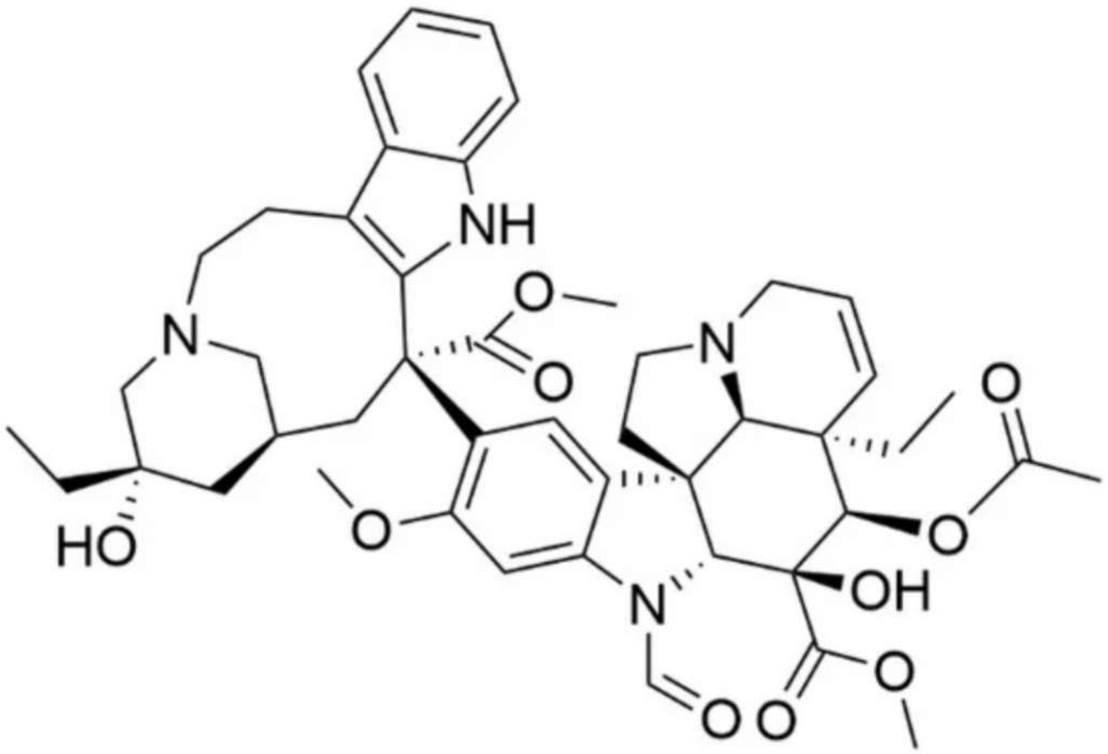
DEVIL FACIAL TUMOUR DISEASE:

NOVEL INSIGHTS THROUGH CELL MECHANICS

A BIOPHYSICAL APPROACH

Group 13: Sulagna Nandi, Nam Nguyen, Sara Osman, Ann Maria Philip, Keira Sponagle



(Škubník et al. 2021)

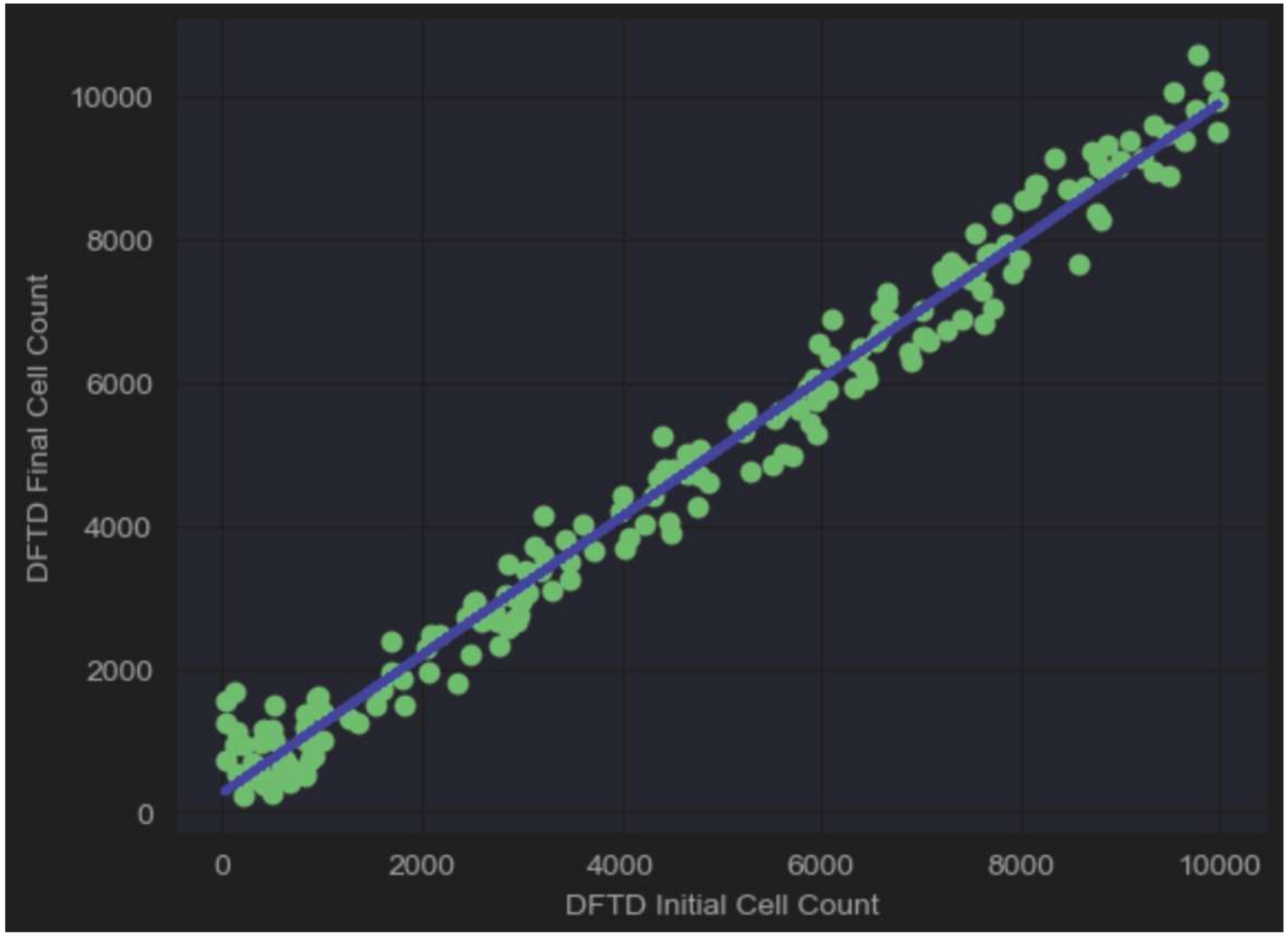
VINCRISTINE

- vinca alkaloid that induces **apoptosis**
- causes **cell cycle arrest** in the metaphase
- disrupts microtubules in **mitosis phase of cell division** and proliferation

COMPUTATIONAL ANALYSIS USING LINEAR REGRESSION

DFTD WITH AND WITHOUT VINCRISTINE TREATMENT

DFTD CELLS WITH VINCRISTINE



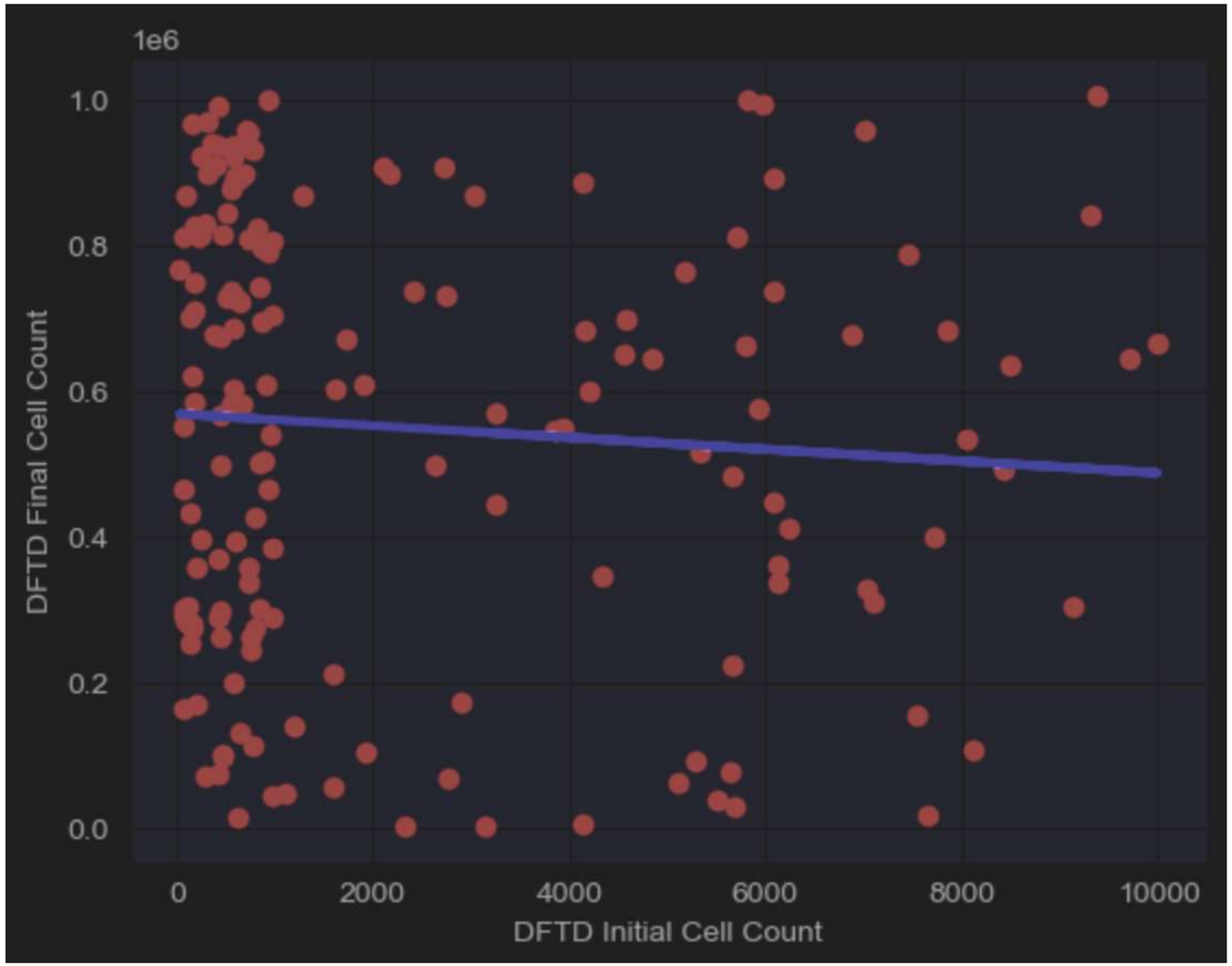
REGRESSION LINE:

$Y = 0.9638X + 261.4$

R^2 VALUE:

0.9804

DFTD CELLS WITHOUT VINCRISTINE



REGRESSION LINE:

$Y = -8.105X + 569453$

R^2 VALUE:

0.0056

INVESTIGATING SEMI-RESISTANCE

We will examine vincristine's mechanism of action in order to further investigate the semi-resistance of DFTD cells.

Why is vincristine-induced mitotic arrest not leading to apoptosis?

INVESTIGATING SEMI-RESISTANCE

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Why is vincristine-induced mitotic arrest not leading to apoptosis?

Evasion of apoptosis is a hallmark of cancer

Cytoskeletal restructuring is a pathway through which cells can evade apoptosis.

BIOPHYSICS AND DFTD

The biophysical perspective offers novel insights into DFTD treatment.

Biophysics and cancer research:

- vincristine treatment **decreases stiffness** in cancer cells
- hypothesized cytoskeletal repair mechanism countering this softening
  - repair causes choline metabolism, **increasing total choline (tCho) levels**

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Biophysics and cancer research:

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Our proposed study's question:

How does vincristine alter cell stiffness in DFT1 cells and what changes in choline metabolism contribute to the cell's response to vincristine treatment?

METHODS OVERVIEW

TECHNOLOGY

Atomic Force Microscopy (AFM) Nanoindentation

Magnetic Resonance Spectroscopy (MRS)

METHODS OVERVIEW

TECHNOLOGY	Atomic Force Microscopy (AFM) Nanoindentation Magnetic Resonance Spectroscopy (MRS)
CELL LINES	DFT1 and human neuroblastoma

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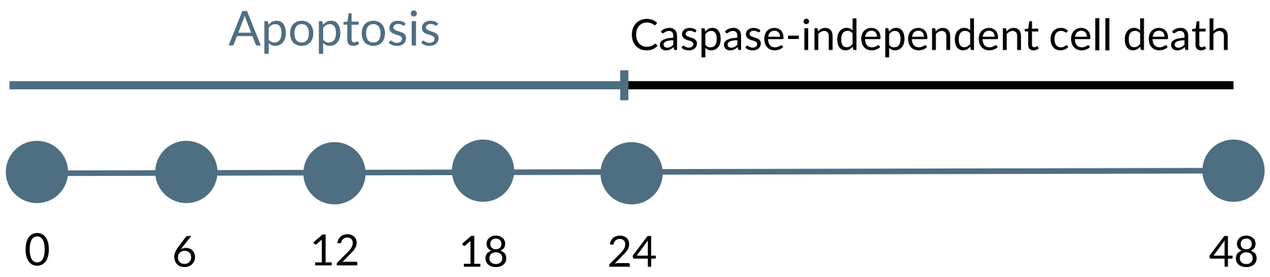
CELL LINES

DFT1 and human neuroblastoma

DURATION



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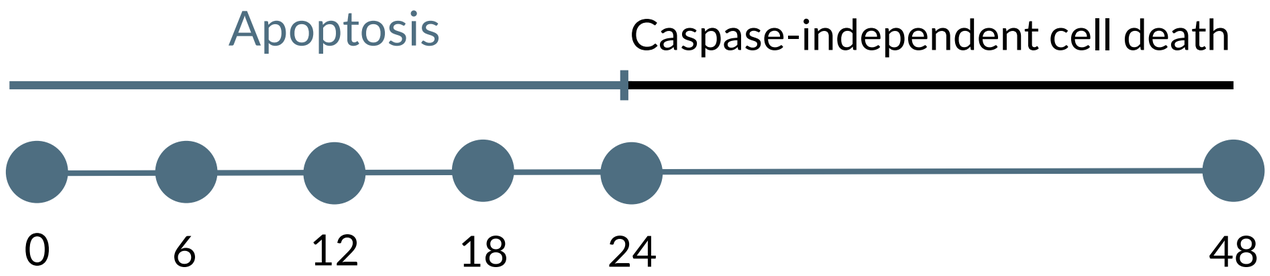
Magnetic Resonance Spectroscopy (MRS)

CELL LINES

DFT1 and human neuroblastoma

DURATION



CONTROLS

Untreated DFT1 and human neuroblastoma experimental groups

CELL LINE PREP

DFT1 cell line C5065

↓

Pinfold et al.
2014

Neuroblastoma cell line SH-SY5Y

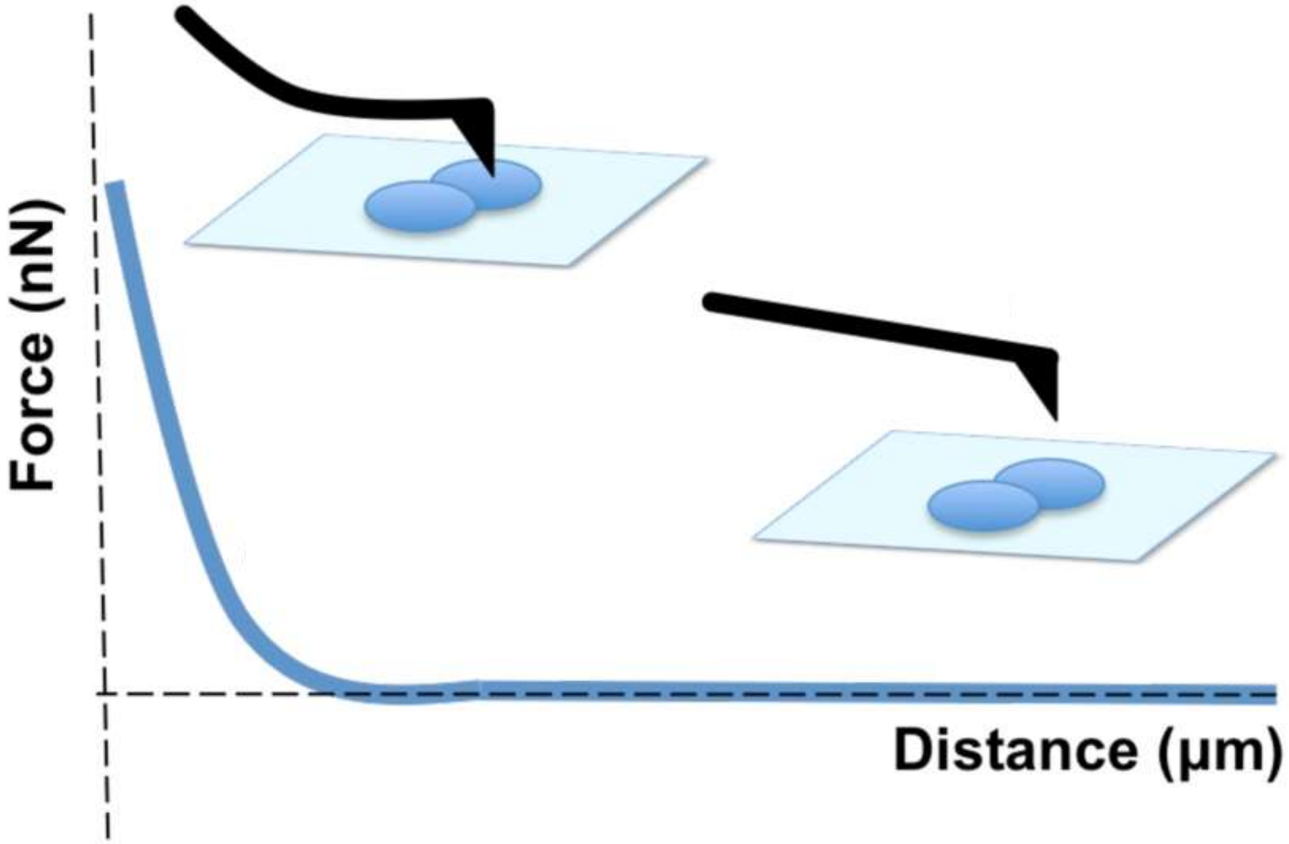
↓

Kaya et al.
2024

Vincristine administration:

- Continuous exposure
- Based off of Tu et al.
- In glass coverslips (AFM) or culture dishes (MRS)

NANOINDENTATION



30 cells per experimental condition

↓

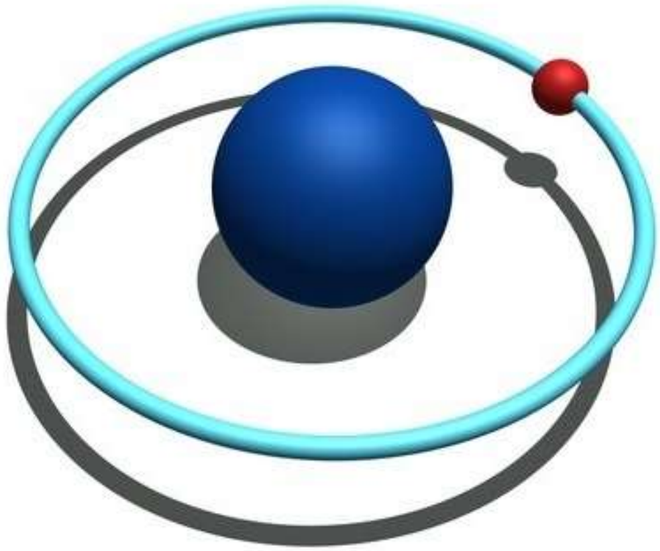
Measured in triplicate

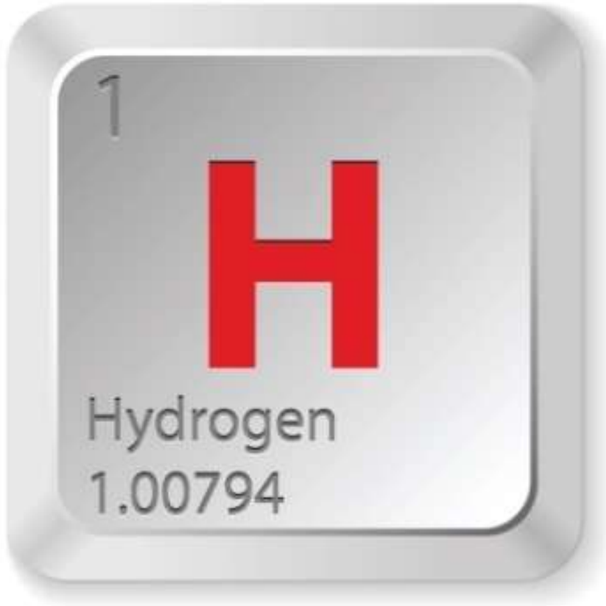
↓

90 force-distance curves per experimental condition

(Aguayo 2016)

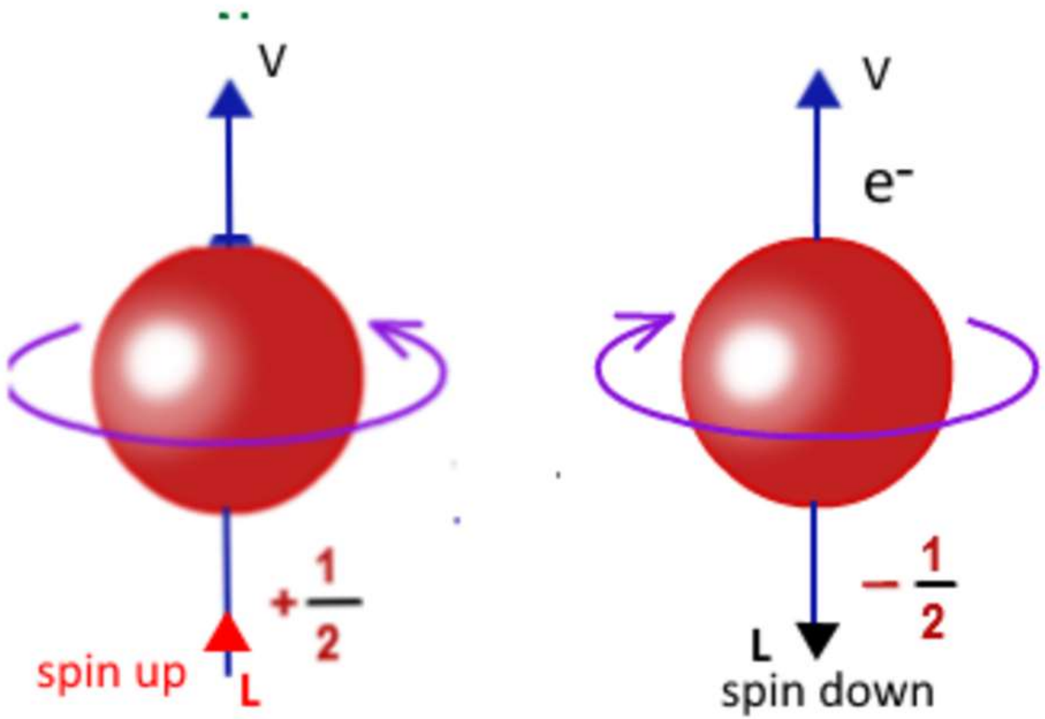
MRS IMAGING OVERVIEW





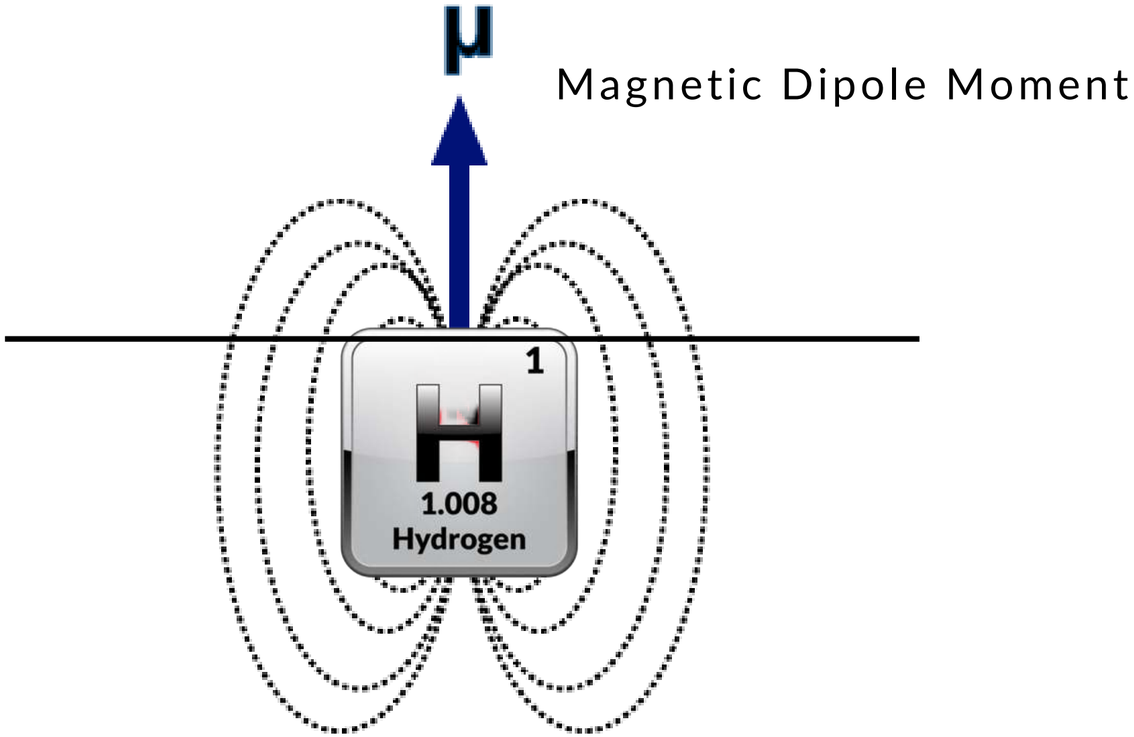
(Blaszczak-Boxe 2015, Reisch 2015)

MRS IMAGING OVERVIEW



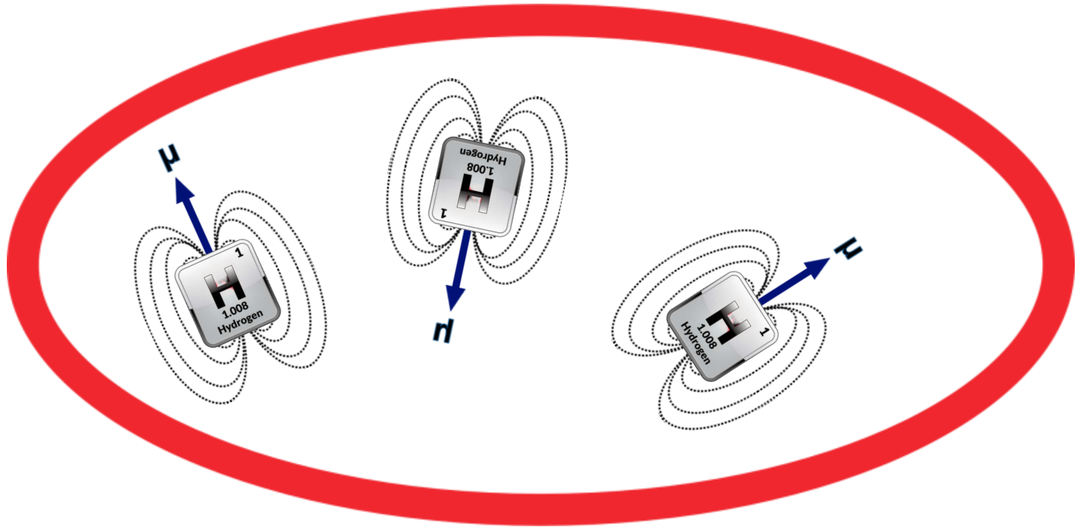
(Jethro 2025)

MRS IMAGING OVERVIEW



MRS IMAGING OVERVIEW

NMR/MRS Machine

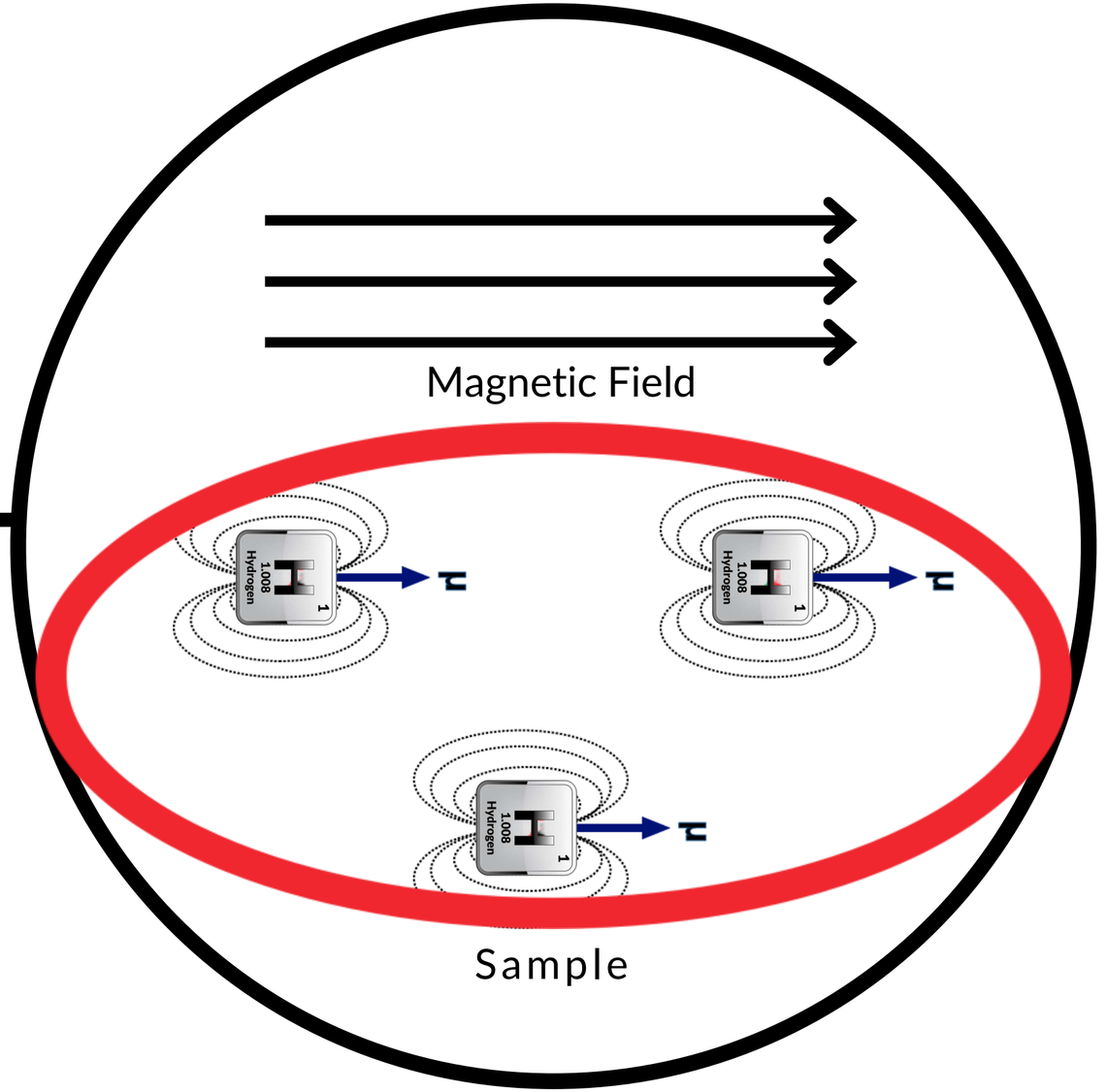


Sample

(Blaszczak-Boxe 2015)

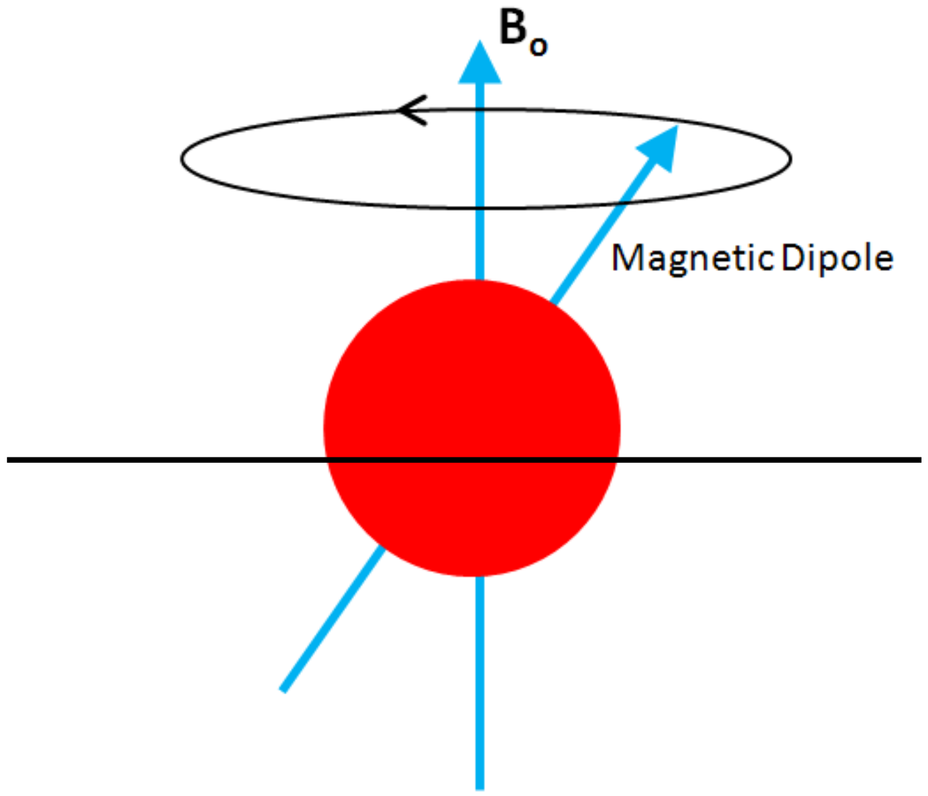
MRS IMAGING OVERVIEW

Inside



Net Polarization

MRS IMAGING OVERVIEW

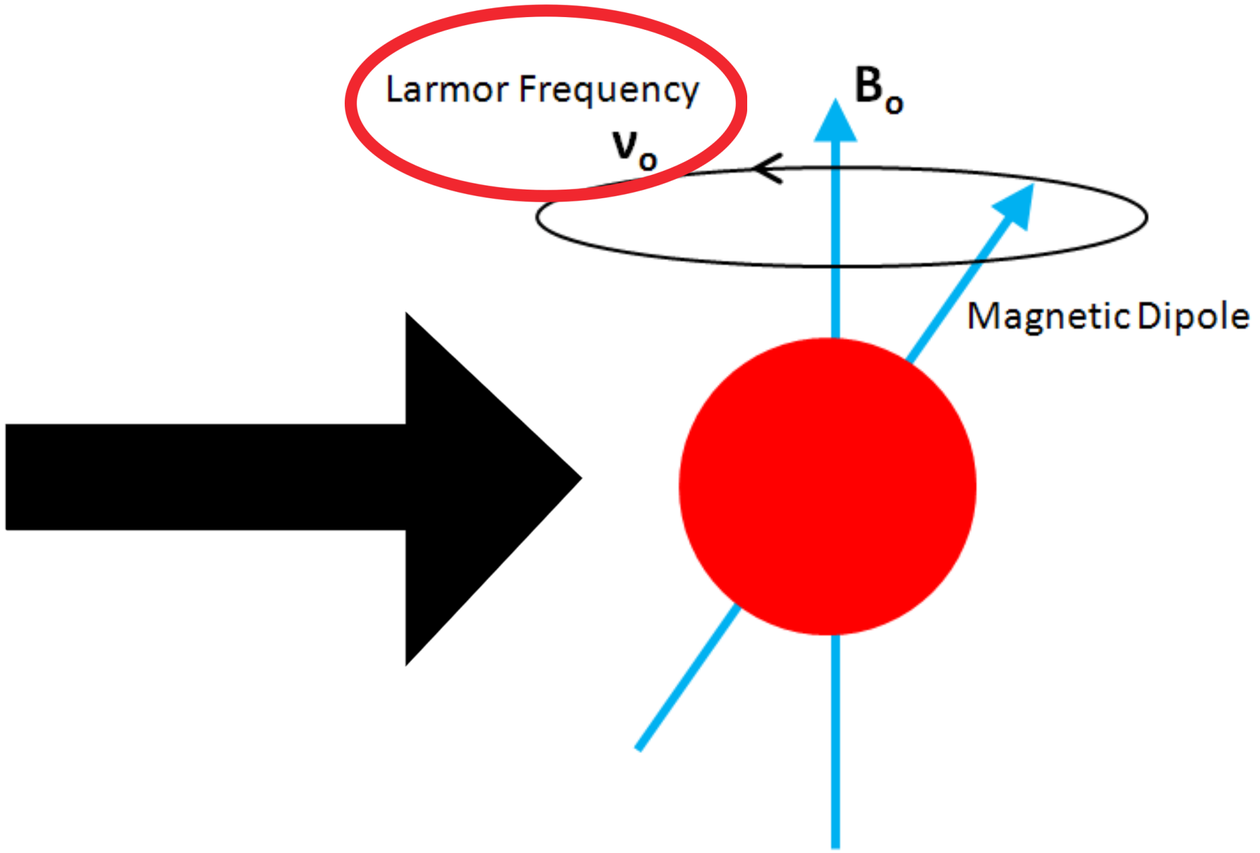


$$\tau = \mu \times B$$

(Bailey 2019)

MRS IMAGING OVERVIEW

$$\tau_{net} = I\alpha = \frac{dL}{dt}$$



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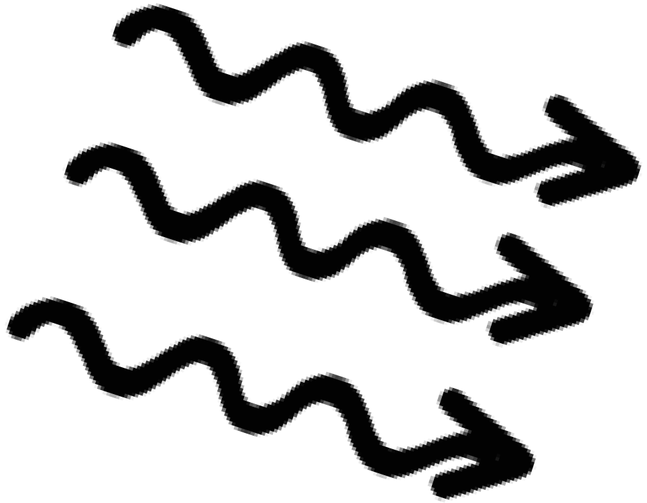
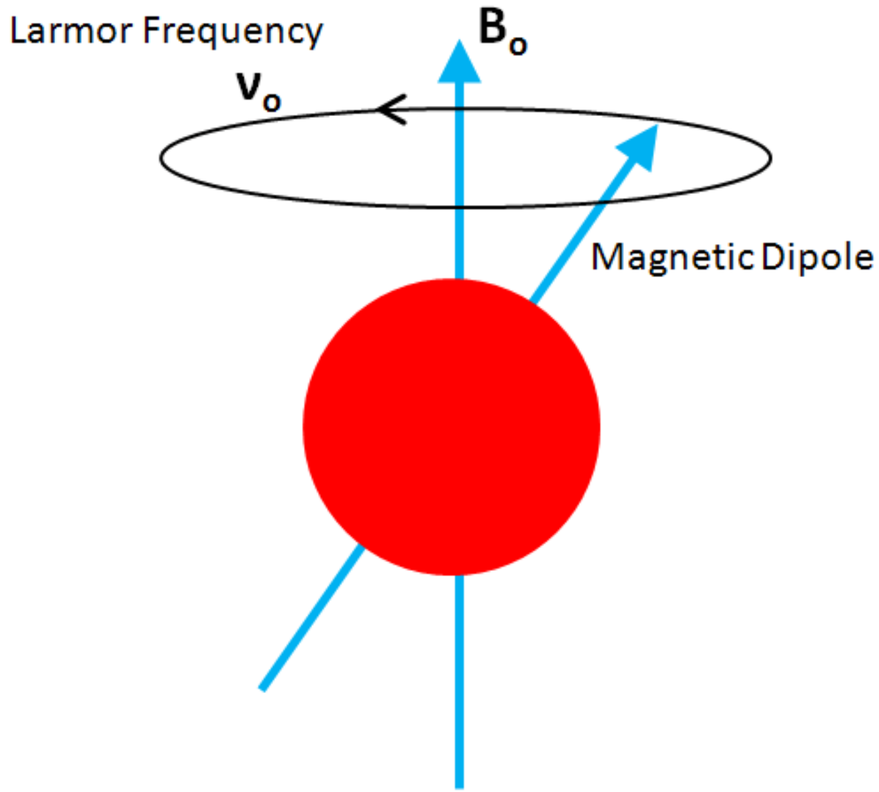


Radiowaves



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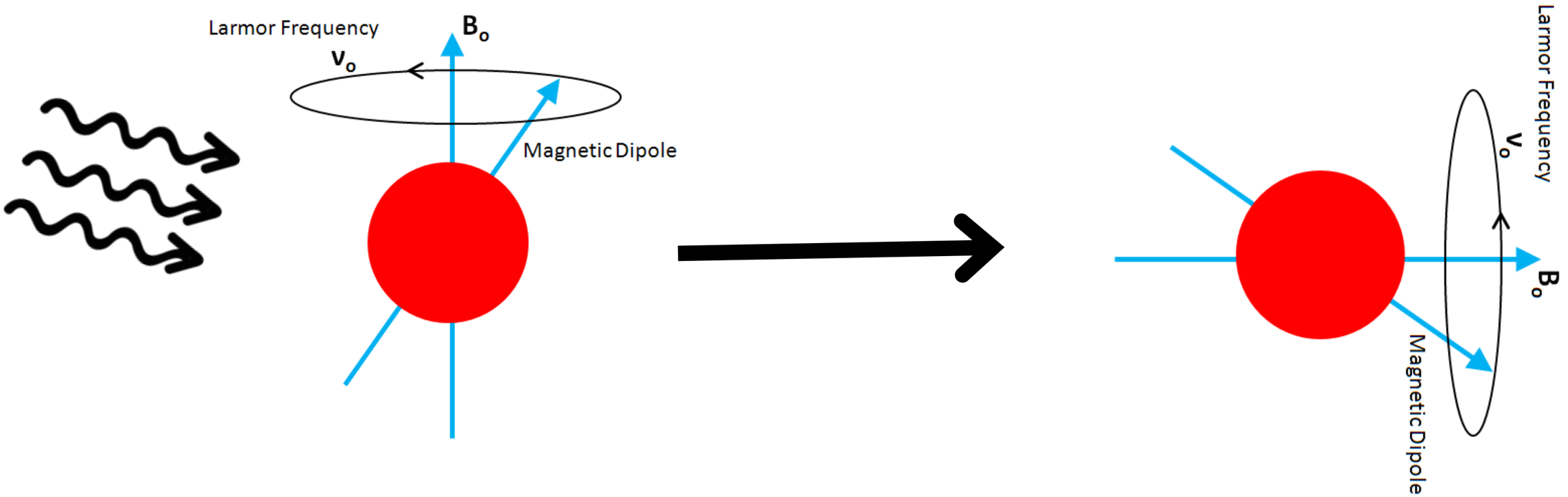

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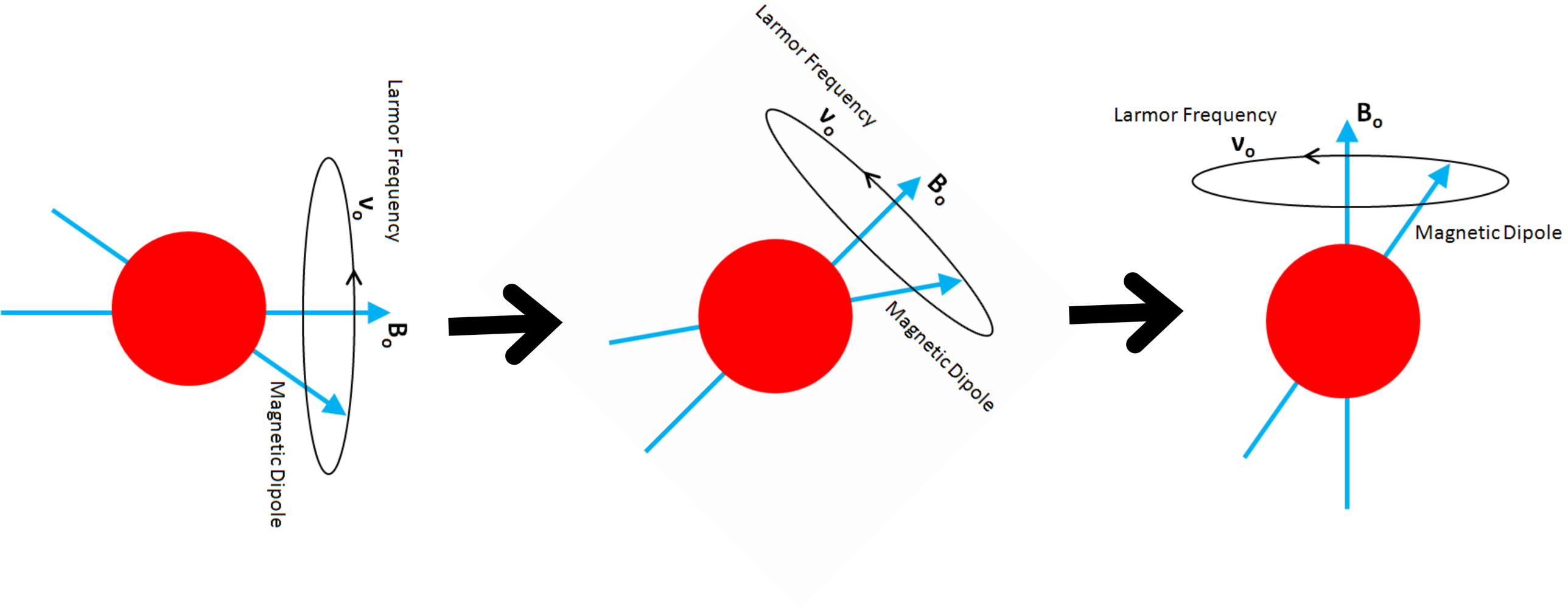

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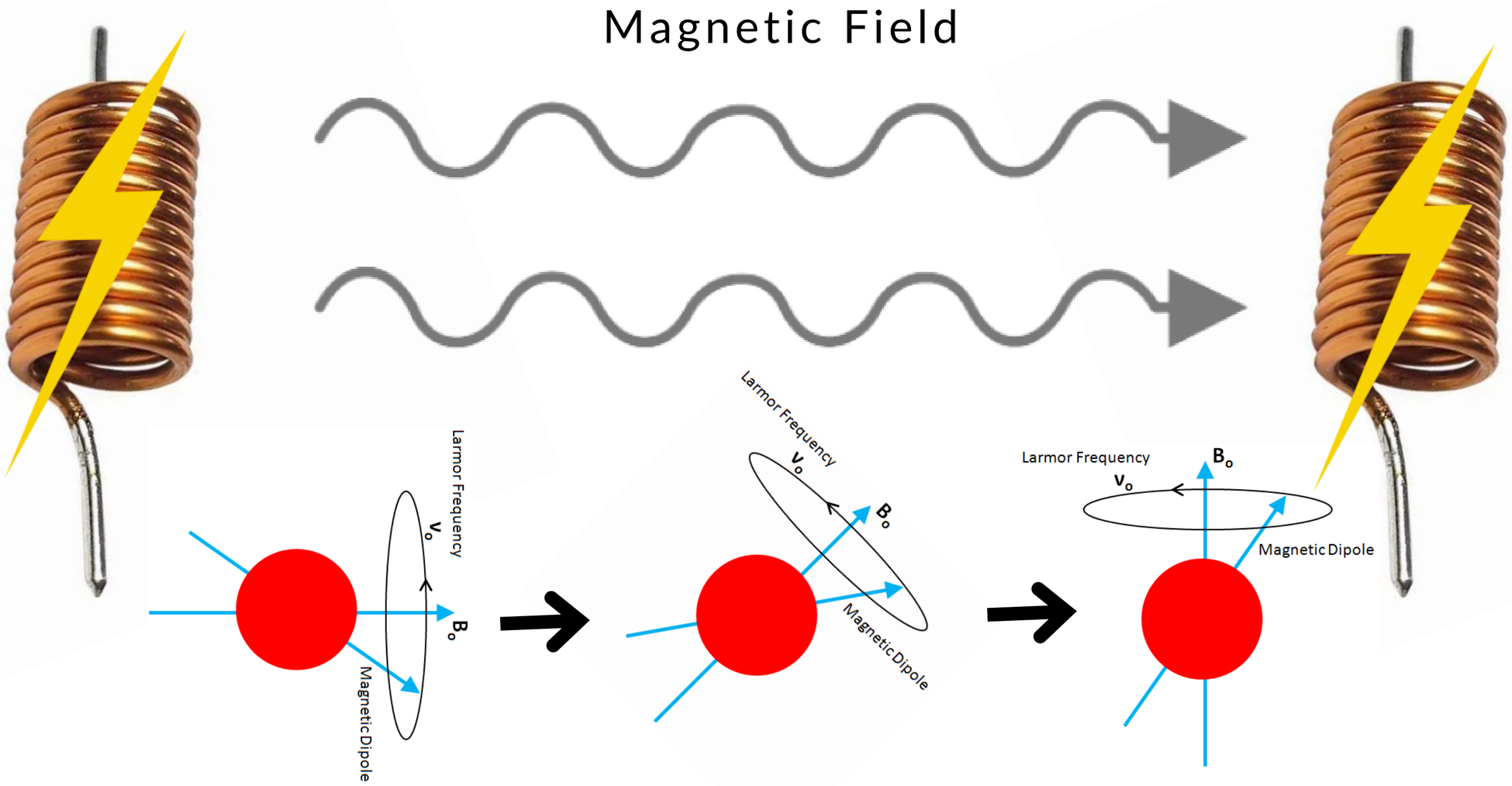

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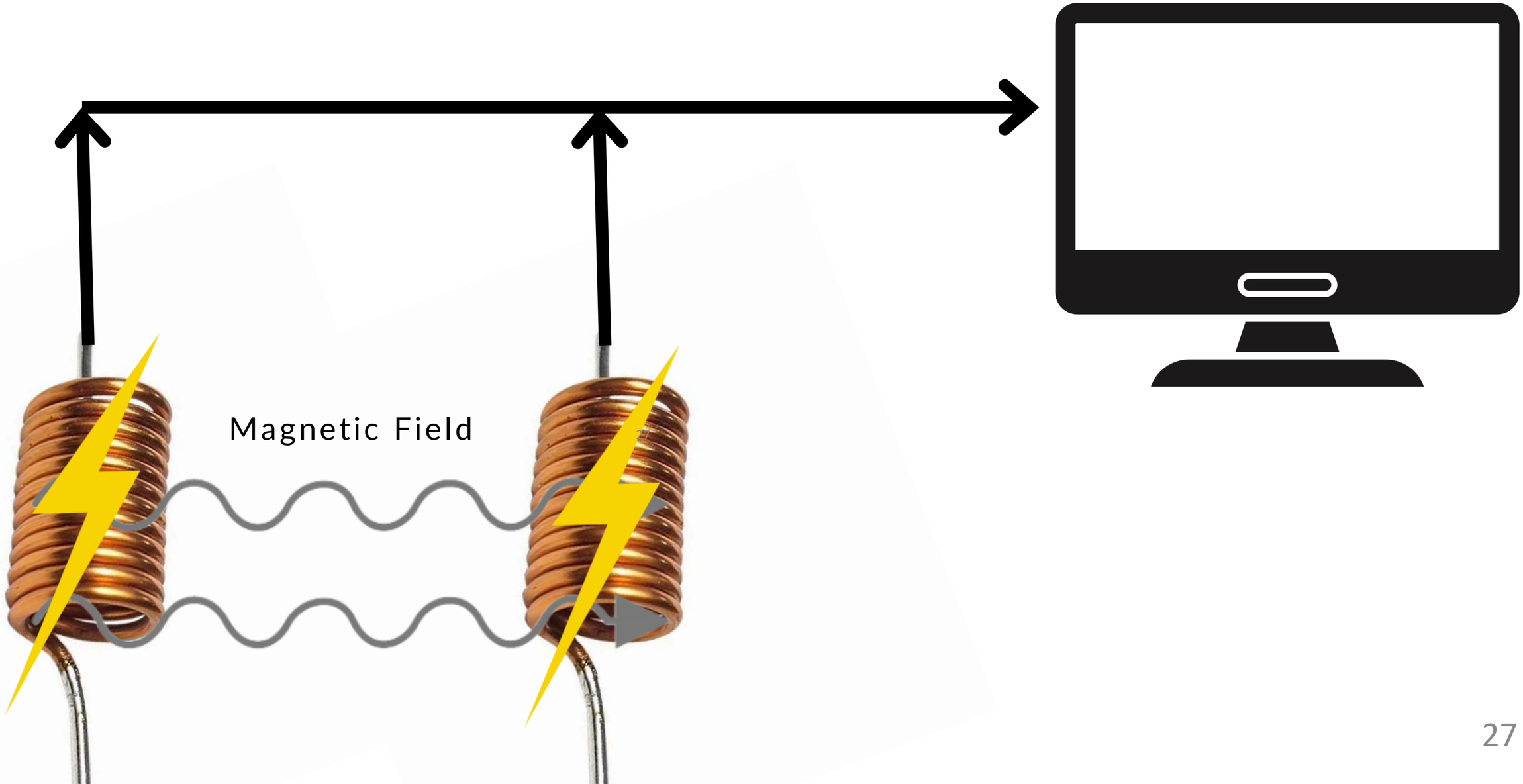

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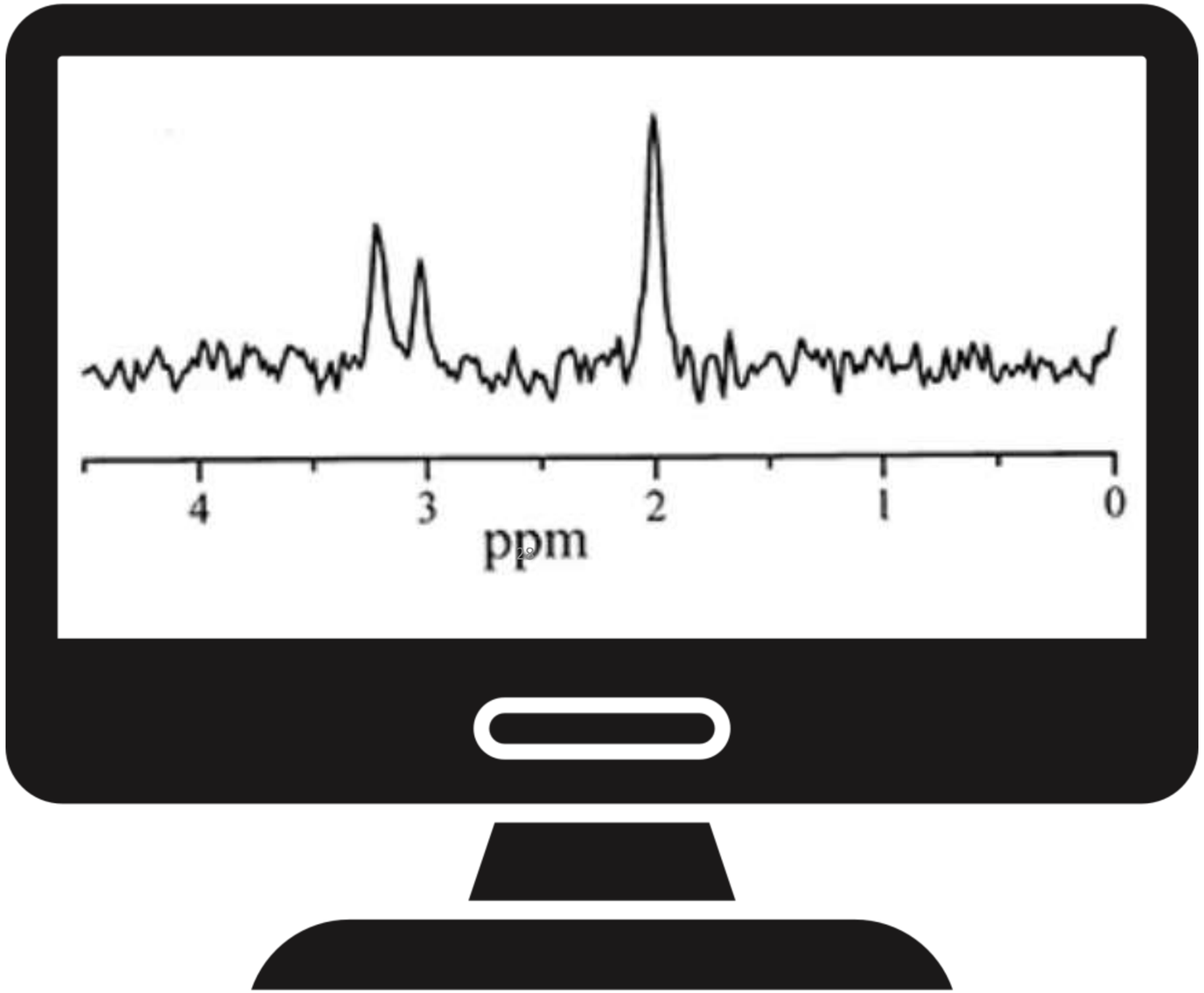

(Robertson and Cox)

MRS IMAGING : TOTAL CHOLINE

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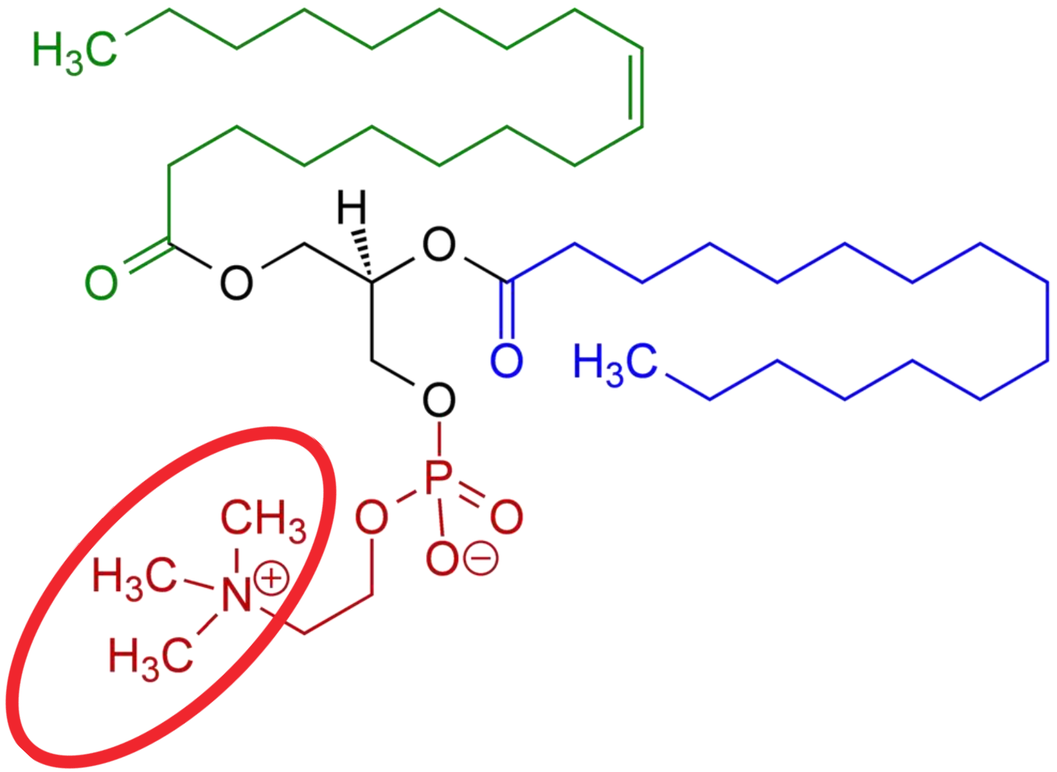
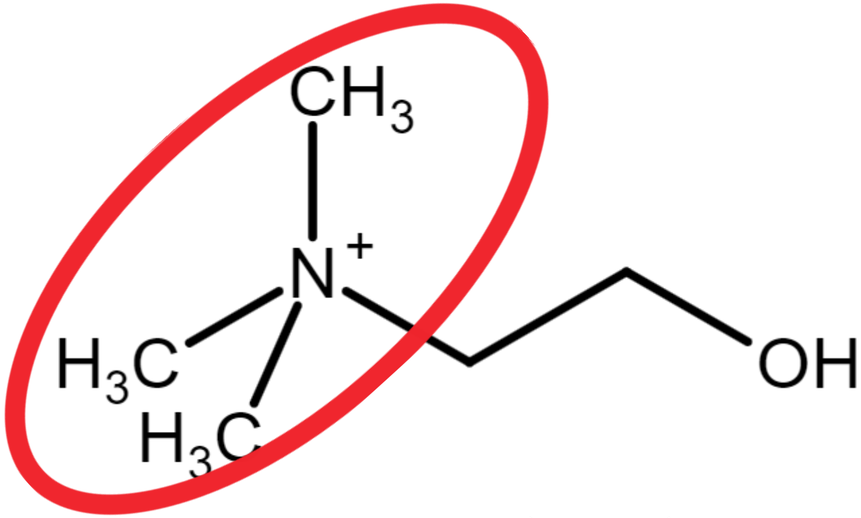
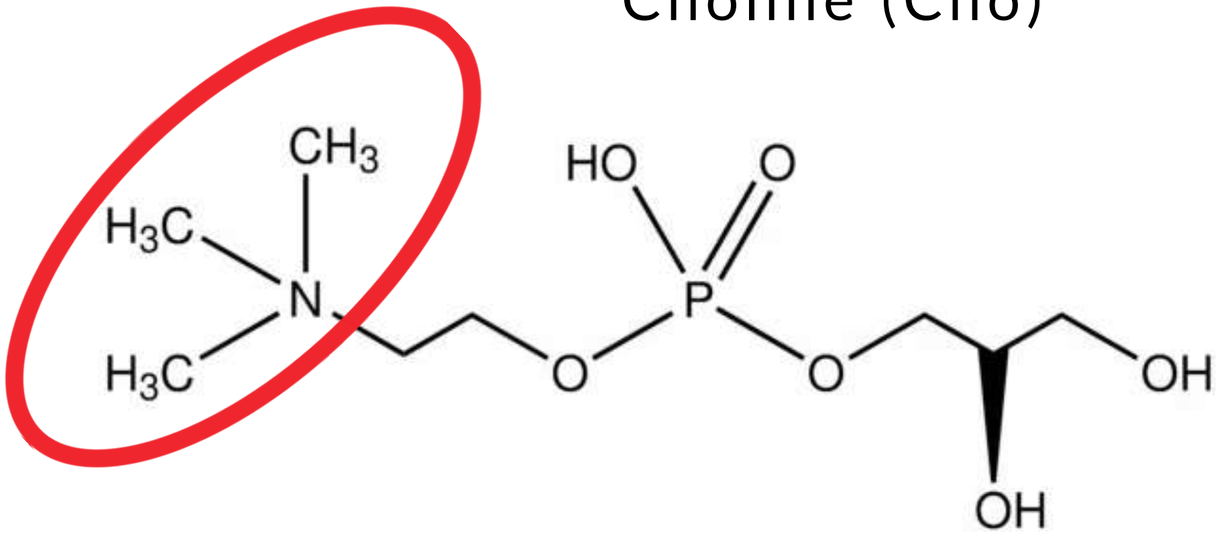


Phosphatidylcholine (pCho)



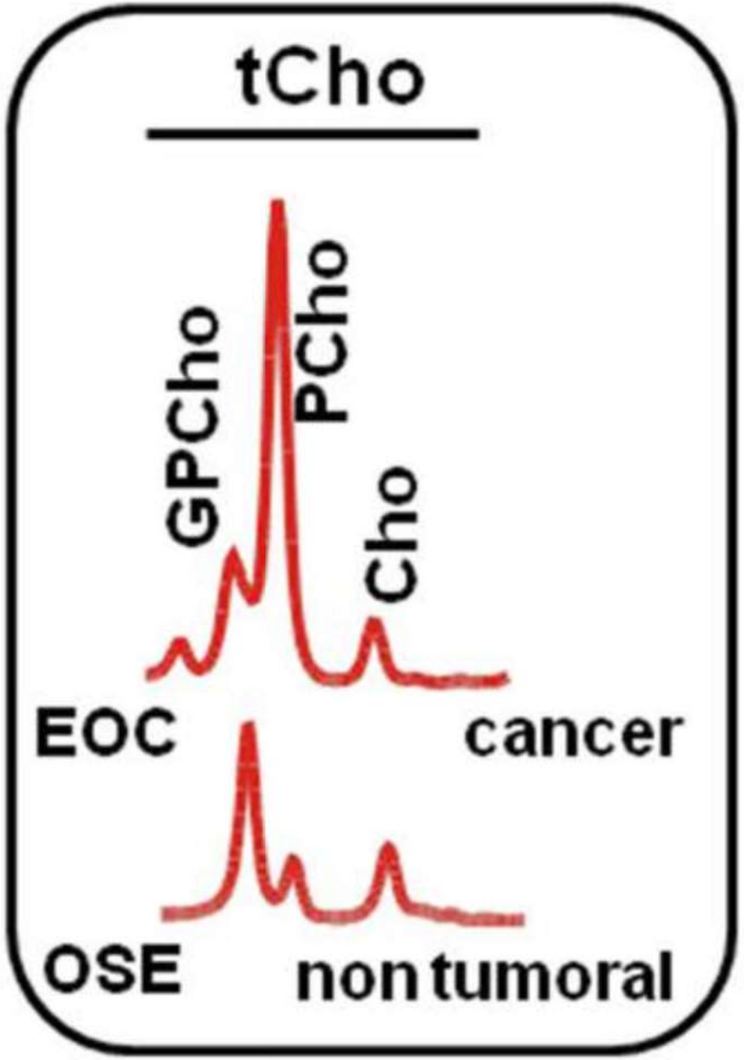
Choline (Cho)



Glycerophosphorylcholine (gCho)

(Sigma-Aldrich)

MRS IMAGING : TOTAL CHOLINE



(Iorio et al. 2021)

OUTCOMES

Cell stiffness	tCho level	Interpretation	Future endeavors
Decrease	Increase		
No change	Increase	Adaptive response	Time-targeted combination therapy
Increase	Increase		

CONCLUSIONS

Novel biophysical perspective, contributing to our understanding of:

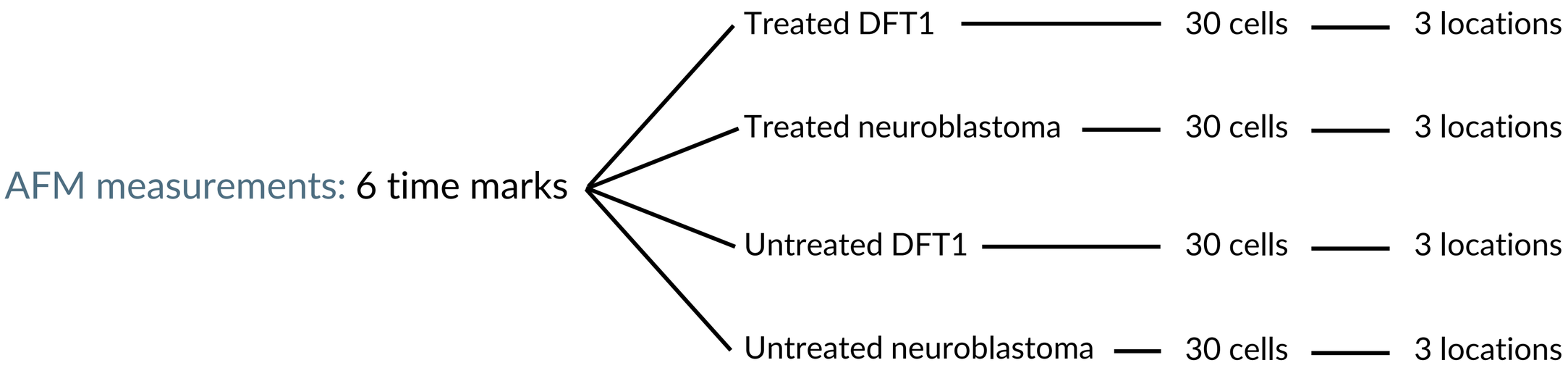
Hallmarks of cancer

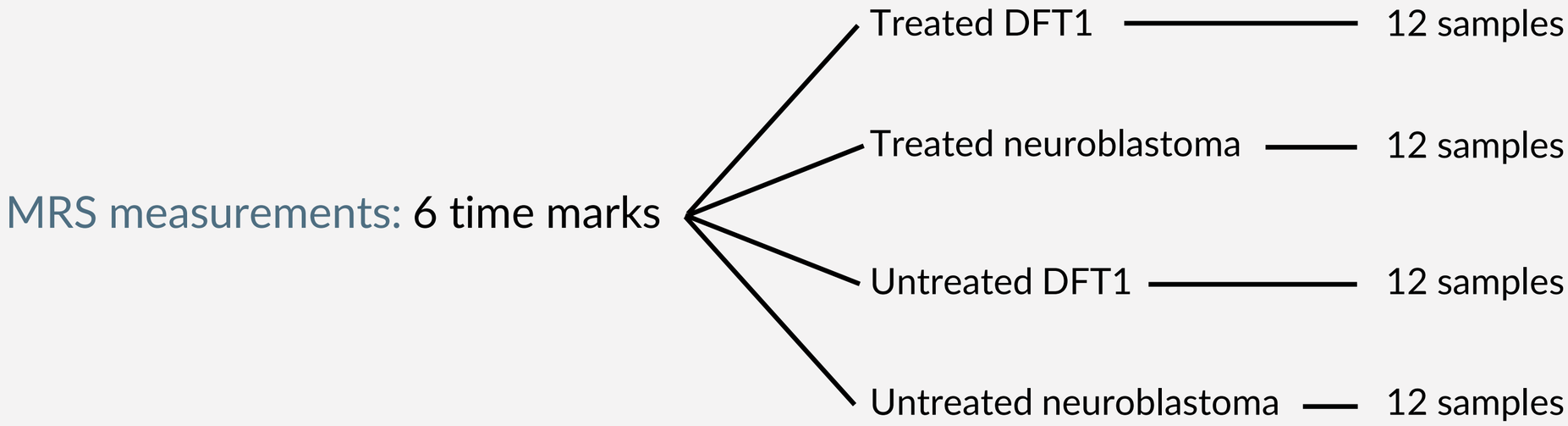
Possibility of combination therapies

Cell mechanics in cancers without clear treatment options

QUESTIONS?

COLLECTED DATA





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COLLECTED DATA

AFM measurements: **720 comparative stiffness values**

MRS measurements: **288 comparative tCho values**

OUTCOMES

Interpretations of combined cell stiffness (AFM) and tCho level (MRS) findings.

AFM / MRS	No change	Increase	Decrease
No change	Complete resistance	Metabolic adaptation	Signs of stress
Increase	Alternate resistance	Resistance and compensation	Inconclusive
Decrease	Destabilization without response	Destabilization with response	Successful treatment

THANK YOU