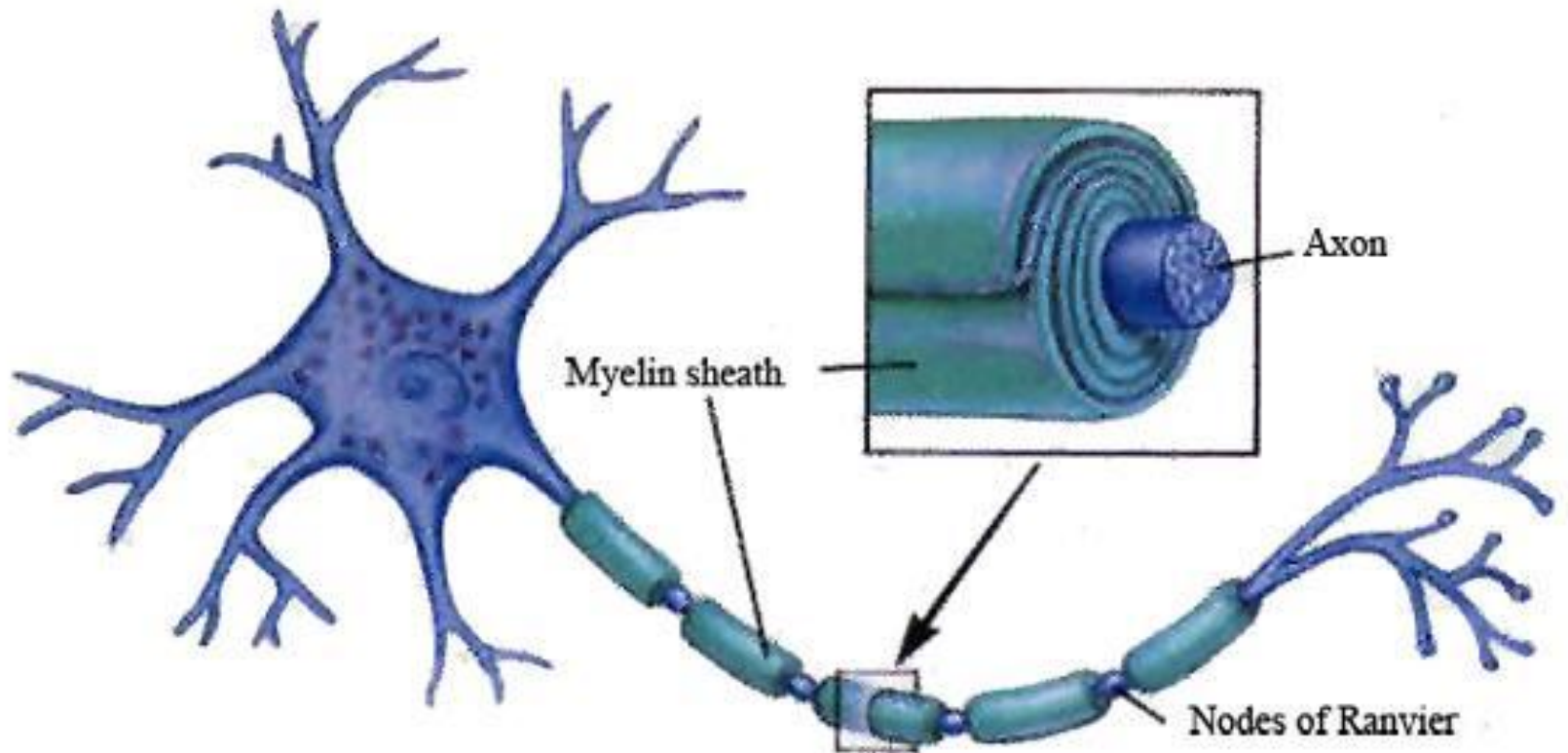


# Tech Spec

*Team Superfly!*

# Remyelination



# Impact

- Numerous diseases deal with demyelination, and symptoms are severe!
- Greatly improve quality of life for many individuals
- 2.1 million people worldwide with Multiple Sclerosis (200 new cases every week in US alone)
- Method of treatment applicable to many diseases

# Our Solution

Engineer a bacterial cell that will:

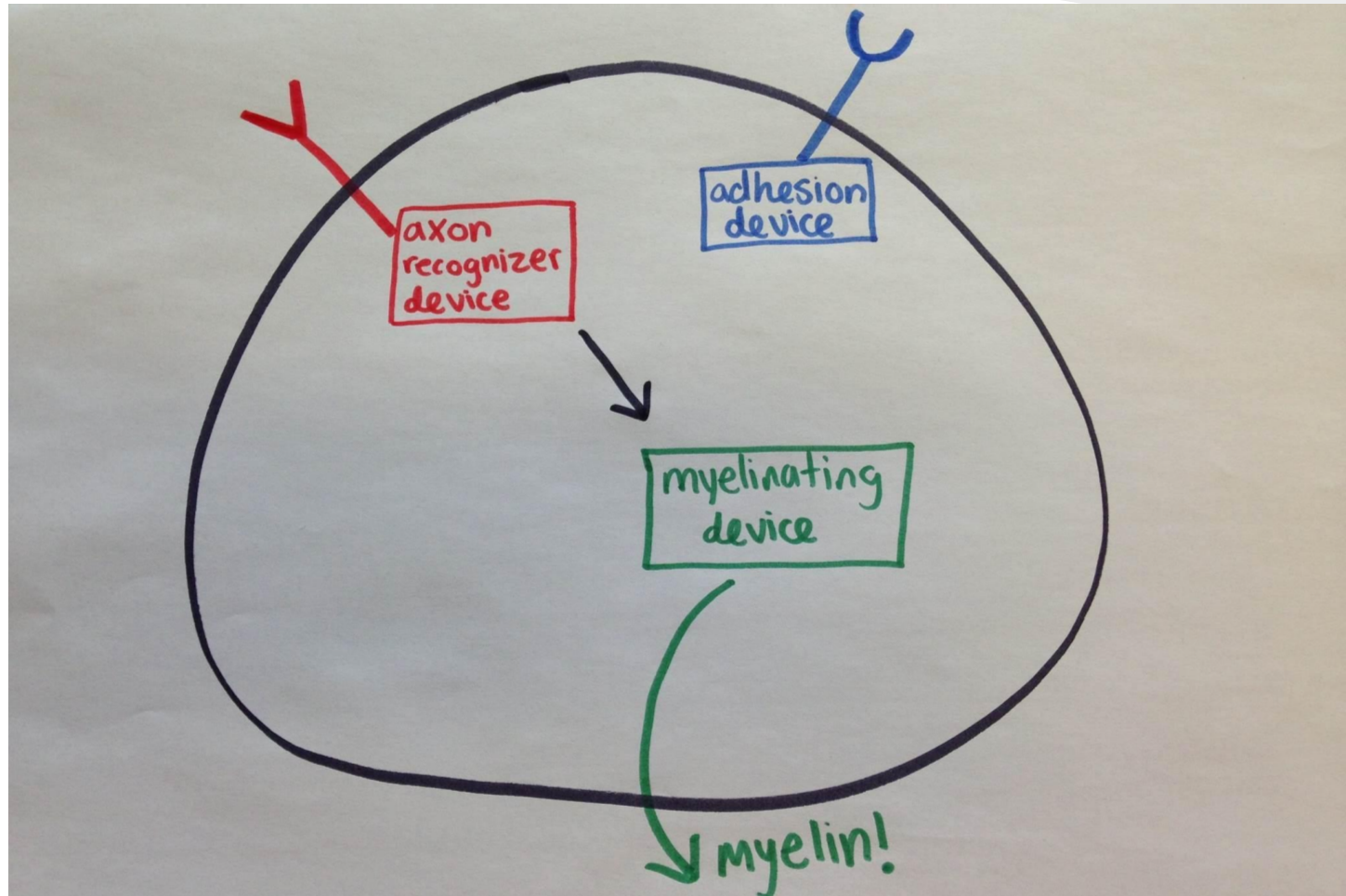
- Recognize demyelinated axons once in the brain
- Adhere to these axons
- Secrete myelin
- Unadhere from the axon once it is appropriately myelinated

Input: Bare axon; Output: Myelin

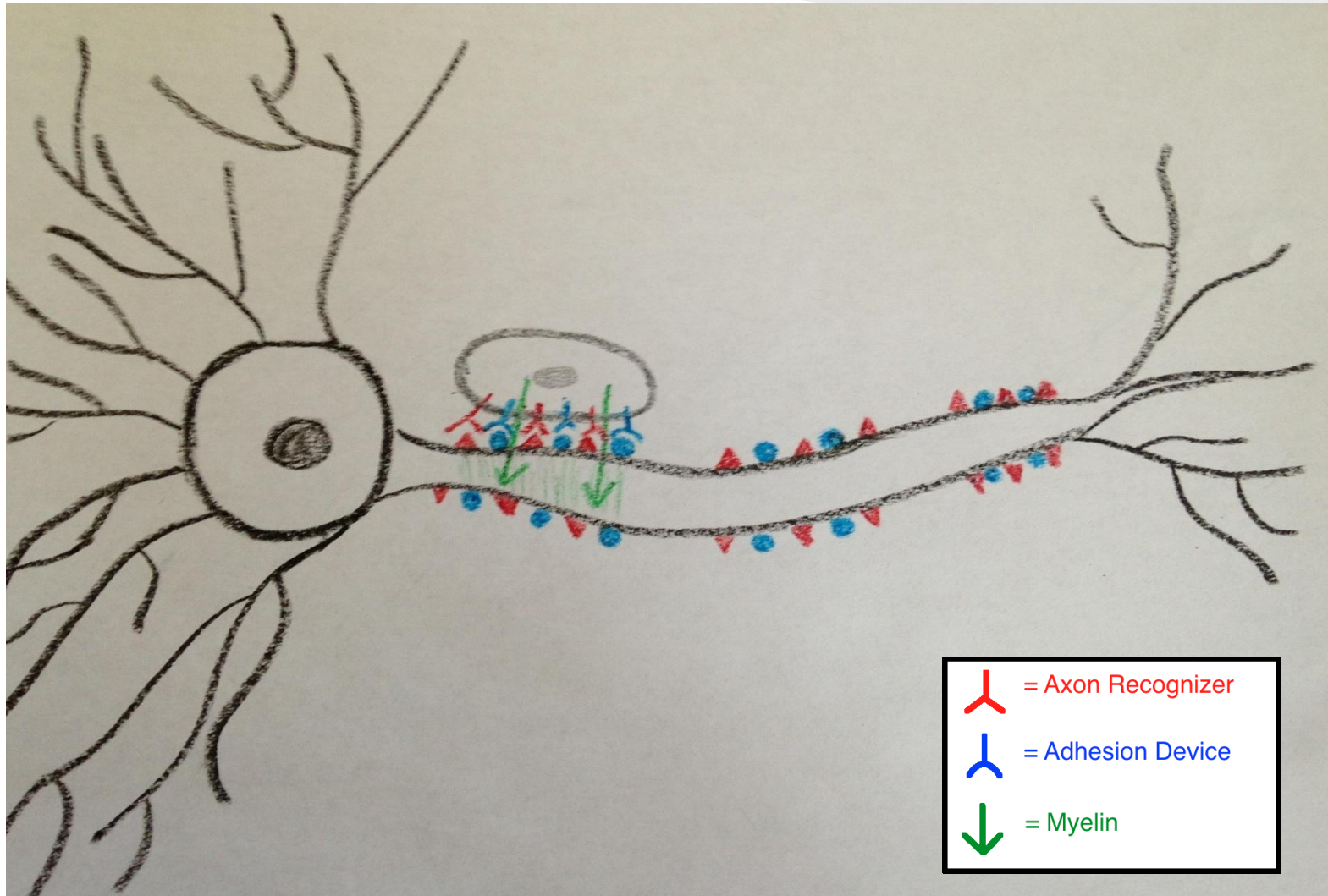
# Device Level Description

1. Axon-cell adhesion device
2. Axon recognizing device
3. Myelinating device

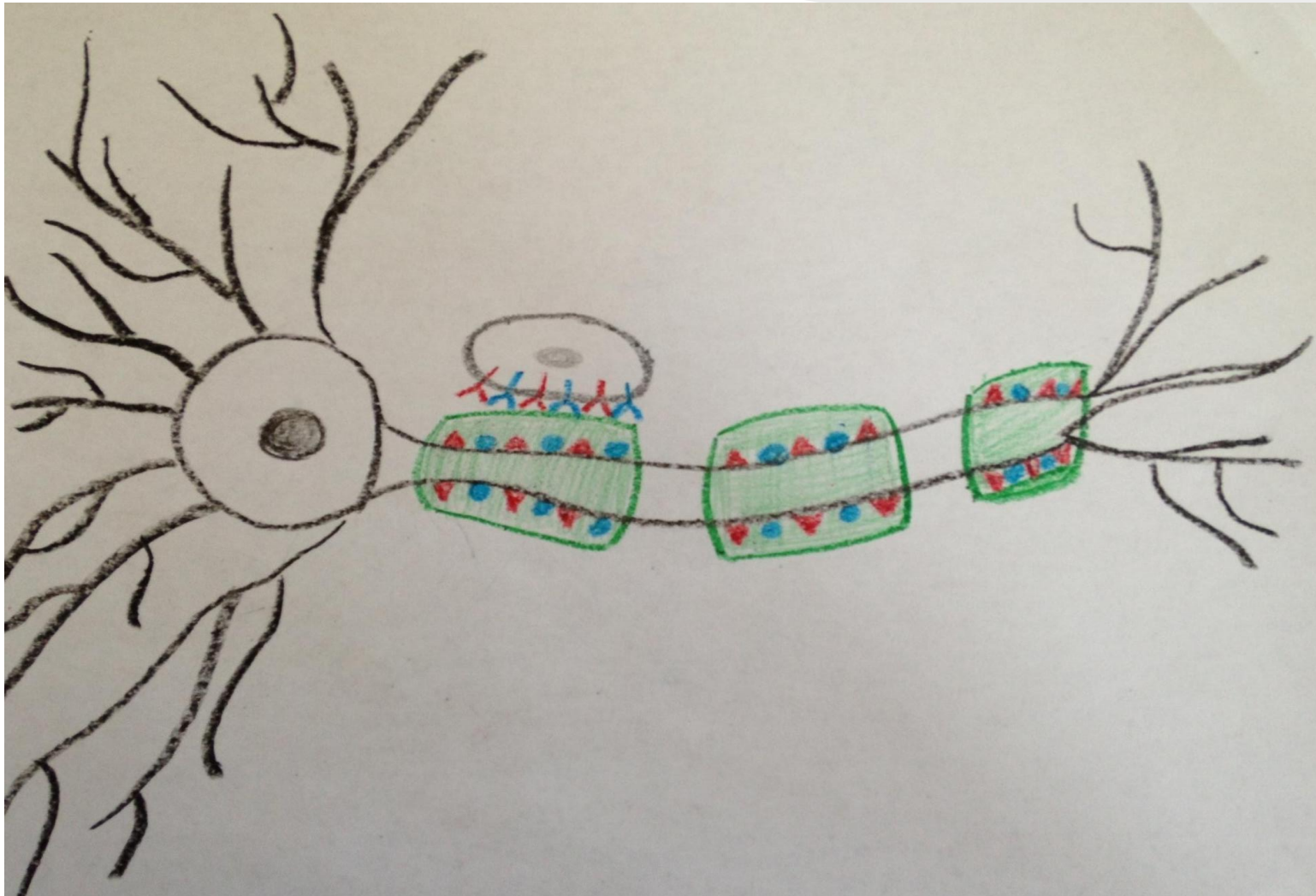
# Device Diagram



# No Myelin?

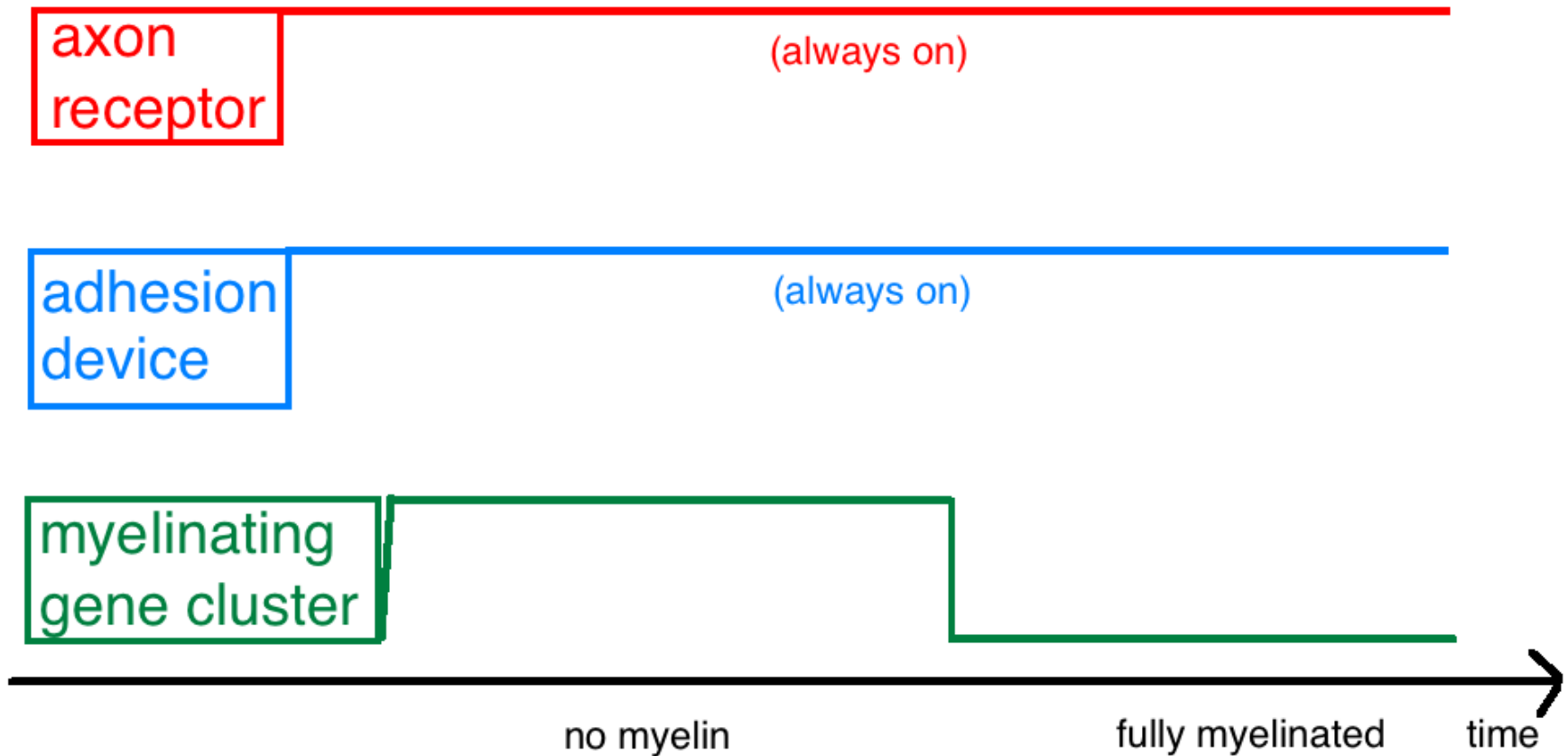


# Already Myelinated?



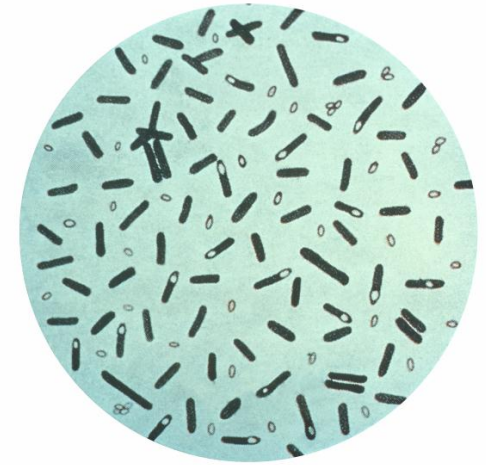


# Timing Diagram



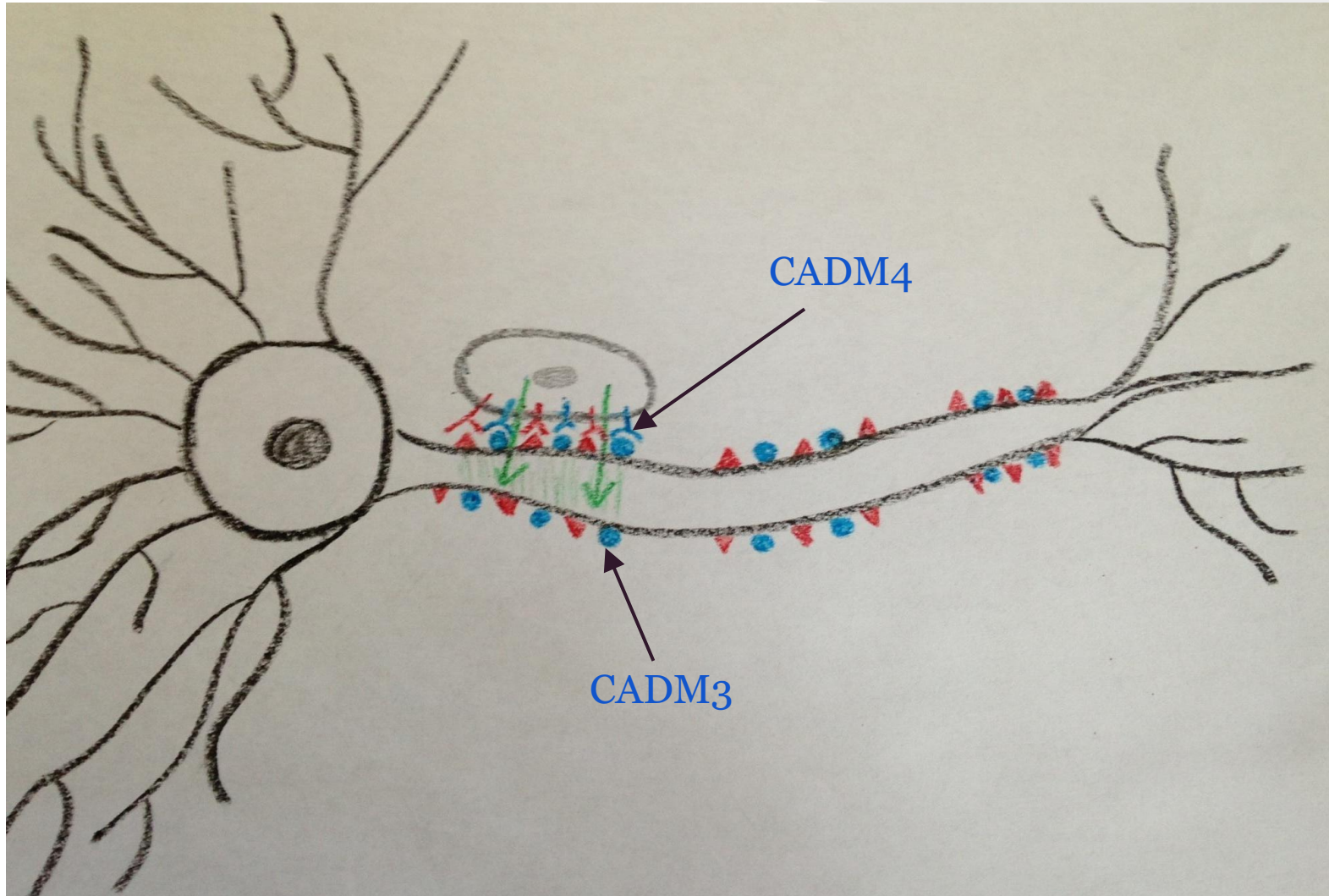
# Chassis

## Clostridium Sporogenes



- Motile, anaerobic bacteria
- Part of the C.Botulinum family, but do not produce neurotoxins
- Currently being used in cancer research to reduce tumor growth
- The spores of the bacteria are small enough to reach the brain and can grow in anaerobic conditions

# Axon-Cell Adhesion Device



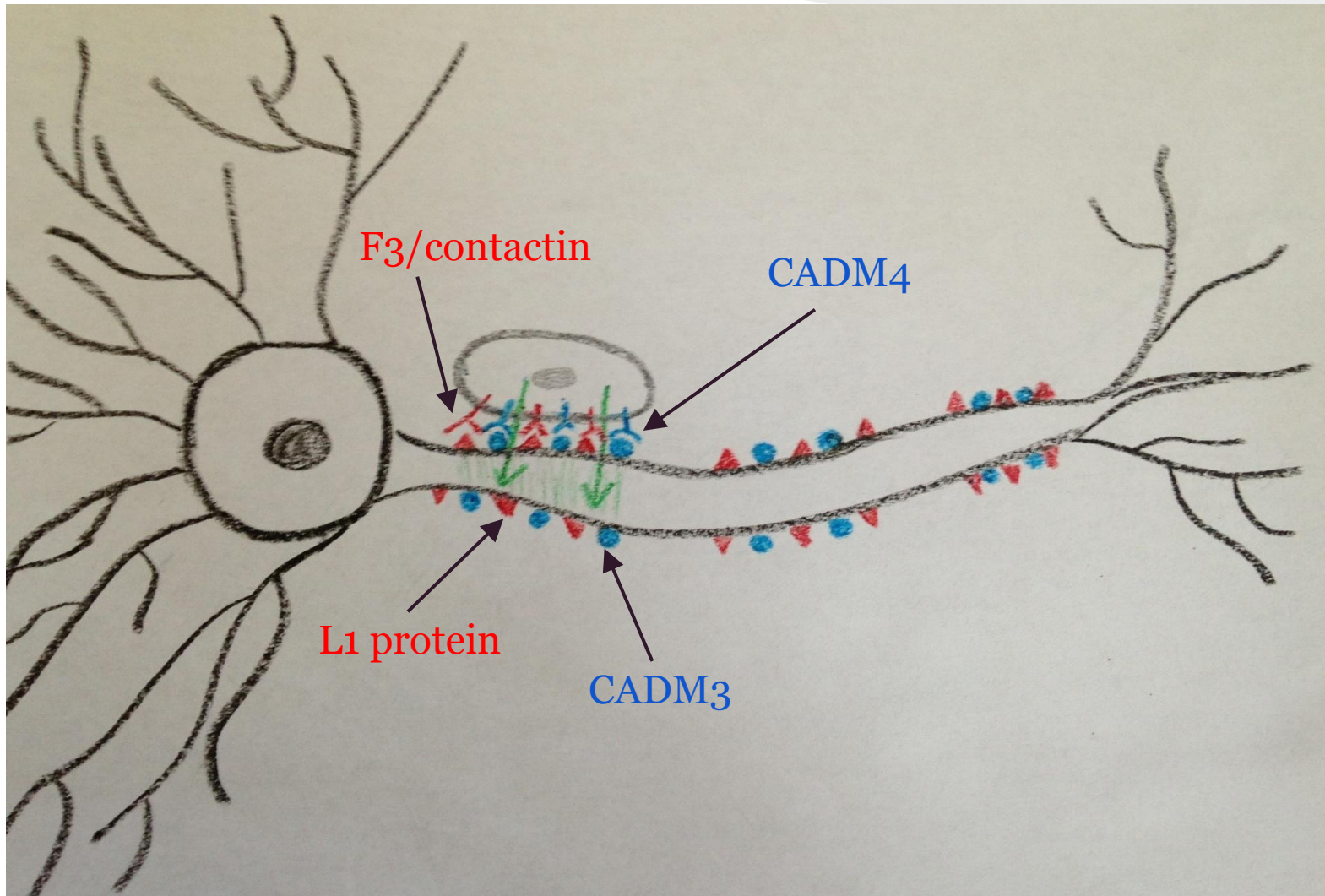
# Axon-Cell Adhesion Device

## CADM4-CADM3 adhesion pair

(CADM = **C**ell **A**dhesion **M**olecule)

- In PNS: CADM4 = Schwann cells, CADM3 = unmyelinated axon
- Gene: CADM4
  - Promoter : HG\_ACW:41758
  - Transcript: CADM4.DAPR07-UNSPLICED
- Debugging: IGSF4C antibodies (N-term)

# Axon Recognizing Device



# Axon Recognizing Device

## F3/Contactin cellular receptor

- L1 (axon) binds to F3/contactin (oligodendrocytes)
- F3/contactin and  $\beta$ 1-integrin stimulate activation of Fyn
- Fyn normally phosphorylates protein hnRNP A2 and begins a signalling cascade
- Gene: CNTN1

F3/Contactin: Immunoglobulin glycoprotein

$\beta$ 1-integrin: Transmembrane receptors that provide information from the extracellular matrix

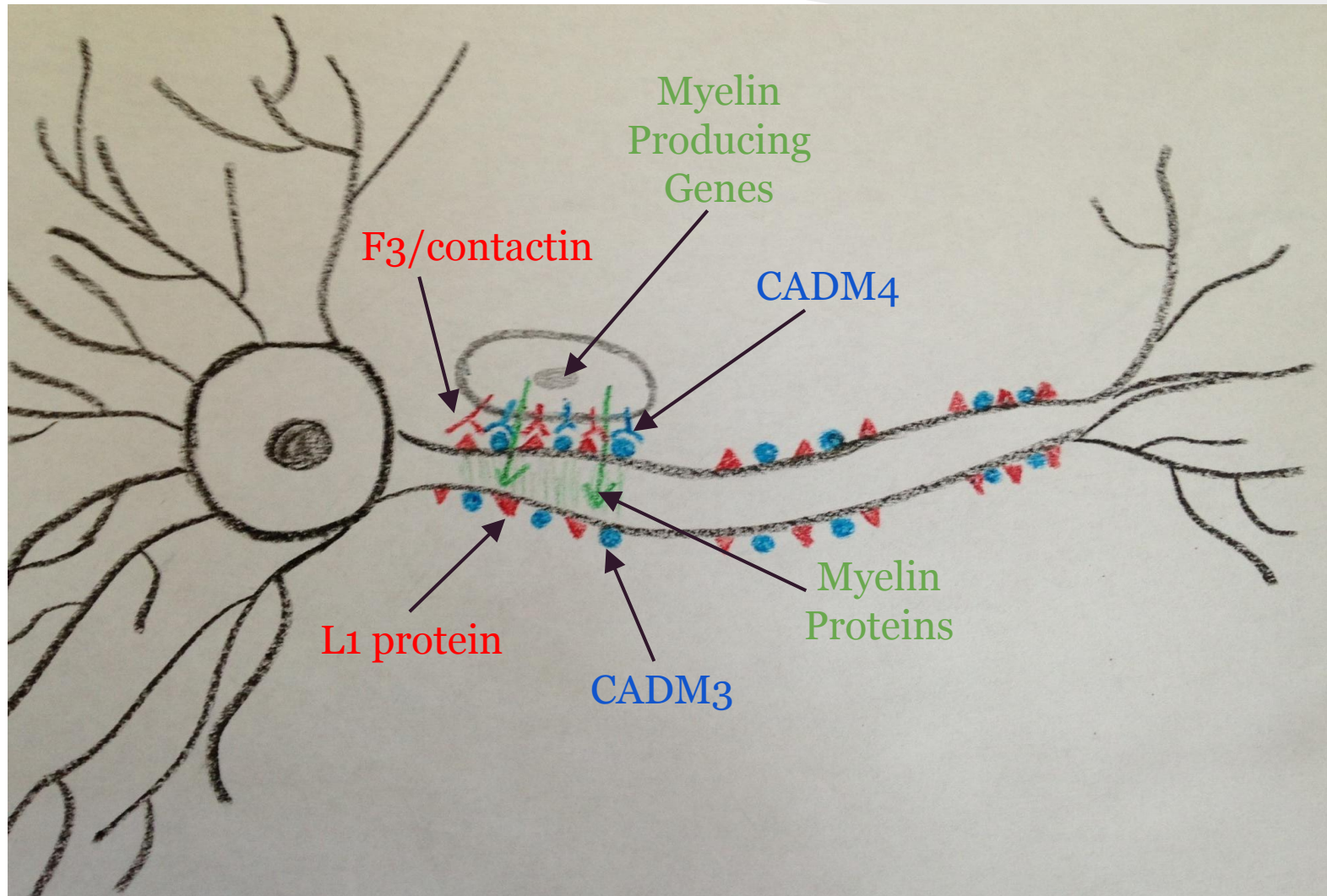
Fyn: A tyrosine kinase molecule

# Control Mechanism

Function: Turn the production of myelin ON when the chassis recognizes the demyelinated axon

- The fyn protein can bind to the HIV LTR promoter to induce the transcription of myelin genes
- Debugging: place HIV LTR promoter on GFP rather than myelin genes, place in isolated cell, record if cell turns green

# Myelin Producing Device





# Myelin Producing Device

Three main glycoproteins produced by Schwann cells:

1. Myelin Protein Zero (Po Protein)
2. Myelin-Associated Glycoprotein (MAG)
3. Peripheral Myelin Protein-22 (PMP-22)

# Myelin Protein Zero

- Encoded by the Myelin Protein Zero gene (MPZ)
- The most abundant protein in myelin
- Acts like an adhesion and protective molecule
- Location:
  - Schwann cells
  - Chromosome 1 (Position 23.3)

# Myelin-Associated Glycoprotein

- Encoded by the MAG gene
- Axon-Glia interactions
- Maintenance of myelin with aging
- Location:
  - Myelinating Schwann Cells

# Peripheral Myelin Protein-22

- Encoded by peripheral myelin protein-22 gene (PMP-22)
- Plays a crucial role in the development and maintenance of myelin
- Location:
  - Primarily in Schwann Cells
  - Chromosome 17 (Position 12)

# Myelin Producing Device

## Debugging:

- Isolate myelin genes with promoter and insert into cell
- Provide the cell with FYN in culture
- Observe whether or not myelin is produced

# Things to look into

- Effects
  - immune system
  - off-target
  - self-destruction?
- Structure
  - Superfly vs. natural myelin
  - myelinating genes
  - myelin leaving the cell
- Debugging
  - wrapping around axon
  - feedback

Go/No Go

**GO!**

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