

# Manganese Neurotoxicity

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# Good Manganese

- Dietary (ingest)
- Mn deficiency can result in birth defects, poor bone formation and increased susceptibility to seizures

# Bad Manganese

- Pulmonary (lungs)
- Manganism: similar to parkinson's disease symptoms include decrease in response speed, irritability, mood changes, and compulsive behaviors

# Manganese Exposure

- Methylcyclopentadienyl manganese tricarbonyl (MMT) used as a substitute for lead in gasoline. (don't worry only about 1% in U.S.!)
- Miners smelters and welders are also exposed

# Studying effects of Manganese

Brain (rat)

Cells

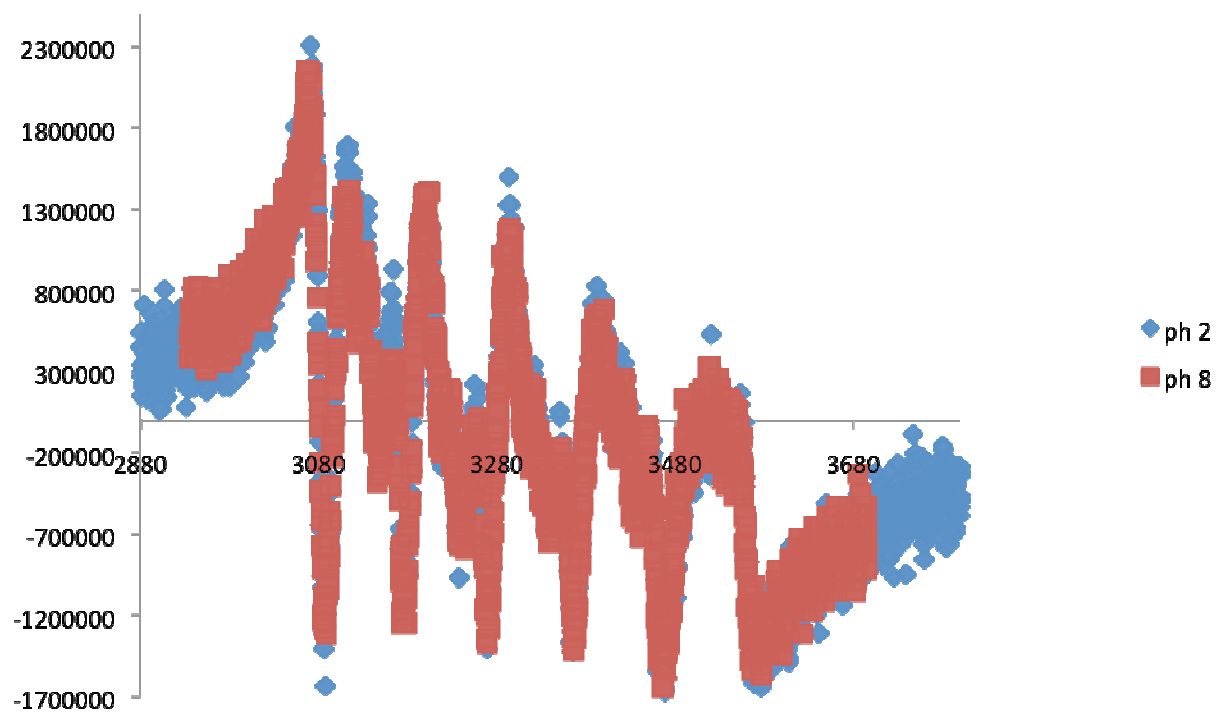
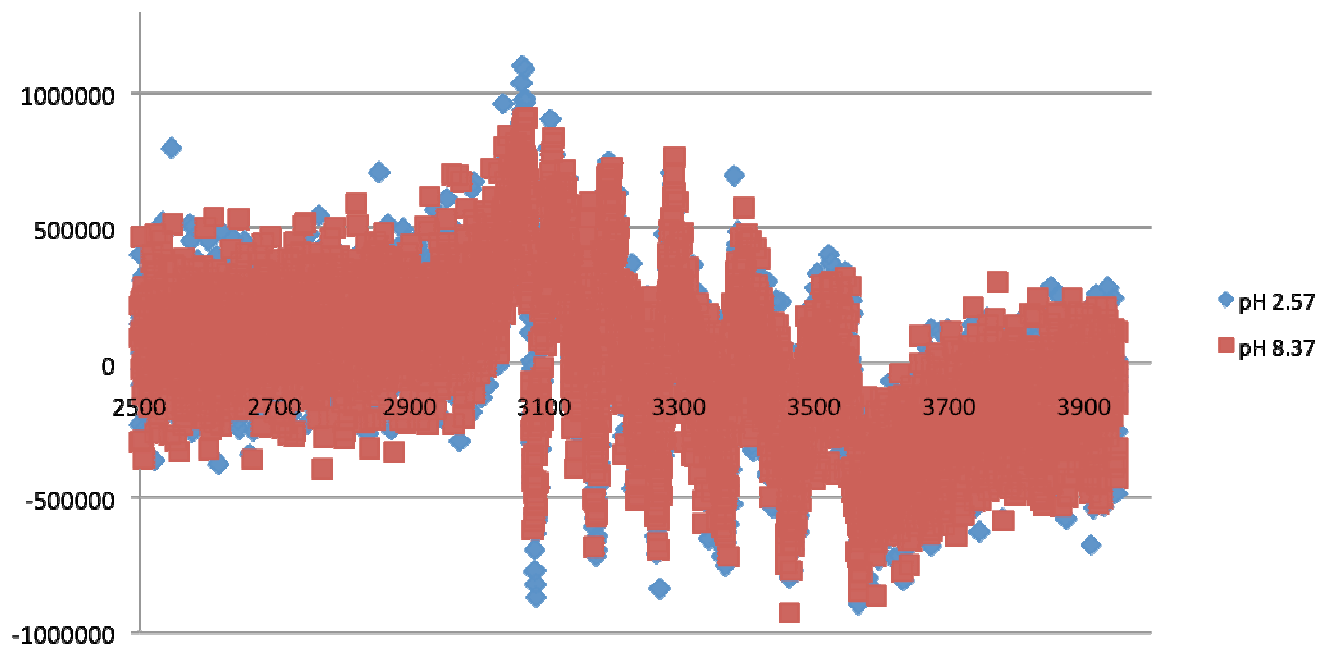
Protein: Aconitase

# Preliminary Work

- Varying pH levels of Mn (II) at different concentrations 5mM, 500uM, 50uM
- 20% glycerol sol.
- 4 different pH

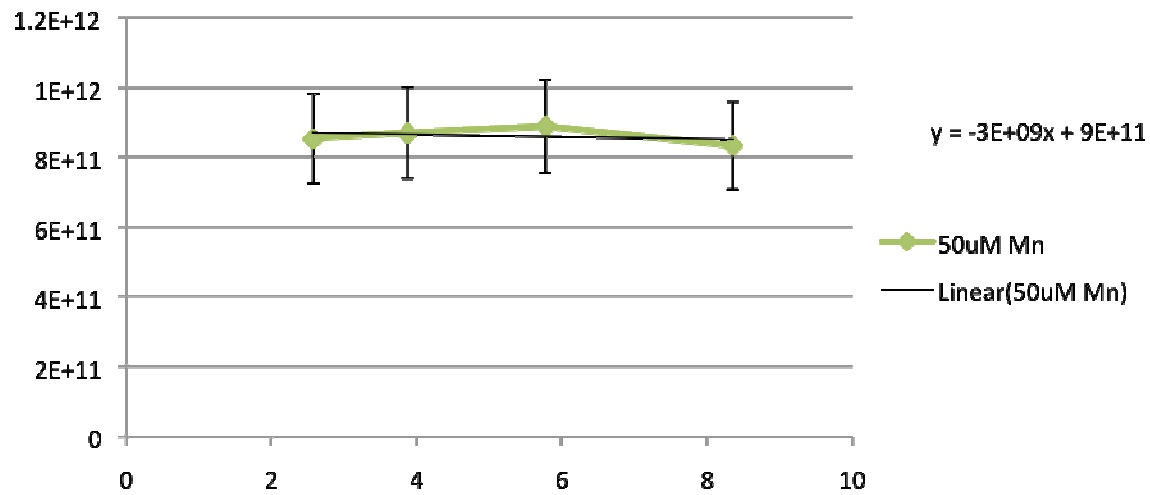
# EPR

- Electron paramagnetic resonance
- is a technique for studying chemical species that have one or more unpaired electrons. The basic physical concepts of EPR are analogous to those of nuclear magnetic resonance (NMR), but it is electron spins that are excited instead of spins of atomic nuclei.
- In the presence of an external magnetic field with strength  $B_0$ , the electron's magnetic moment aligns itself either parallel ( $m_s = -1/2$ ) or antiparallel ( $m_s = +1/2$ ) to the field, each alignment having a specific energy (Zeeman effect).



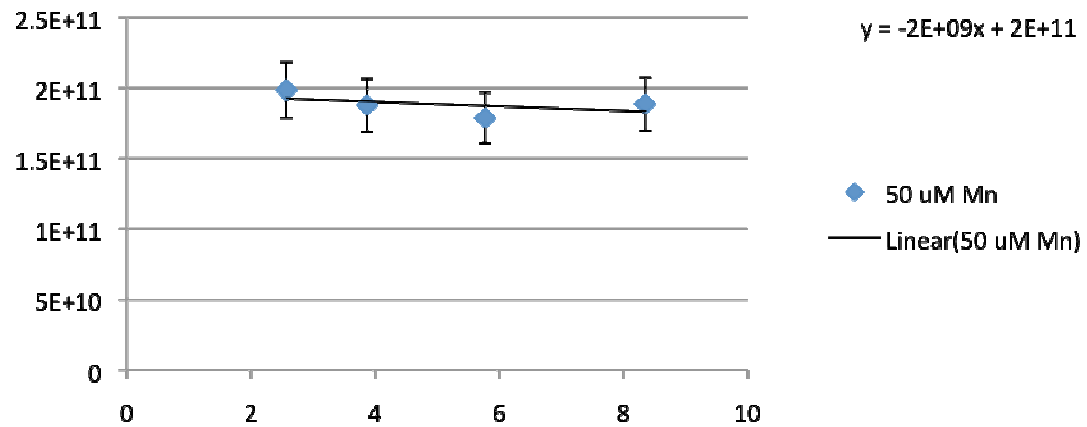


## Integration Method

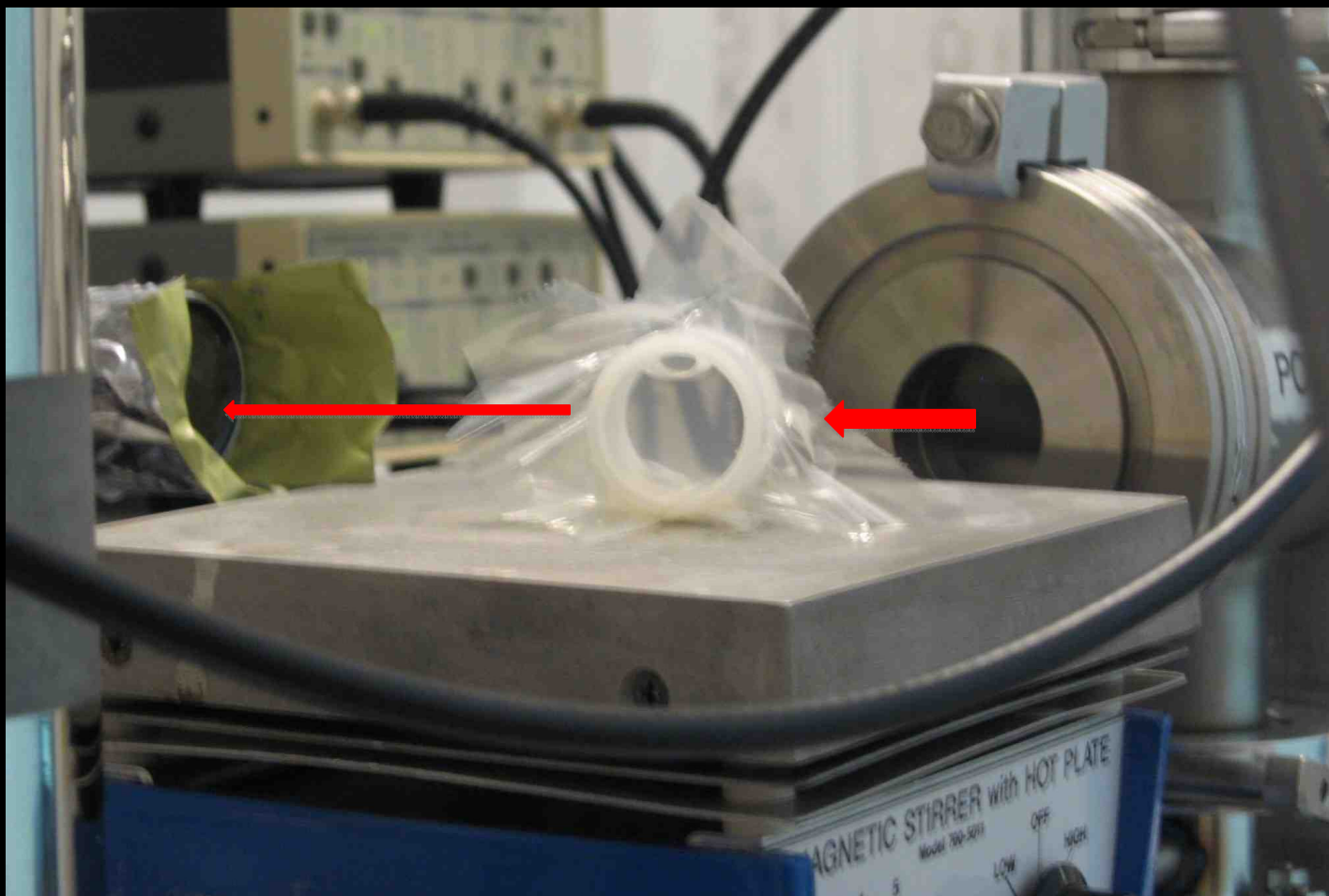


~3.57%

## 50uM Mn

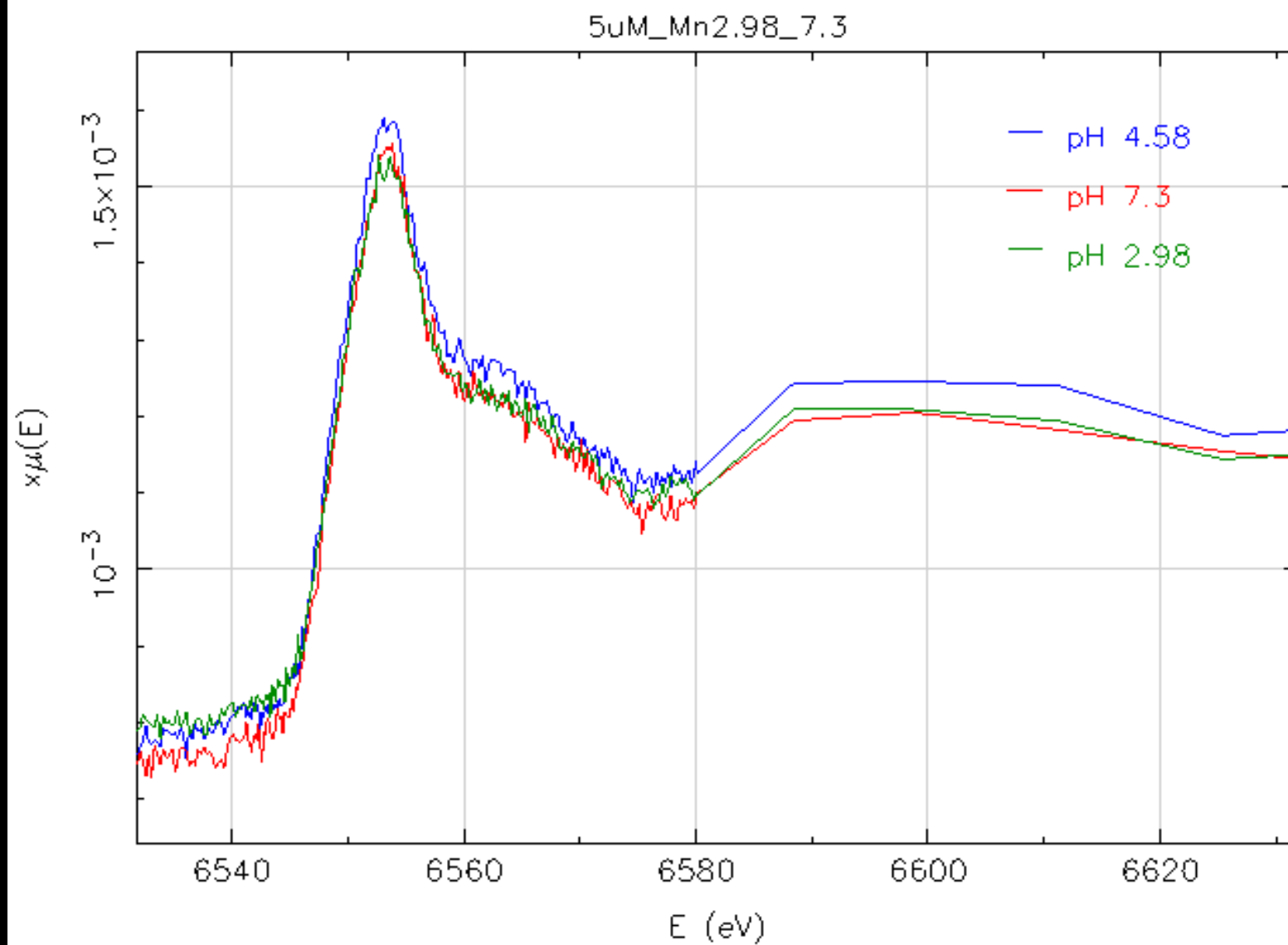


~6.14%



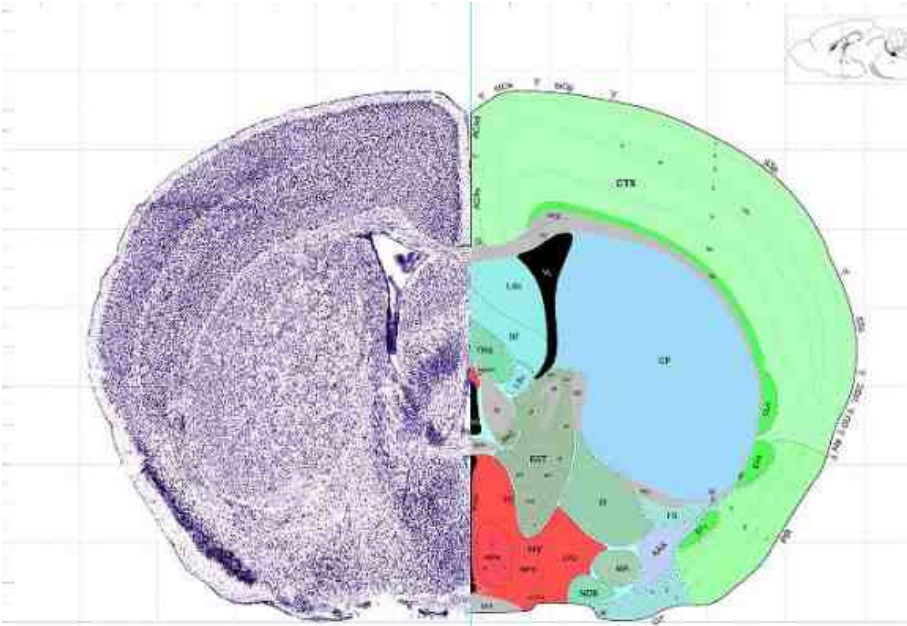
# APS Measurements





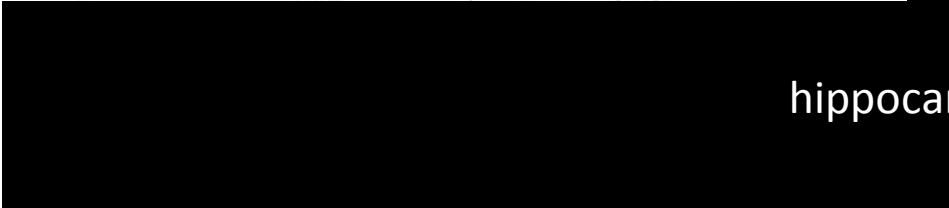
# Brain

- Synchrotron X-ray fluorescent (11.5 kev)
- metal distributions in rat brain
- Mn exposed vs. Control
- Globus pallidus, striatum of the basal ganglia, hippocampus



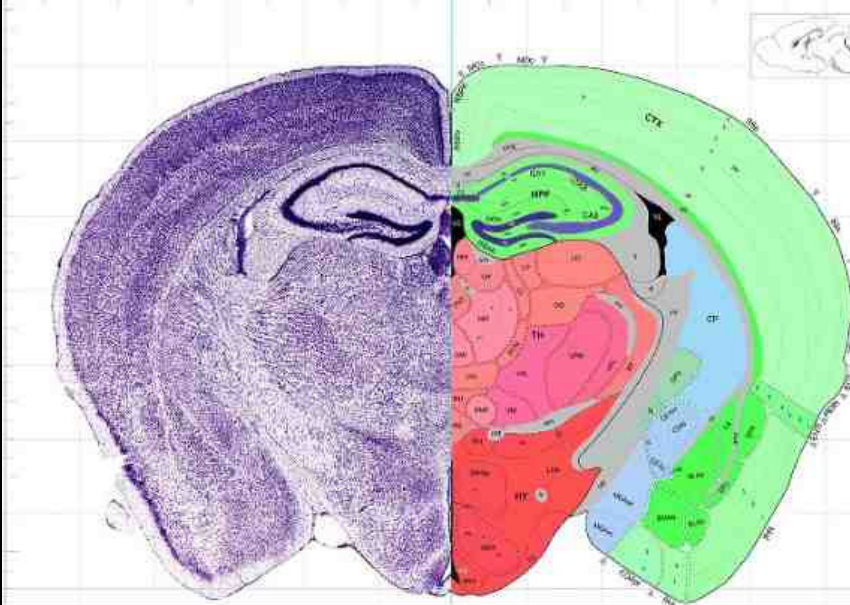
A coronal section of a mouse brain with various regions highlighted in color. The cerebral cortex is purple, the corpus callosum is black, and the lateral ventricle is light blue. The globus pallidus is highlighted in green. Other regions like the hippocampus and striatum are also visible in different colors.

Globus pallidus



A coronal section of a mouse brain with various regions highlighted in color. The cerebral cortex is purple, the corpus callosum is black, and the lateral ventricle is light blue. The hippocampus is highlighted in red. Other regions like the globus pallidus and striatum are also visible in different colors.

hippocampus

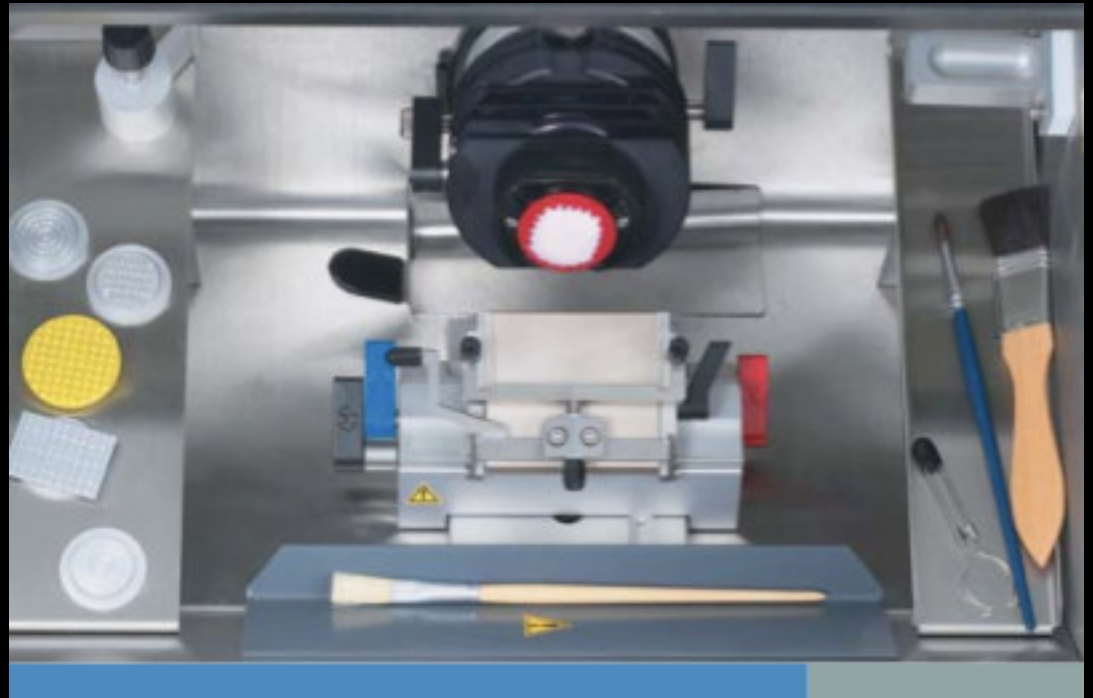


A coronal section of a mouse brain with various regions highlighted in color. The cerebral cortex is purple, the corpus callosum is black, and the lateral ventricle is light blue. The striatum of the basal ganglia is highlighted in red. Other regions like the globus pallidus and hippocampus are also visible in different colors.

striatum of the basal ganglia

<http://mouse.brain-map.org/launchviewer.do?plane=coronal&initialIndex=61>

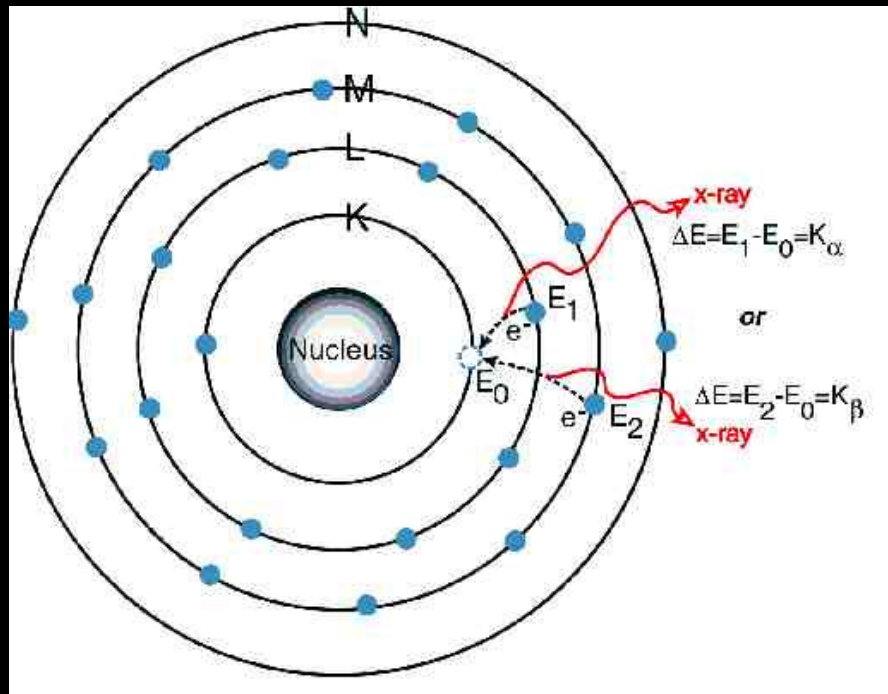




<http://www.thermo.com/com/cda/product/detail/1,1055,10121433,00.html>

# Beamline 10.3.2

## X-Ray Florescence



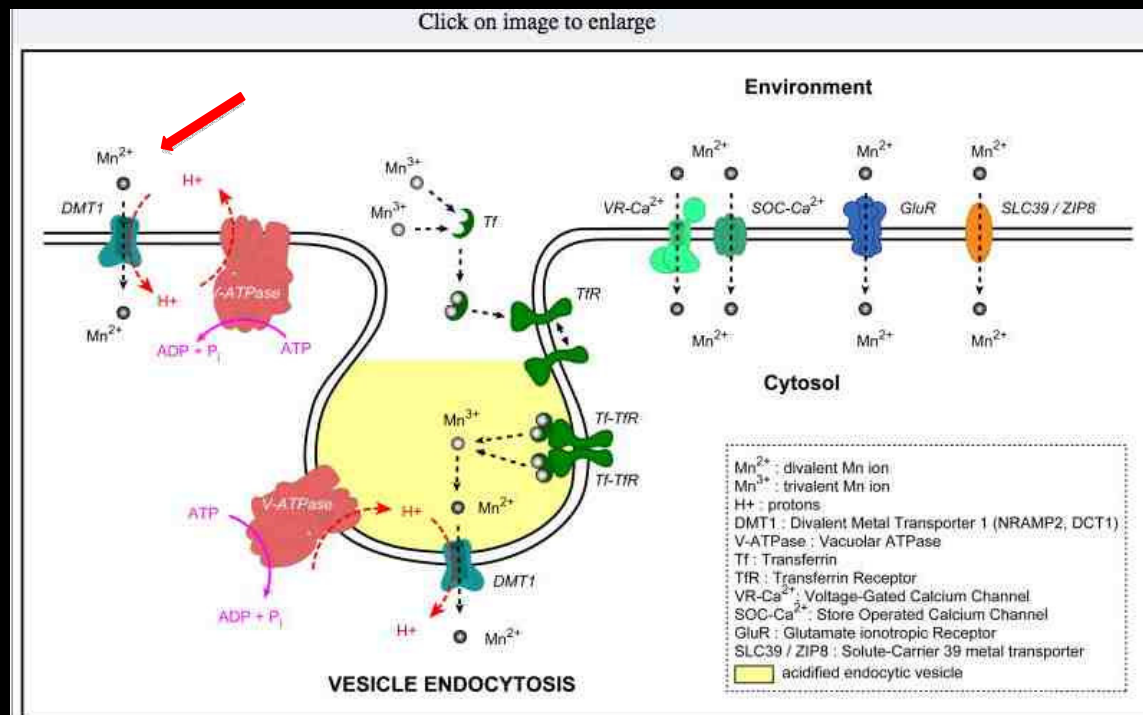
<http://www.fastcomtec.com/fwww/xray/xrf.html>



# Theories

1.  $\text{Mn}^{2+} \rightarrow \text{Mn}^{3+}$

2. Increased Mn = Increase of Fe and decrease of Fe storage protein (Blood Brain Barrier)



<http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2501114>

# Preliminary Results

plate 21 R4\_control 90\_decontam  
red-Fe 0-2000  
green Cu 0-1000  
blue compton 8000-30000

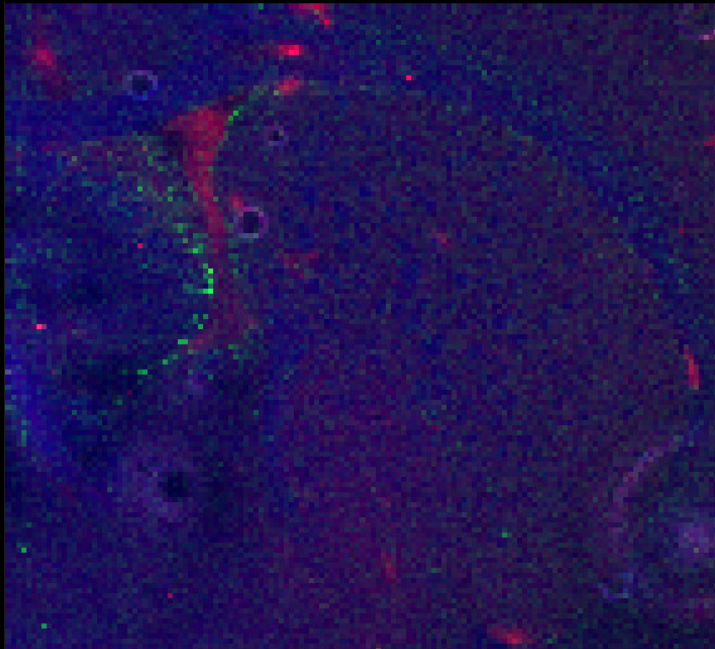


plate 21 R7\_Mn\_222\_decontam  
red-Fe 0-2000  
green Cu 0-1000  
blue compton 8000-30000

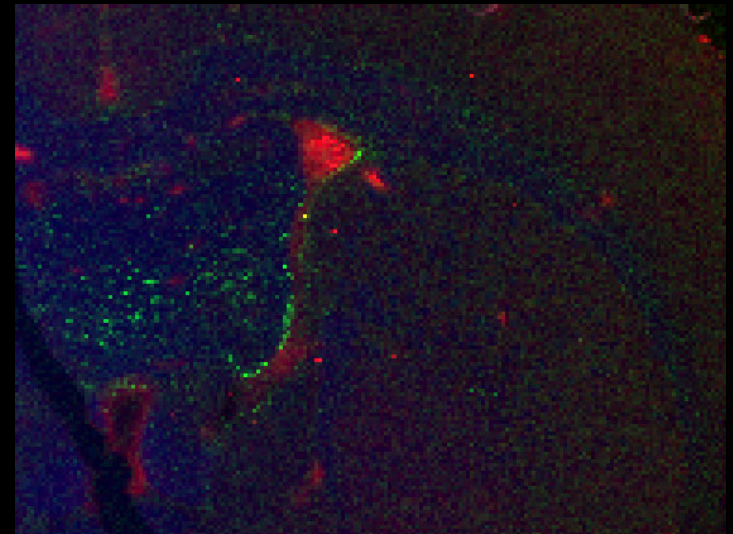


plate 27 R1\_control 17\_decontam  
red-Fe 0-2000  
green Cu 0-1000  
blue compton 8000-30000

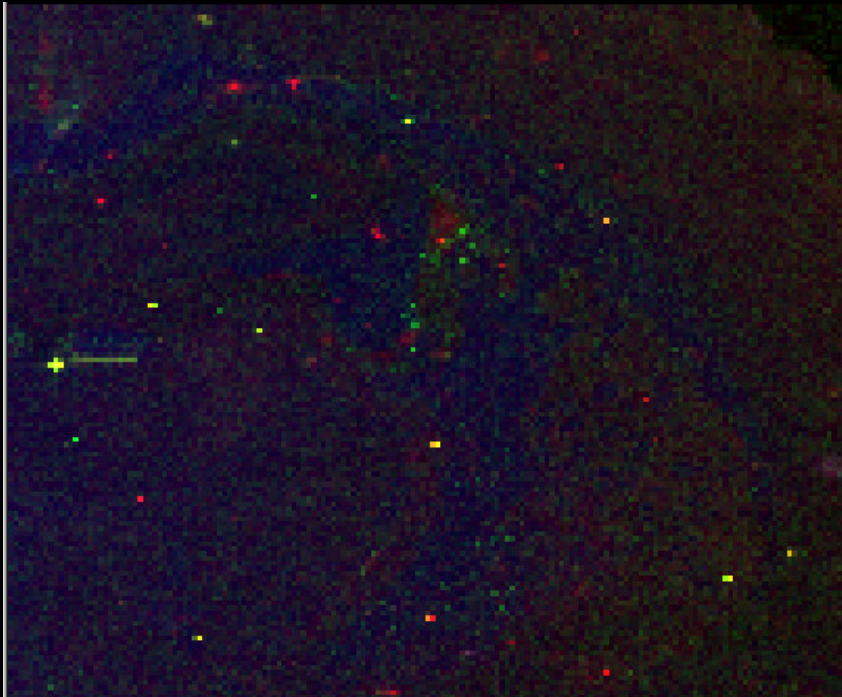
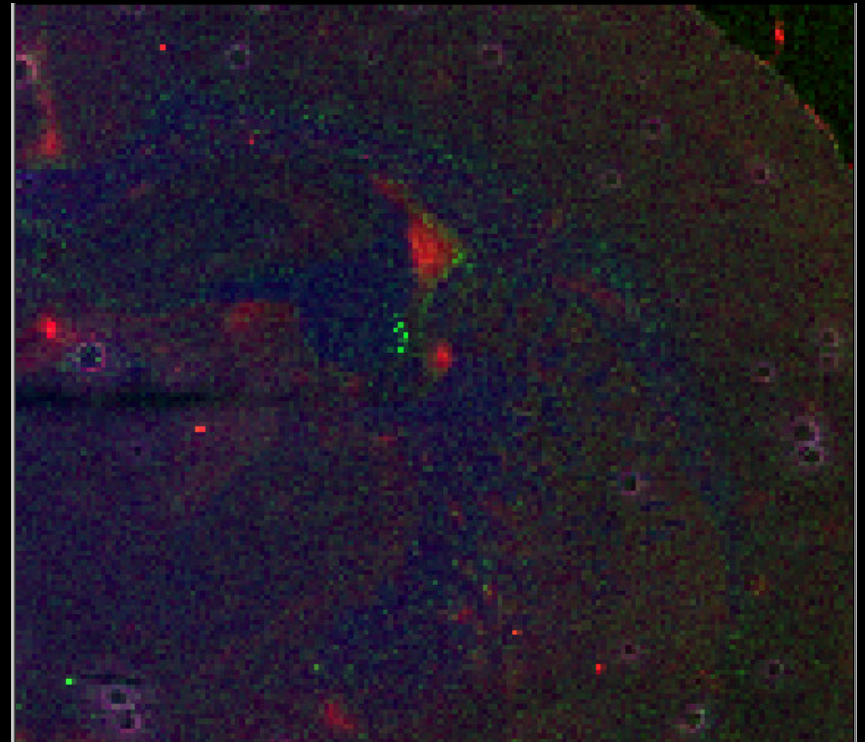
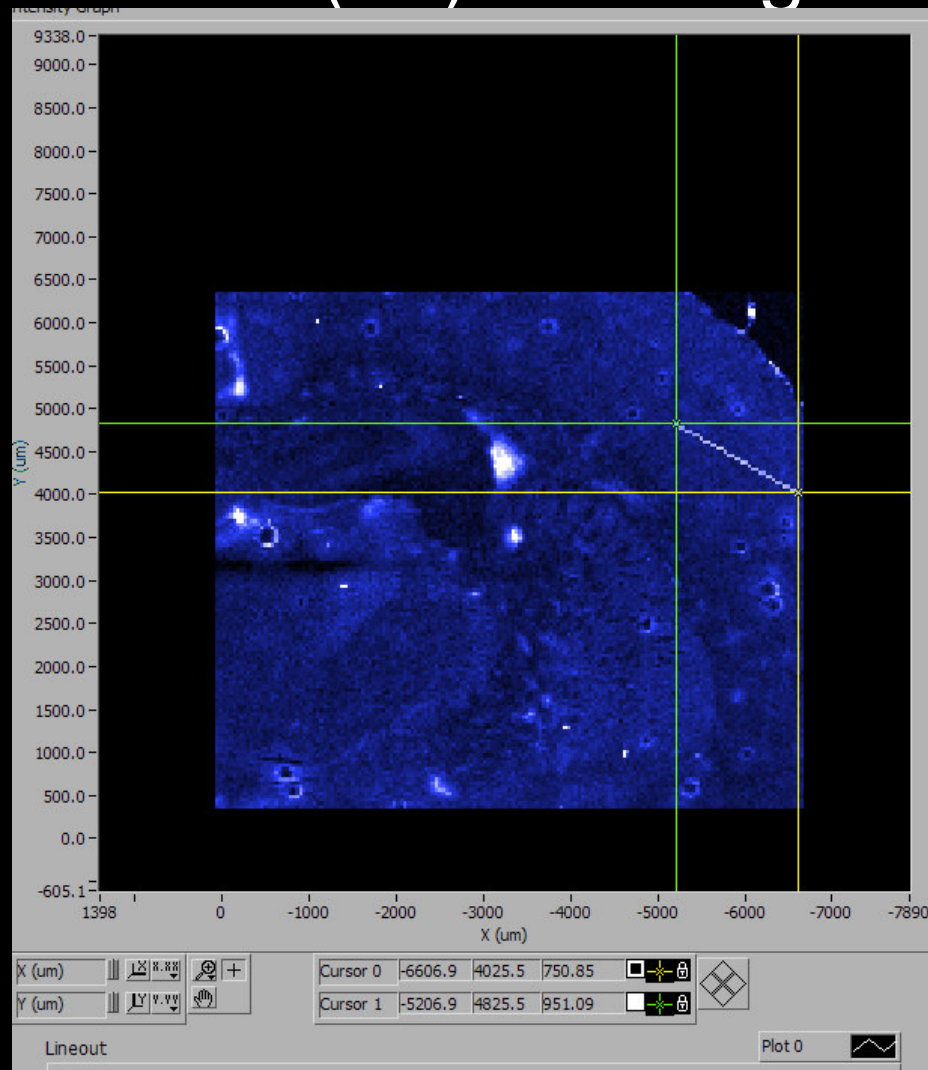


plate 27 R2\_Mn 47\_decontam  
red-Fe 0-2000  
green Cu 0-1000  
blue compton 8000-30000



# Mn (47) Fe Integration over cortex

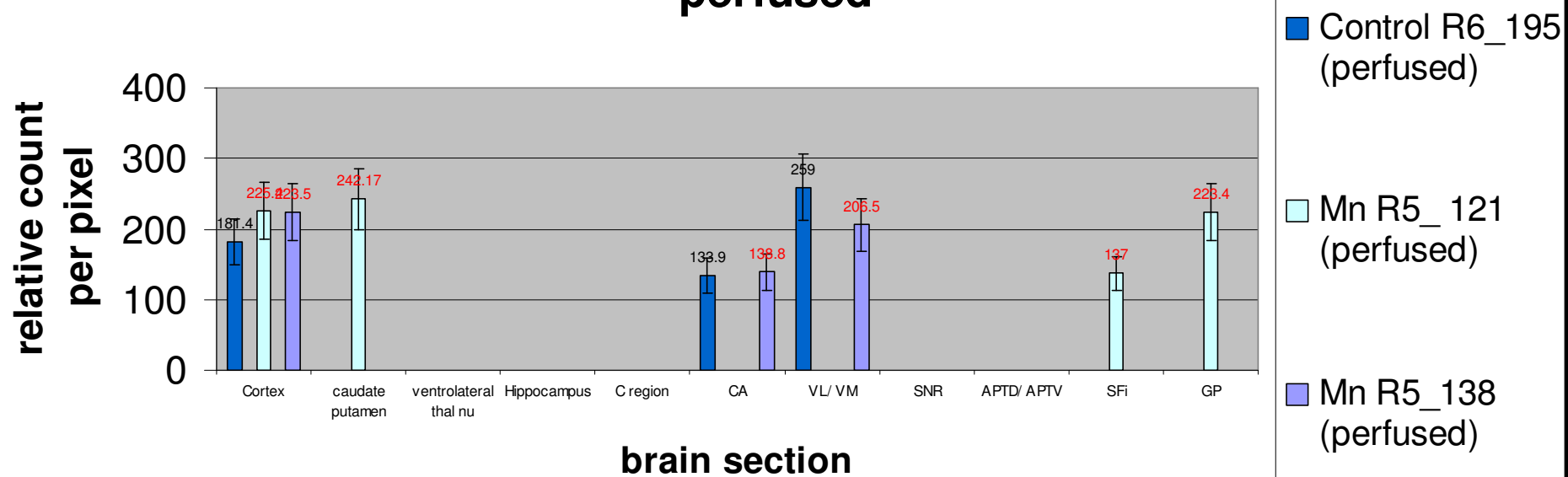


Pixel sum	Pixel min	Pixel max
199167.27	136.62	444.45
# pixels X		
21		
# pixels Y		
36		
Pixel average		
263.45		
Density (sum/area)		
0.16		

40 μm x 40 μm pixels



## Iron concentration in Mn treated and untreated rat brains . perfused



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& *argonne*

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Single Cell thickness analysis (10um)

Manganese Detection

# Conclusions

There is a slight decrease in  $\text{Mn}^{2+}$  concentrations as pH is increased that could be due to  $\text{Mn}^{2+}$  converting to  $\text{Mn}^{3+}$

Preliminary analysis suggests that there is an increase of Fe concentration when there is significant Mn exposure

# References

- 1. Minjares, R.J.; Walsh, M.; Blumberg, K. Methylcyclopentadienyl Manganese Tricarbonyl (MMT): A Science and Policy Review. *The International Council of Clean Transportation* **2009**, 1-36.
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- 2. Comments on the Gasoline Additive MMT (methylcyclopentadienyl manganese tricarbonyl). *Fuels and Fuel Additives*. U.S. Environmental Protection Agency.  
[http://www.epa.gov/oms/regs/fuels/additive/mmt\\_cmts.htm](http://www.epa.gov/oms/regs/fuels/additive/mmt_cmts.htm)
- Catherine Au, A. Benedetto, M Aschner. Manganese transport in eukaryotes: the Role of DMT1. *NeuroToxicology*. 2008. 569-576
- 3. Gulson. B.; Mizon, K.; Korsch, M.; Louie, H.; Wu, M.; Stauber, J.; Davis, J.M.; Taylor, A. *Environmental Research* **2006**, *100*, 100-114.
- Preliminary analysis (slides 18-21) were done by researchers at Berkley, Y. Puskar, G. Robison