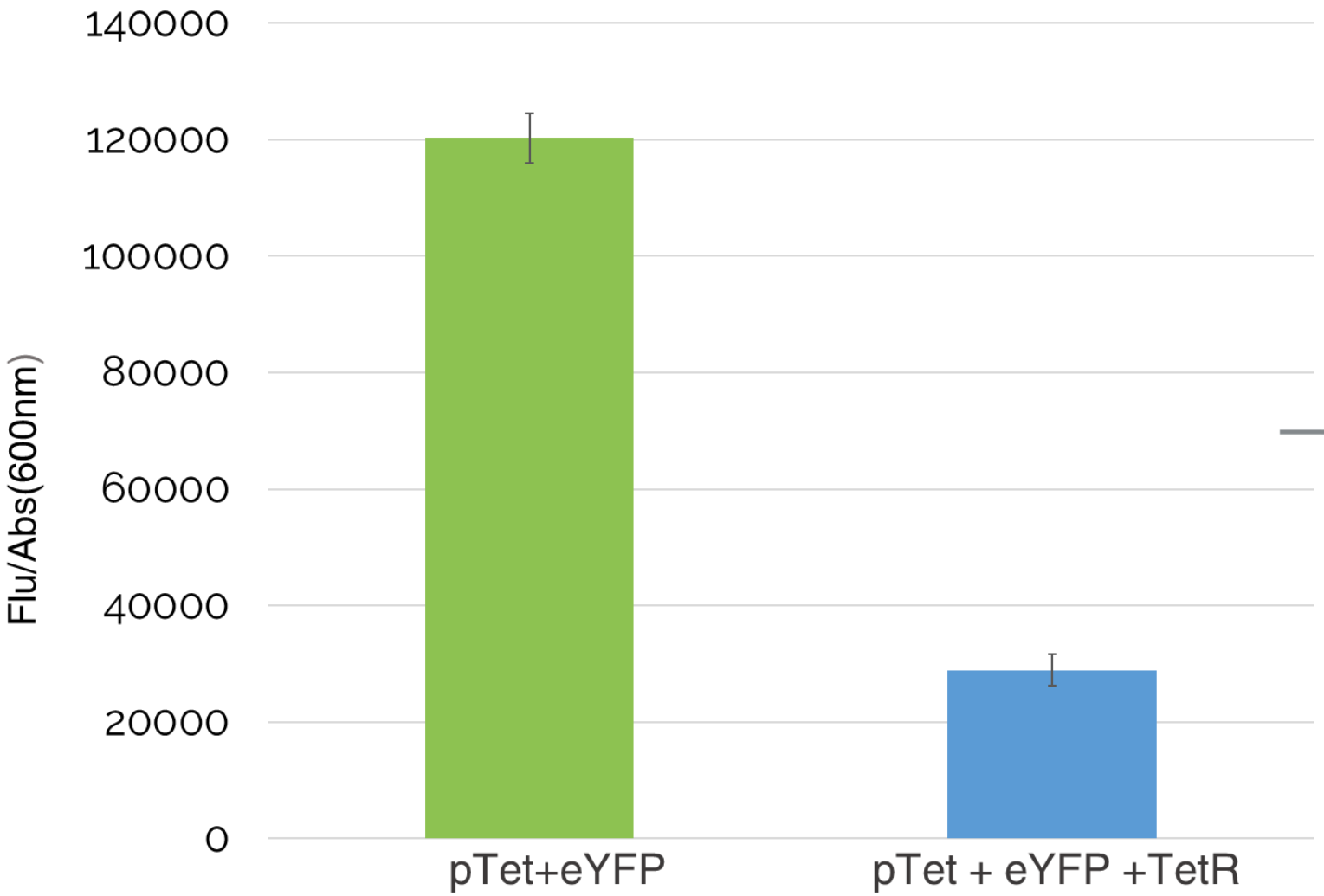
pTet-eYFP Was Designed as Proof-of-Concept for DNA Added to System

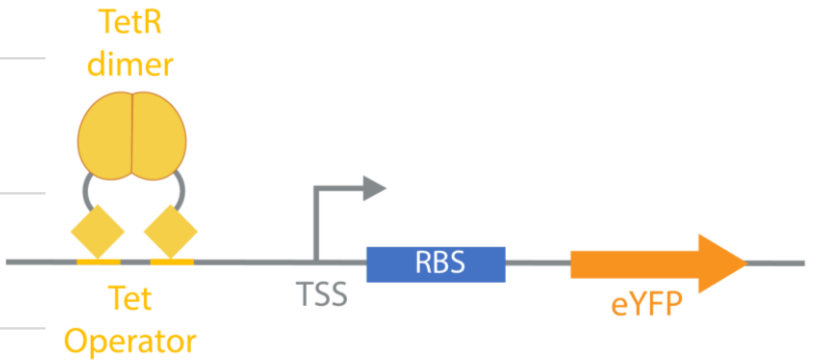


Strong RBS Increases Hirudin Production Rate

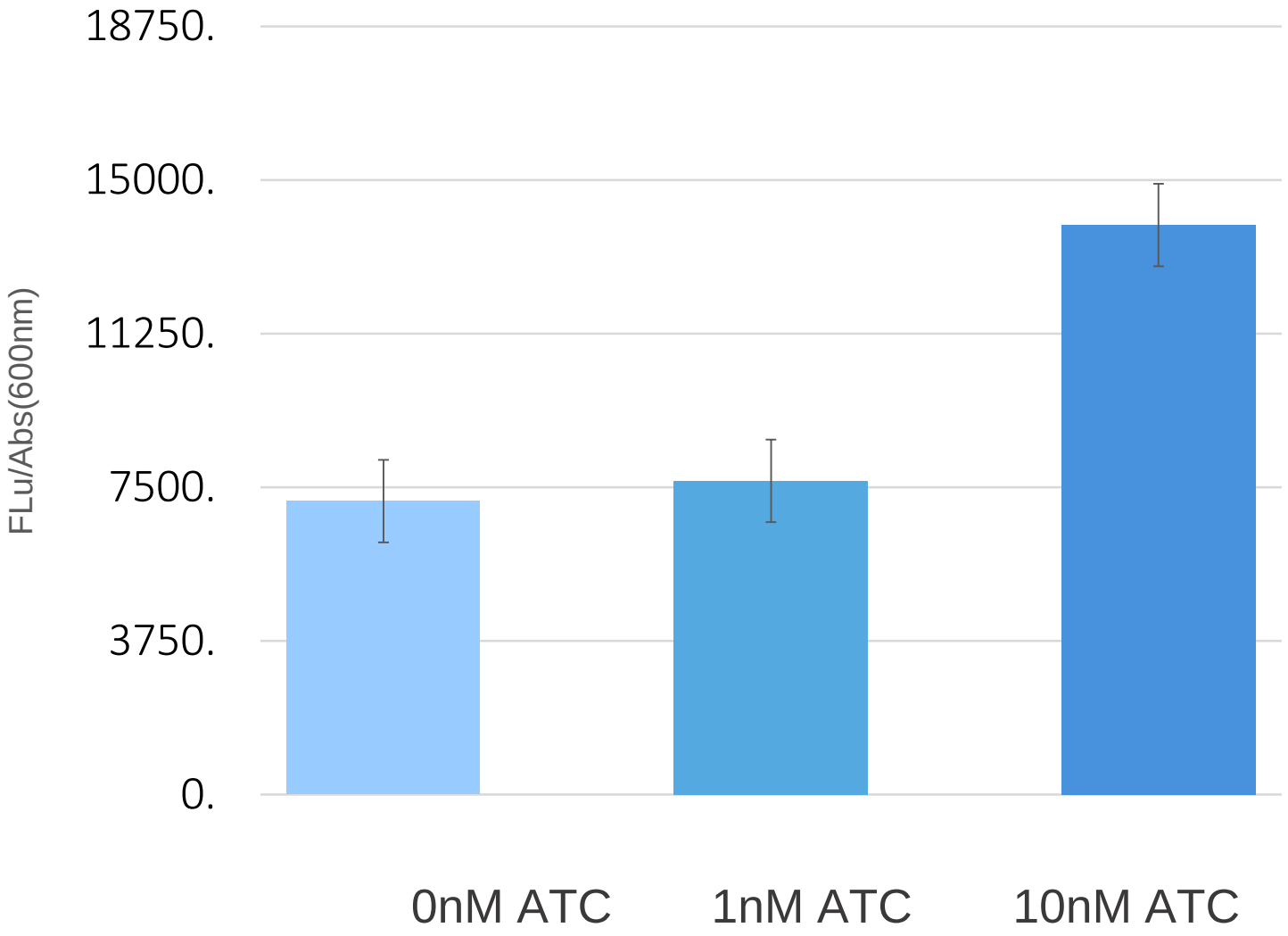


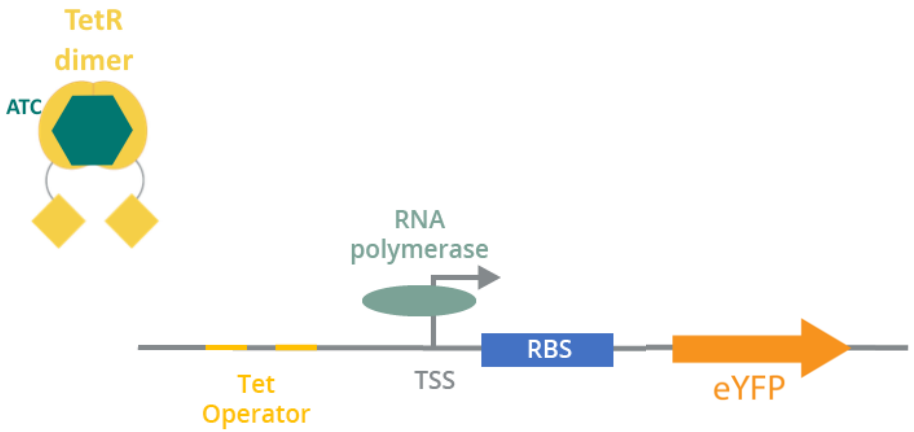
pTet-eYFP is repressed by TetR





Repression of pTet-eYFP can be Relieved by Addition of ATC



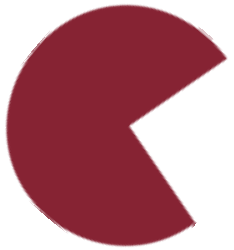


Protein-Based Circuitry Overview

Inactive TEV protease

Cruzipain

Active TEV protease

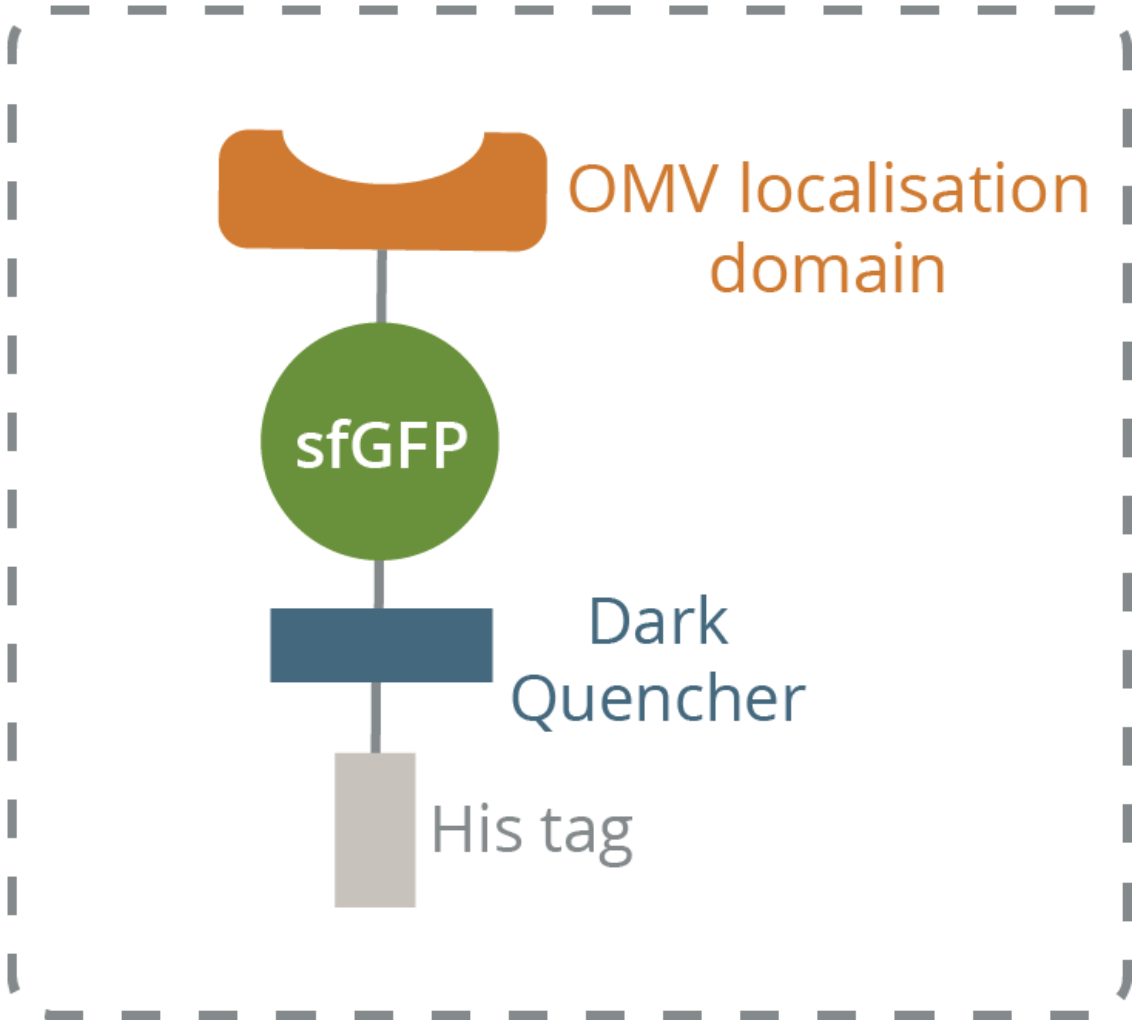


Prevents Blood Clotting

Proof-of-Concept Parts to Investigate Protease Action at Outer Membrane Vesicles

Use in our diagnostic

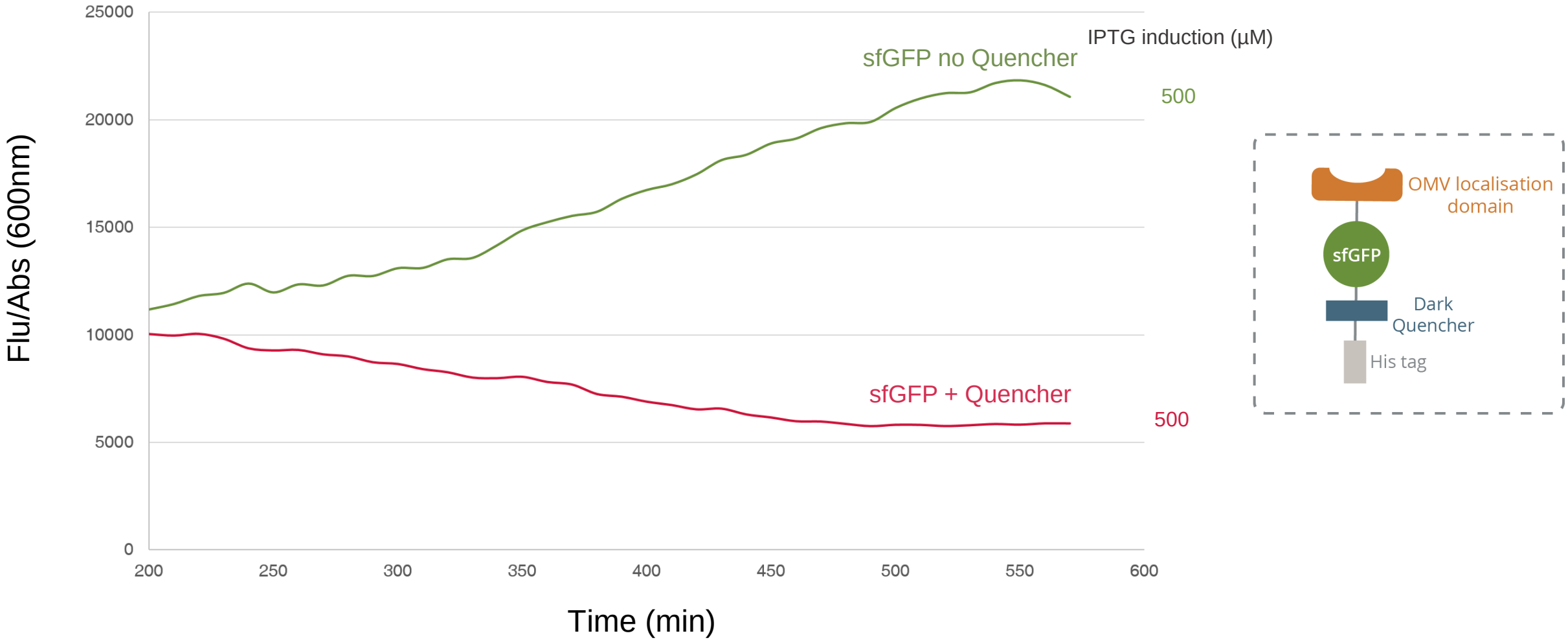
- Simulates activation of our system by Cruzipain
- Can also be used to test the activation of TEV in our output



Use for future teams

- Investigating targeted delivery to OMVs

Cleavage by TEV Protease Significantly Increases sfGFP fluorescence



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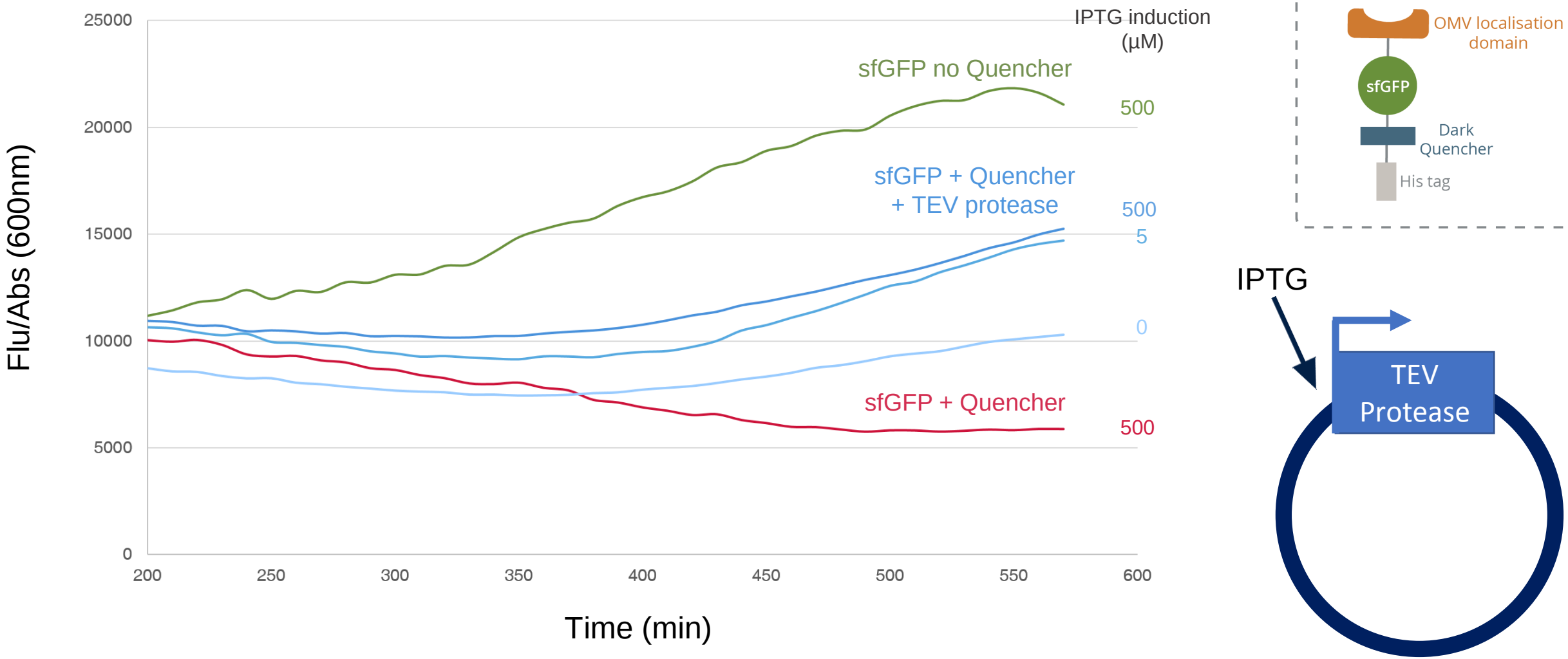


The 4Es Framework for Applied Design

Dr Cristina Alonso-Vega, Expert in Infectious Disease (University of San Simon)

Helped develop an understanding of the current political, social and economic landscape in Bolivia that ould impact the implantation of our design

Centre for Health, Law and Emerging Technologies (HeLEX) and Innovation for Science, Innovation and Society (InSIS)

We had sustained dialogue about the ethical and social issues related to our project, which heavily influenced our applied design

Dr Piers Millet, Senior Research Fellow at Future of Humanity Institute (University of Oxford)

Piers gave us his expert opinion on the current direction that regulation may be moving in; and elped evaluate our cell free report

Ease of Use

Equipment
Presentation
Training

Economics

Materials
Transport
Delivery

Environment & Safety

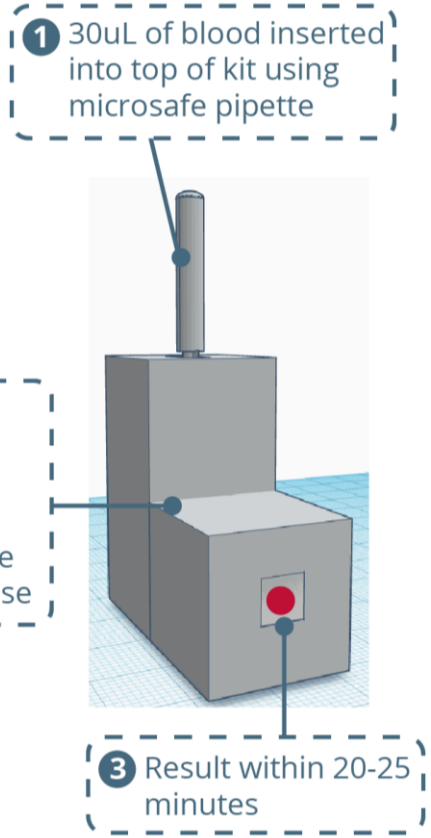
Risks
Sustainability
Disposal

Effectiveness

Clarity
Sensitivity & specificity
Speed

Our Final Kit

Prototyped using paper, cardboard, CAD and 3D printing



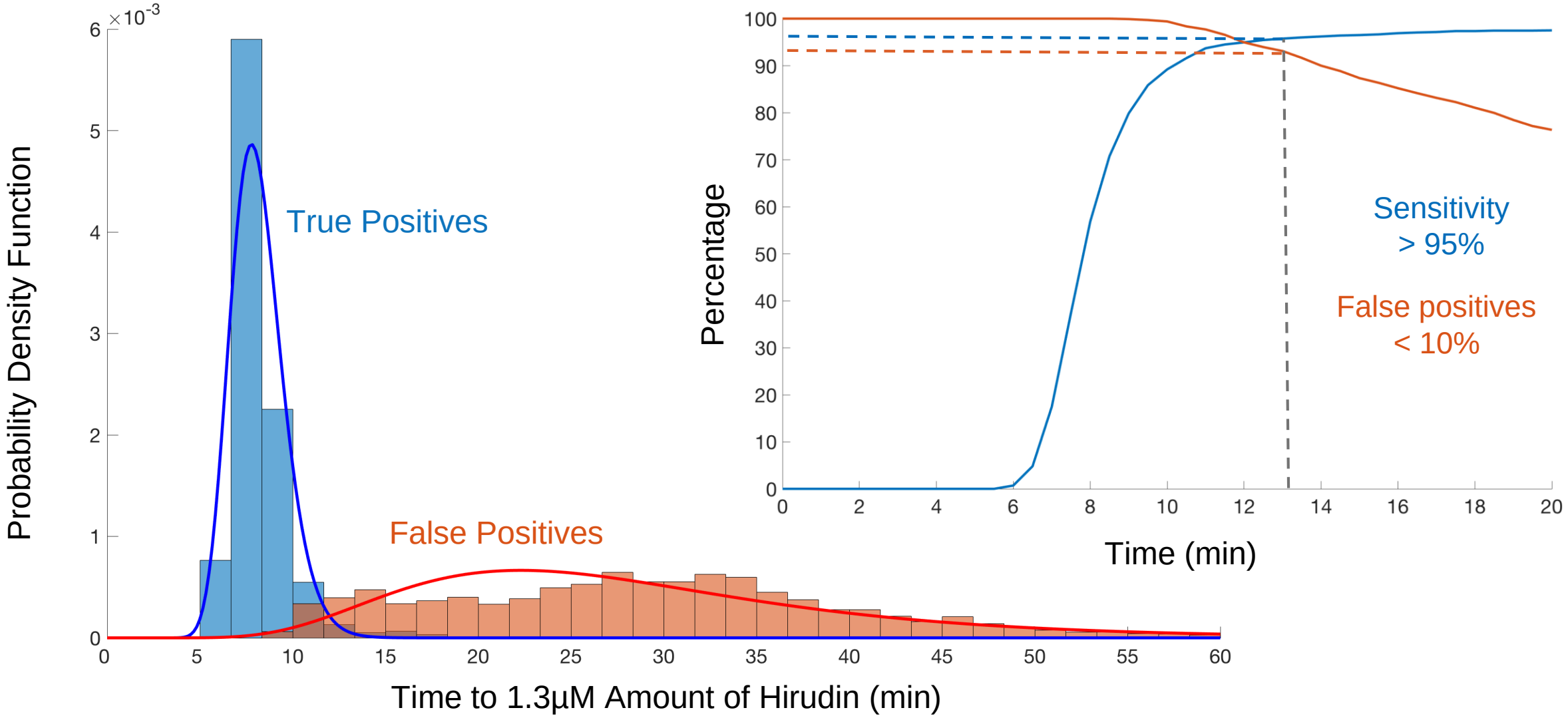
Meets the 4Es framework criteria

Ease of Use	At all levels of medical infrastructure
Economics	$3.90 – cheaper than current options
Environment & Safety	Fully contained and cell-free
Effectiveness	Rapid, point-of-care diagnostic

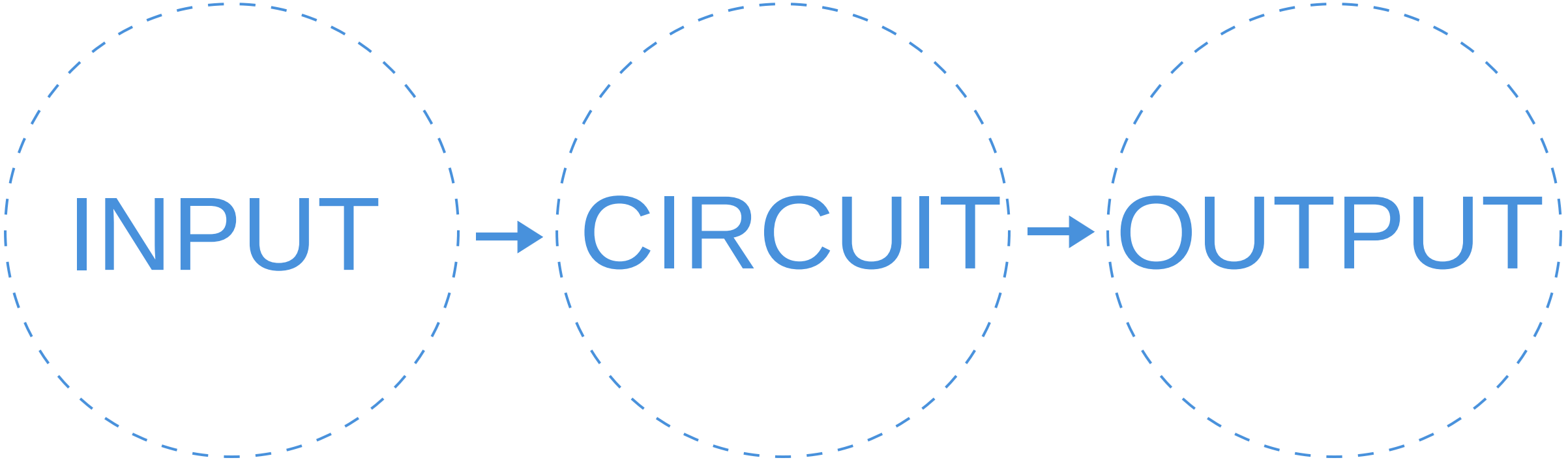
Dr Tempest van Schaik, researcher in Biomedical Engineering (Science Practice)

Helped us to understand the importance of cheap and easy prototyping for our kit to maximise efficiency and potential

Stochastic Modelling Highlighted Effectiveness of System



Where Do We See Cruzi Going?



Where Do We See Cruzi Going?

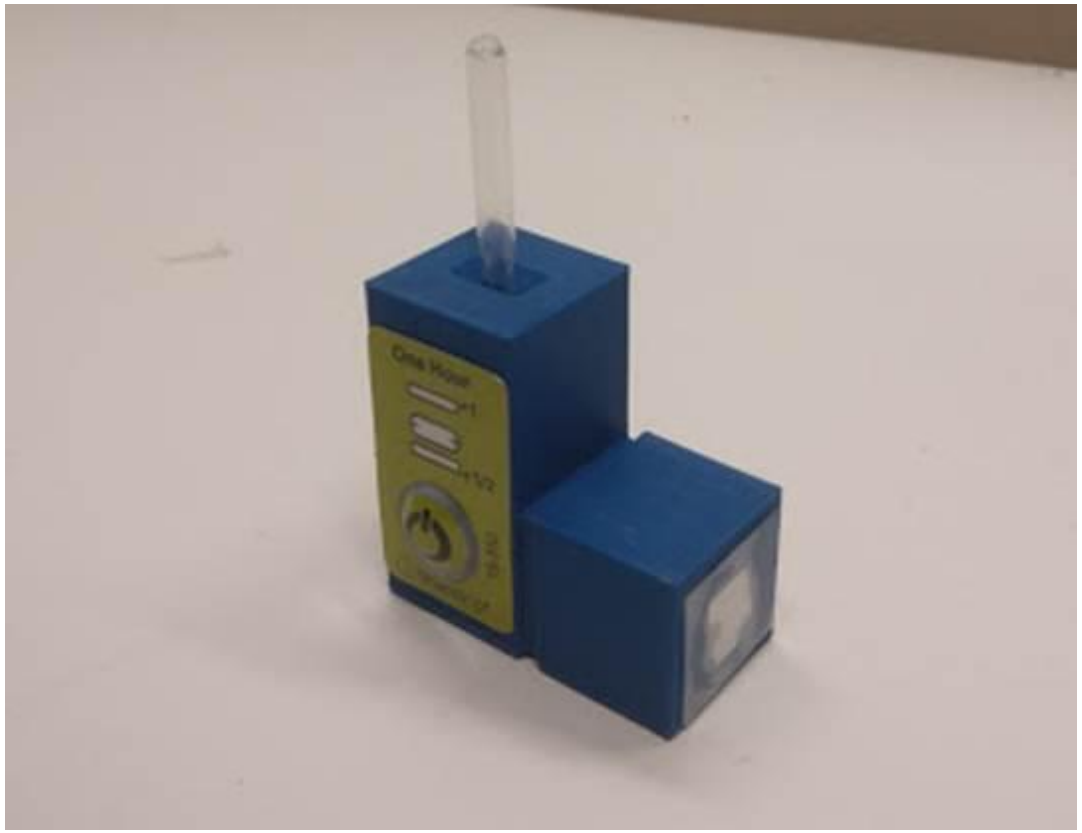
INPUT

African Sleeping sickness
(Rhodesain)

Schistosomiasis
(Cercarial elastase)

Toxoplasmosis
(Cathepsin L)

Sepsis
(LasA)



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- Professor Michael Bonsall
- Harrison Steel
- Associate Professor Maike Bublitz

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Sam Bannon
Professor Mike Bonsall
Professor Jaila Dias Borges Lalwani
Professor Yves Carlier
Dr Scott L Diamond
Sarah Dragonetti
Dr. Darragh Ennis
Dr. Matteo Ferla
Drs David and Carol Harris
Dr Miguel Hernan Vicco
Professor Matt Higgins
Professor Mark Howarth
Professor Michael Laffan
Professor Emilio Malchiodi
Dr. Piers Millett
Dr. Michael Morrison
Eileen Murphy
Professor Keith Pardee
Dr. Ben Riley
Tim Ring
David Sprent
Juan Solano
Alfons Van Woerkom
HeLEX and InSIS

Collaborations

Amazona
AQA Unesp
City of London School
EPFL
Judd School
Northwestern
McMaster II
TEC CEM