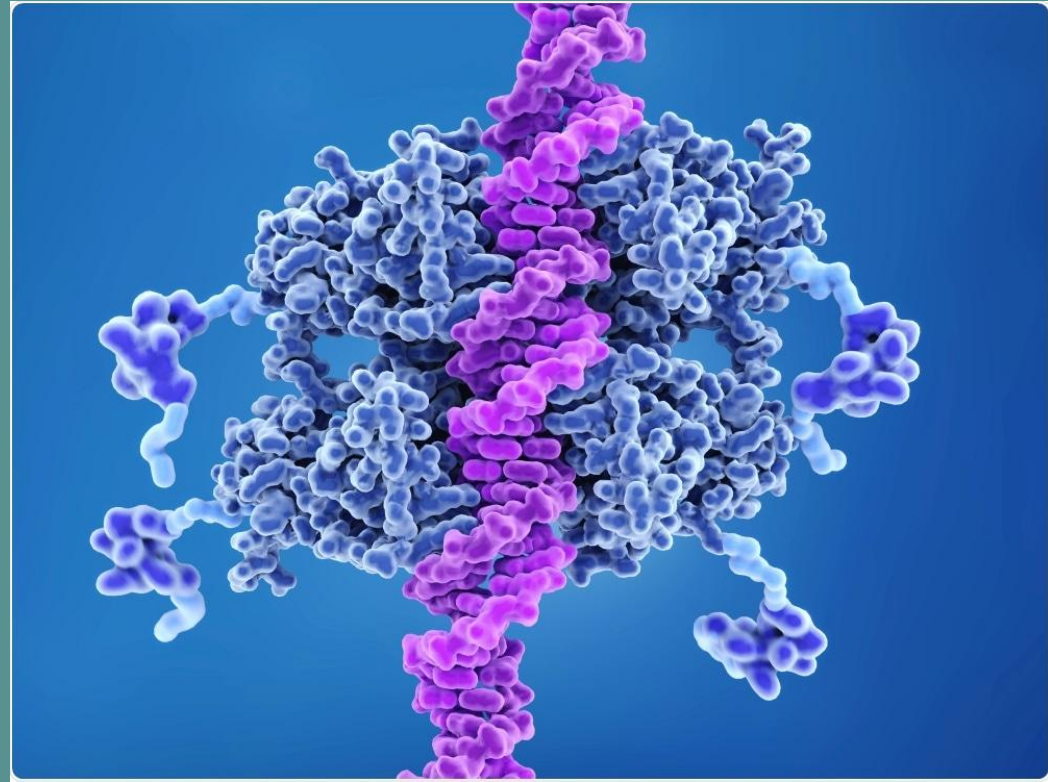


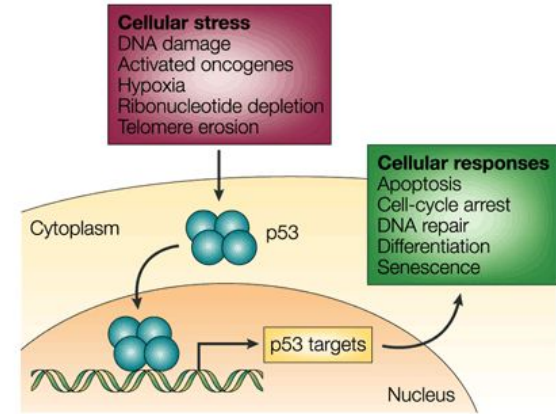
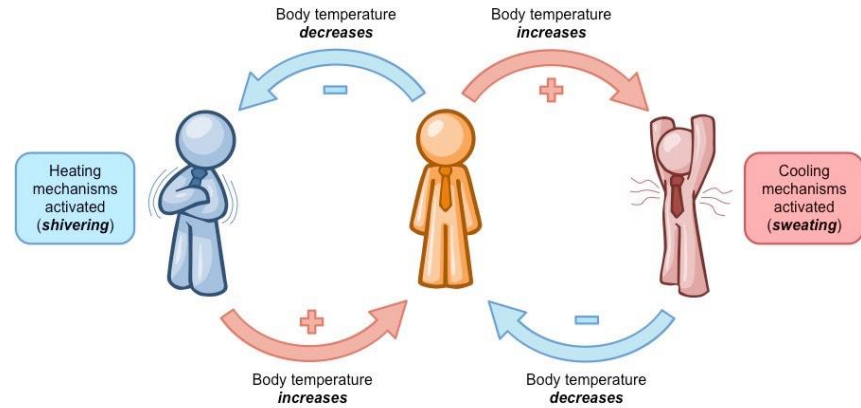
p53 and DNA damage

William Cesaretti

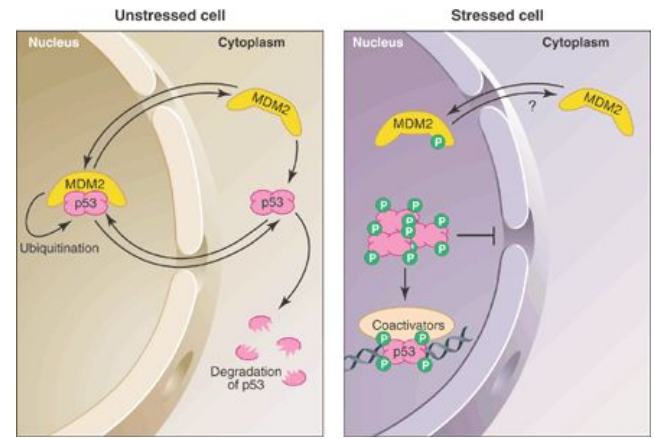


Biological Background

- p53 is a protein to stop tumors
- MDM2 is a protein that suppresses p53
- Increase in p53 causes MDM2 production, thereby decreasing the level of p53
- Positive/negative feedback loop



Biological Background cont.

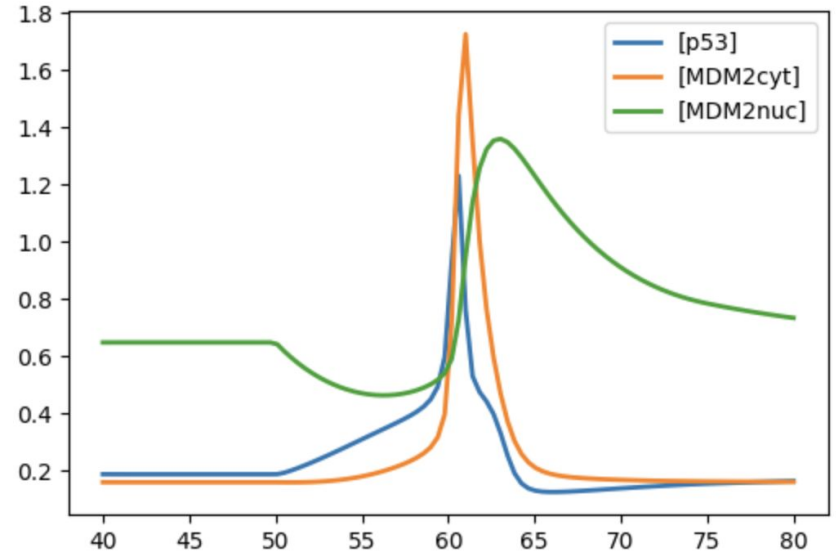


- DNA damage -> p53 accumulates to help fix the damage or kill cell (apoptosis)
- Researchers have found levels of p53 and MDM2 rise and fall in pulses post DNA damage
- They investigated the function of pulses



The models

- Models already exist (used SBML -> Antimony translator [online](#))
- Default params see picture
- Protein signaling network
- Note: This is just the first model I found
- Will look at others



Model One

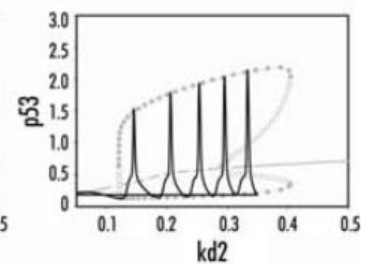
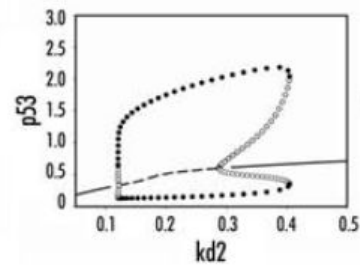
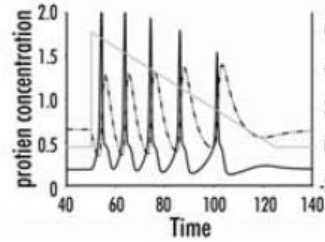
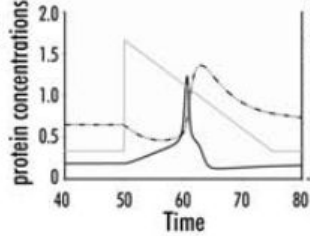
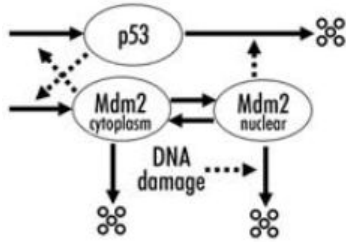
Equations 1, 2, 3; $[Mdm2^*] = [Mdm2_{nuc}]$, $[p53^*] = [p53]$

$$(4) \quad \frac{d[p53]}{dt} = k'_{s53} + k^*_{s53} \cdot \frac{[Mdm2_{cyt}]^4}{J^4_{s53} + [Mdm2_{cyt}]^4} - k_{d53} \cdot [p53]$$

$$(5) \quad \frac{d[Mdm2_{cyt}]}{dt} = k'_{s2} + k^*_{s2} \cdot \frac{[p53]^4}{J^4_{s2} + [p53]^4} - k_i \cdot [Mdm2_{cyt}] + k_o \cdot [Mdm2_{nuc}] - k^*_{d2} \cdot [Mdm2_{cyt}]$$

$$(6) \quad \frac{d[Mdm2_{nuc}]}{dt} = k_i \cdot [Mdm2_{cyt}] - k_o \cdot [Mdm2_{nuc}] - k_{d2} \cdot [Mdm2_{nuc}]$$

Model cont.





My goal

- Alter models by adding parameters and manipulating equations
- Further explore combinations of models to draw new conclusions
- Create a UI to allow users to simulate an environment and see the change p53/MDM2 in response to the DNA damage in the given environment





Thank you

I'd appreciate any critiques, questions, or thoughts.



References

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