



ADDRESSING NEURODEGENERATIVE DISEASE: NANOZYMES SHOWCASING EXCEPTIONAL ANTIOXIDANT PERFORMANCE

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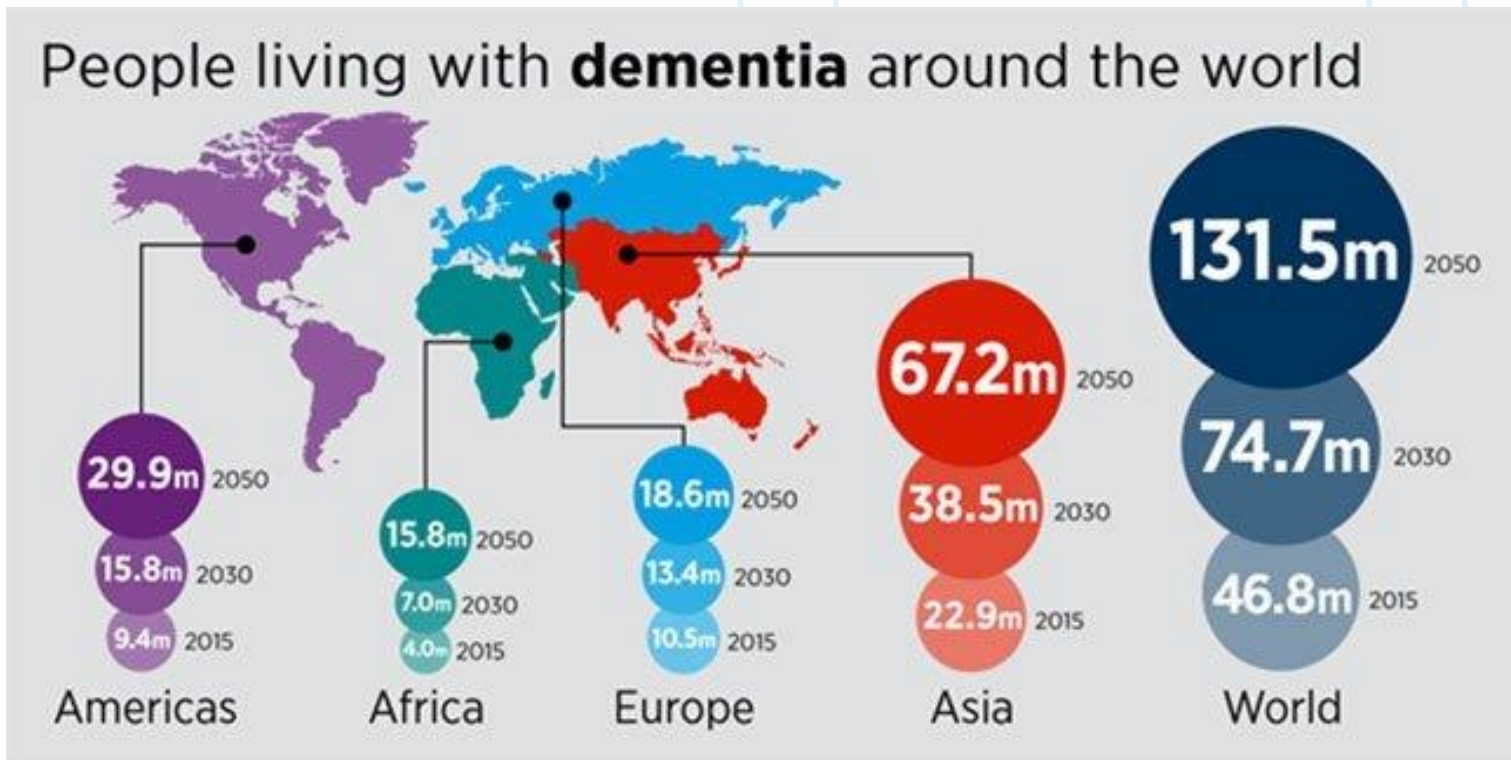
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Intro

AD in numbers



\$368 billion



\$742 billion



\$818 billion

World Alzheimer Report 2015. The Global Impact of Dementia. An analysis of prevalence, incidence, cost and trends. *Alzheimer's Disease International, 2015.*



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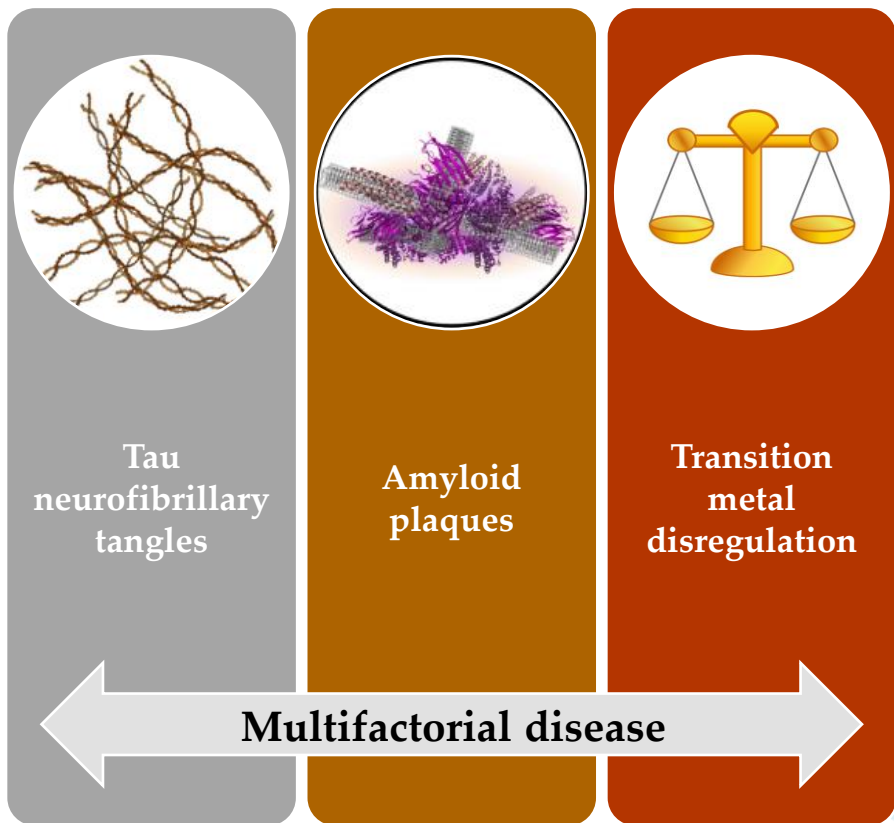
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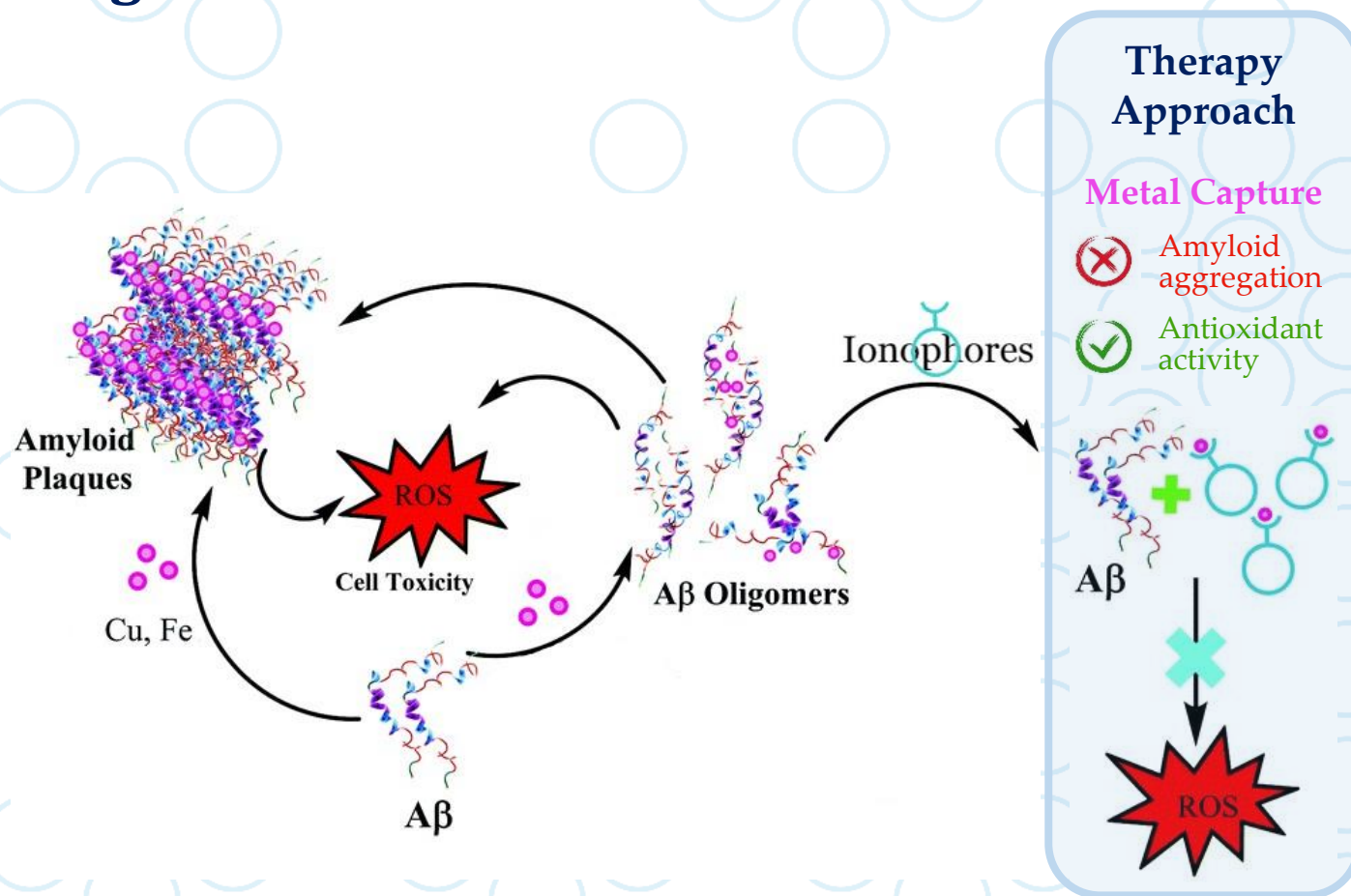
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Intro

Neuropathological hallmarks of AD



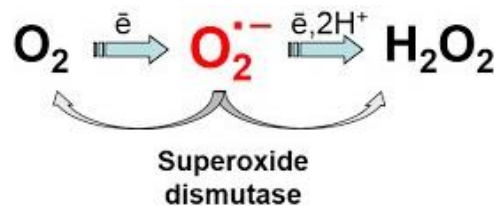
Nat. Rev. Neurol. 2019, 15, 73–88.



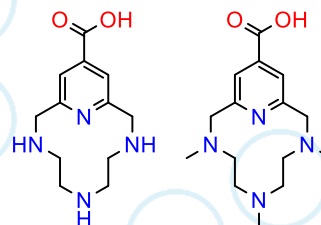
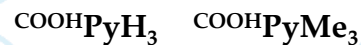
(Adapted) *Metallomics*, 2019, 11, 64–84.

Project

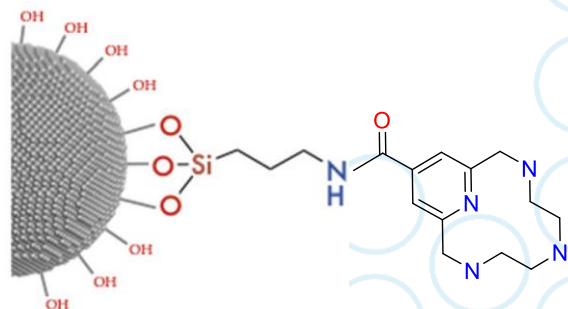
Innovation



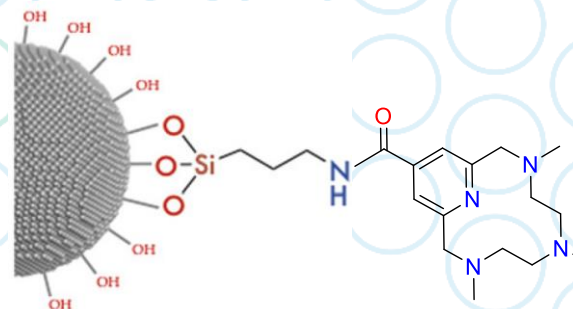
Antioxidant scaffold
Chem. Commun.
2013, 49, 2712.



Introduction of carboxyl group for NP functionalisation
Chem. Commun., 2022, 58, 5021–5024.



BNP-COOHPyH₃



BNP-COOHPyMe₃



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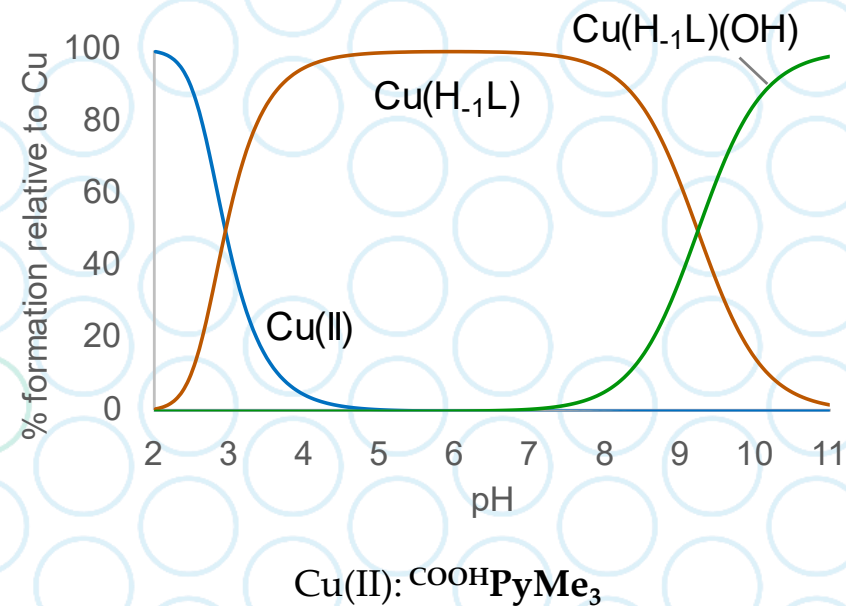
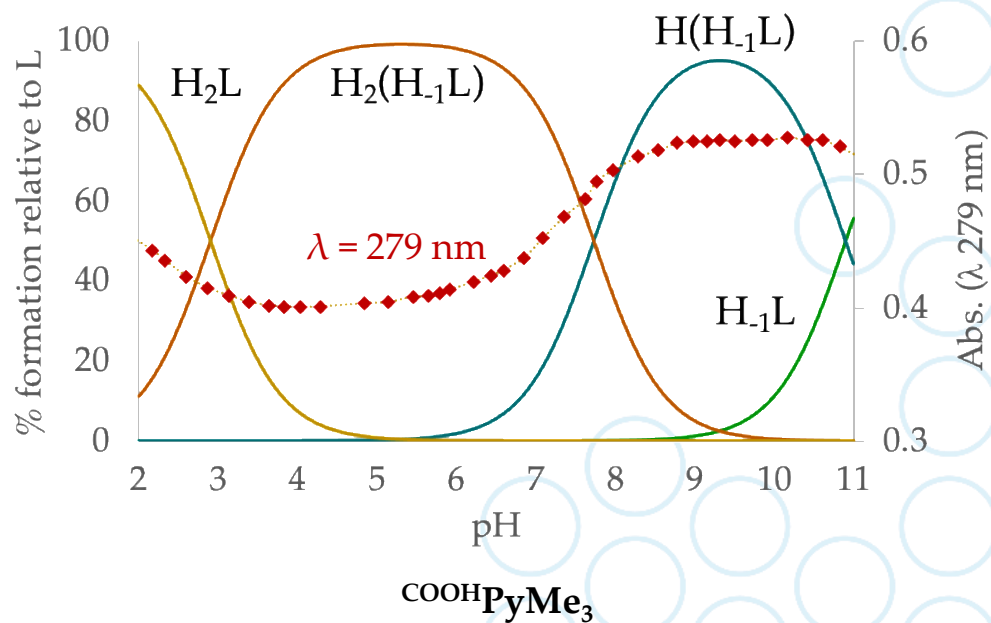
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Results

Equilibrium studies



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Results

System	IC ₅₀ (μM)	k _{cat} (10 ⁶ M ⁻¹ s ⁻¹)
Cu-COOHpyH ₃	0.36(1)	9.7
Cu-COOHpyMe ₃	0.29(3)	12.3
Cu-HpyH ₃	2.1(4)	1.7
Cu-HpyMe ₃	2.9(6)	1.2
Cu-BNP-COOHpyH ₃	0.071(6)	51.1
Cu-BNP-COOHpyMe ₃	0.155(6)	22.6
Cu(ClO ₄) ₂	1.1(1)	2.7
CuZn-SOD	0.010(2)	430

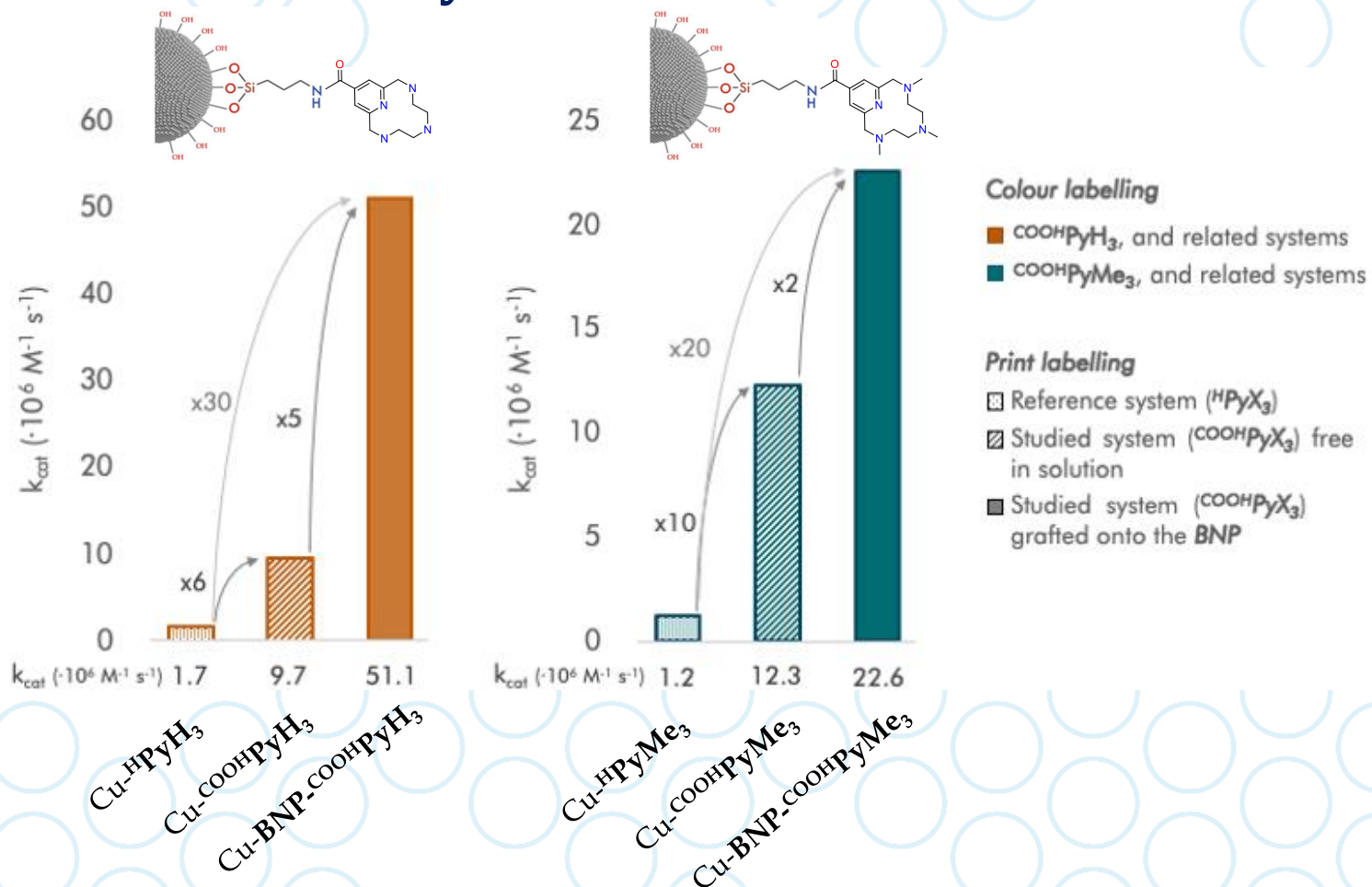
Chem. Commun., 2022, **58**, 5021–5024.

Inorg. Chem., 2018, **57**, 10961–10973.

McCord-Fridovich method

- L. K. MacDonald-Wicks, L. G. Wood, M. L. Garg, *J. Sci. Food Agric.* 2006, **86**, 2046–2056.
- C. Beauchamp, I. Fridovich, *Anal. Biochem.* 1971, **44**, 276–287.
- J. M. McCord, M. Crapo, I. Fridovich, *Superoxide and Superoxide Dismutases*, Academic Press, New York, 1977.
- L.W. Oberley, D. R. Spitz, *Method. Enzymol.* 1984, **105**, 457–464.

SOD Activity



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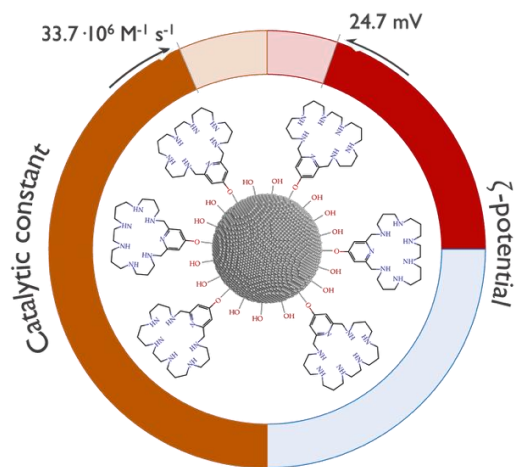
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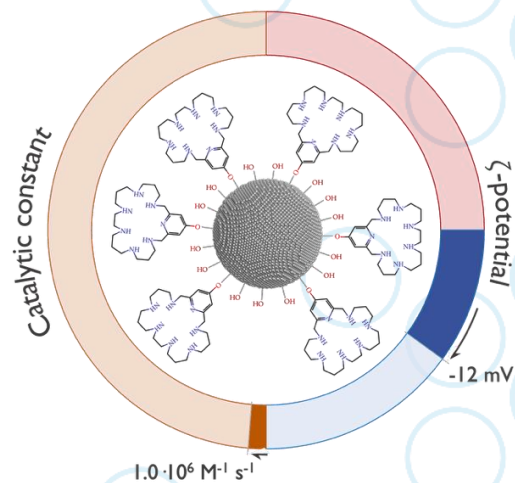
Results

Why BNPs increase activity?

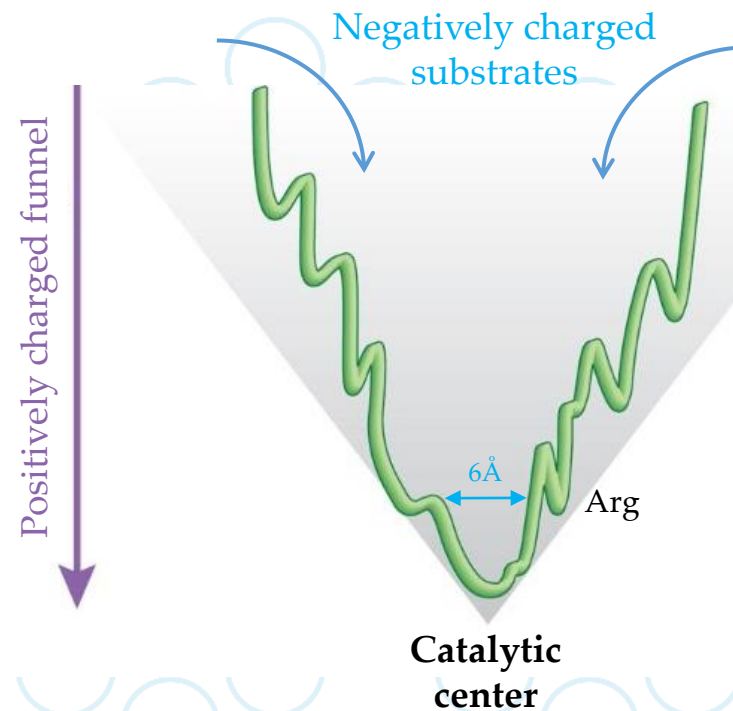


More **positive** surface charge,
higher SOD activity

RSC Adv. 2019, 9, 41549.



More **negative** surface charge,
lower SOD activity



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Conclusion

Take-home message

- ❑ Neurodegenerative disease is becoming a serious concern in an increasingly aging society
- ❑ Coordinative efforts are needed from multiple Life Sciences to address it
- ❑ Medicinal Chemistry faces major challenges due to the complexity of this disease
- ❑ Antioxidant complexes can help rebalancing transition metal regulation and eliminating beta-amyloid plaques to reduce the symptoms
- ❑ BNP not only increase their activity but also open a huge range of new vehiculation possibilities



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A Supramolecular Chemistry Group



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