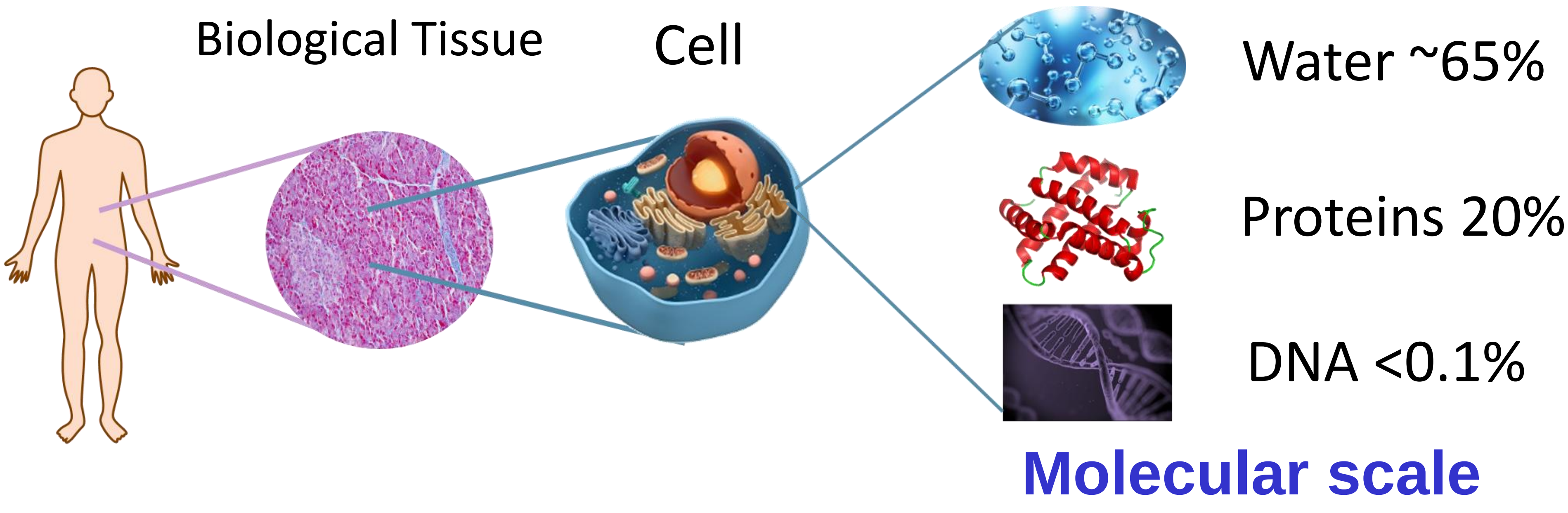
Radiolyse de l'eau et de biomolécules à haut débit de dose

Q. Raffy[1]

A. Arnone[1], S. Chefson[1], A. Danvin[1], C. Galindo[1], P. Peaupardin[1], M. Pelliciolli[1], T. Kusumoto[2], S. Kodaira[2], A. Nasreddine[3], F. Kuntz[3], N. Arbor[1], R. Barillon[1]

[1] IPHC, Strasbourg, France
[2] NIRS-QST, Chiba, Japan
[3] Aerial-CRT, Illkirch, France

Context: Radiotherapy



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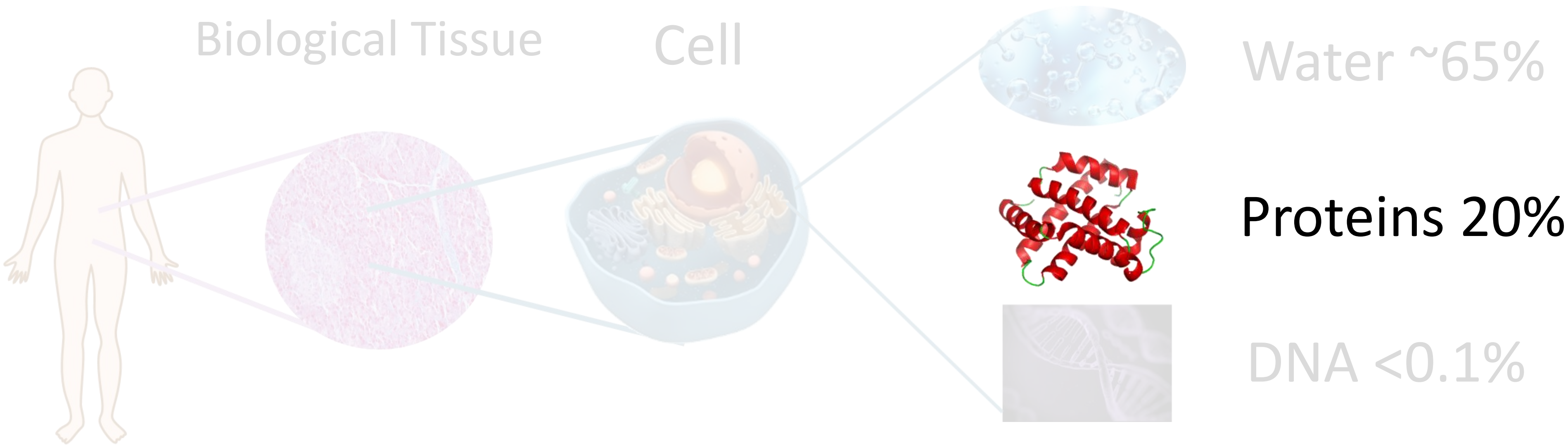
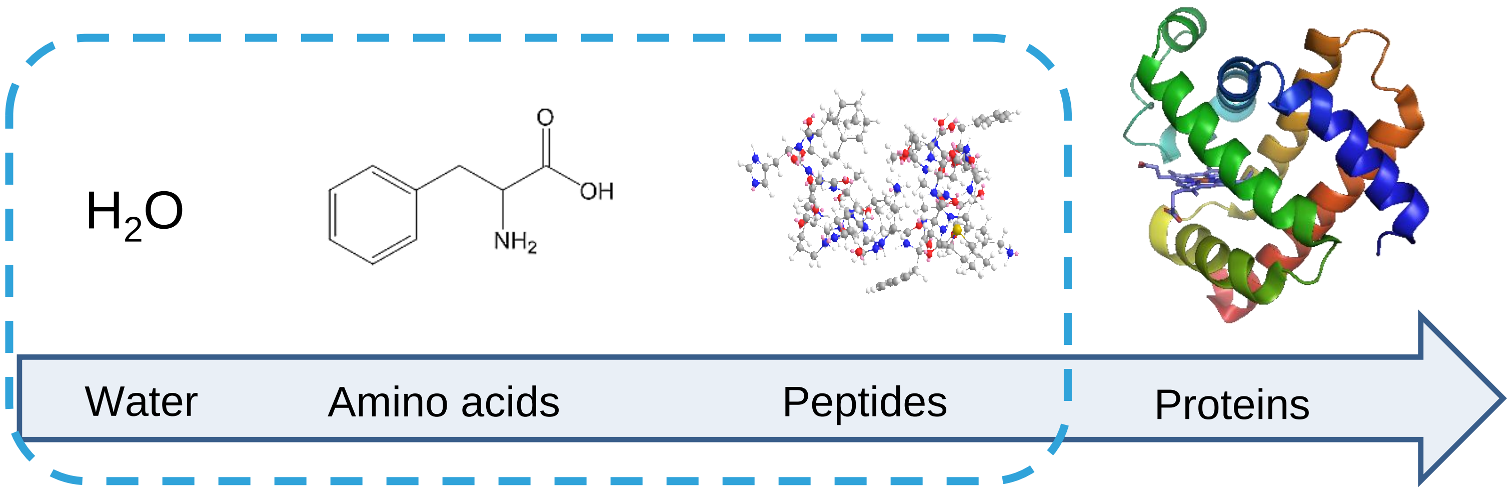


Molecular scale

Systematic experimental study



- **LET effect** (ions - RX / e^-)
  Fragmentation CLINM
  Hadrontherapy
- **Dose-rate effect**
  FLASH therapy

- Geant4-DNA Simulations
Coll. DeSIs, IPHC

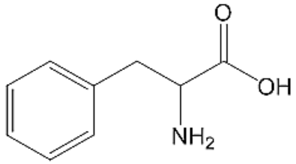
Context: Radiotherapy

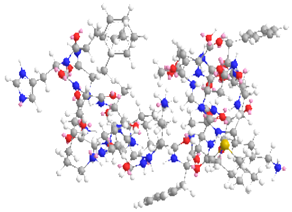
QST	CNAO	CYRCÉ	ICUBE	GANIL	ICANS	Aerial
H, He, C 6 – 400 MeV/u	C 120-400 MeV/u	H 24 MeV	H 2 MeV	^{8}Li, C 64 MeV/u	RX 6 MV	RX / e^{-} 1 et 10 MeV

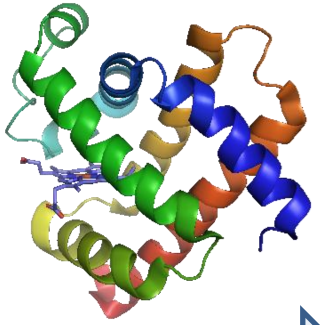
ARRONAX: H, 68 MeV

Systematic experimental study

H_2O







Water → Amino acids → Peptides → Proteins

- **LET effect** (ions - RX / e^{-})
  Fragmentation CLINM
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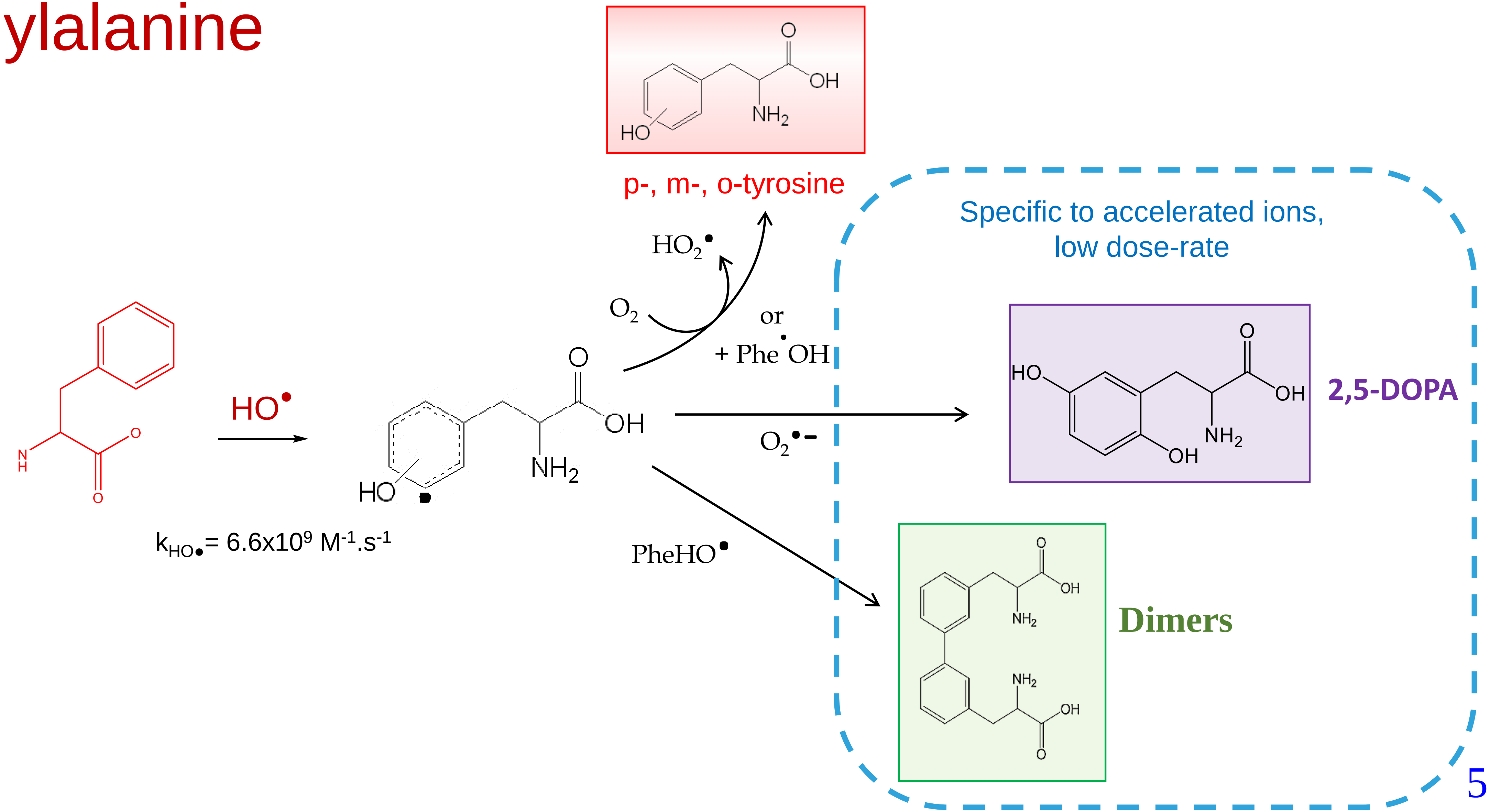
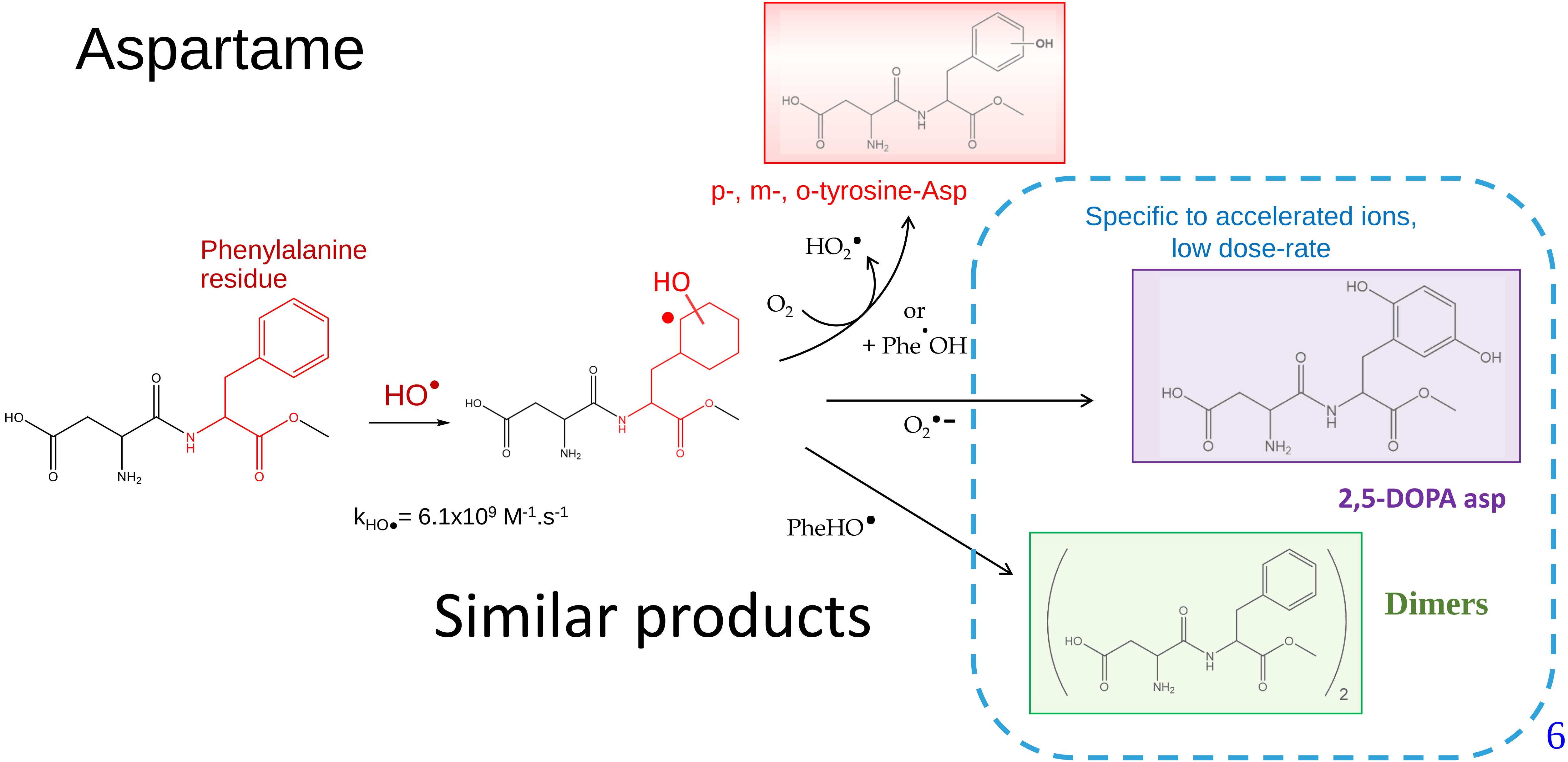
Radiolysis of Phenylalanine and Aspartame

Phenylalanine



Radiolysis of Phenylalanine and Aspartame

Aspartame



Similar products

Water radiolysis: $HO^\bullet$ and e^-_{aq}

Quantification by scavenging ➔ Molecular probes. Indirect method

Radiolytic yield: $G = 100 \times \frac{N}{E}$ species/100eV

$$t_S = \frac{1}{k \times C}$$

Scavenging time:
depends on probes concentration

Hydroxyl radical $HO^\bullet$

Hydrated electron e^-_{aq}

Precek, M. *et al*, *Radiat. Res.*, **2022**, *197*, 131-148

Yamashita S. et al, *Radiation Physics and Chemistry* **2008**, *77* (4), 439–446.

LaVerne, J. A. and Yoshida, H. *J. Phys. Chem.*, **1993**, 10720

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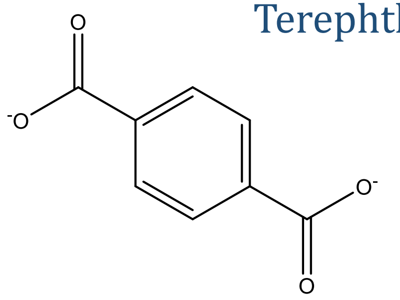
Hydroxyl radical $HO^{\bullet}$

Organic probe

Terephthalate (TA)



KBr/Formate

$G(HO^{\bullet}) = G(H_2O_2)_{Formate} - G(H_2O_2)_{KBr}$

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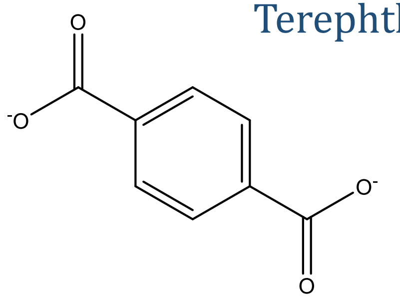

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Hydrated electron e^-_{aq}

Organic probe: Glycil-glycine

$$^{+}NH_3CH_2CONHCH_2CO_2^- + e^-_{aq} + H_2O \rightarrow {}^{\cdot}CH_2CONHCH_2CO_2^- + NH_4^+ + OH^-$$

Inorganic probe: $NaNO_3$ / Na_2HPO_3

Formation of NO_2^-, quantification by colorimetry

Under Argon

$e^-_{aq} + O_2 \cancel{\rightarrow} O_2^{\bullet -}$

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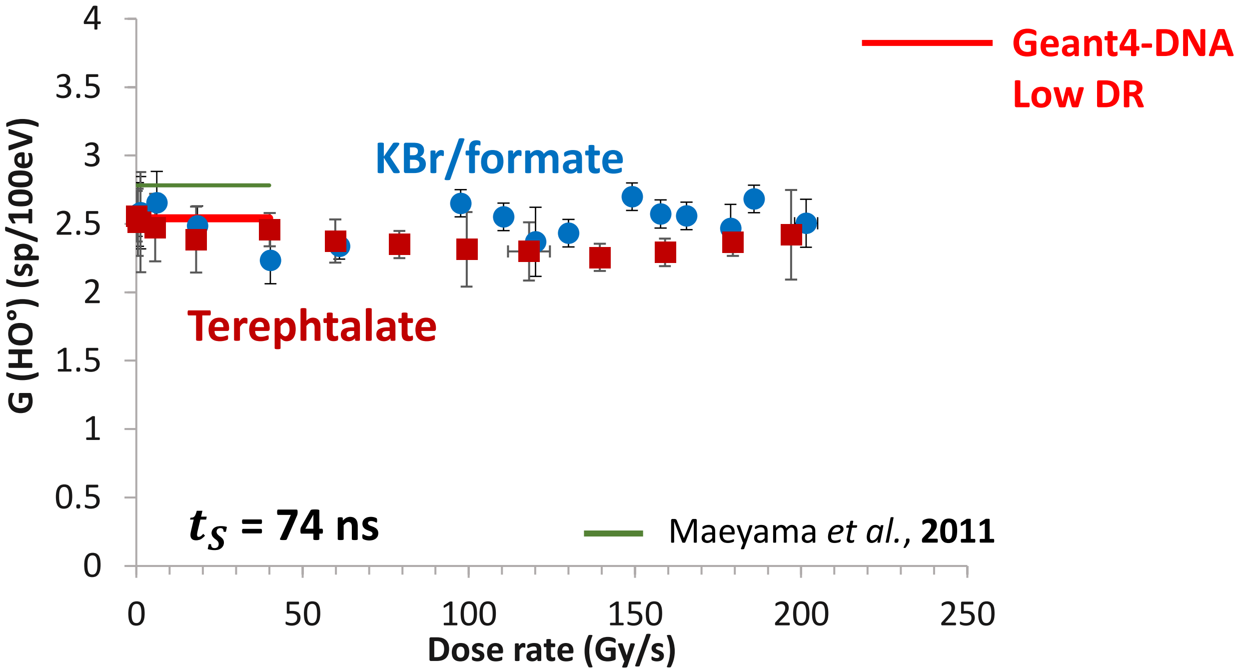
24 MeV protons - Water radiolysis ($HO^{\bullet}$ and e^{-}_{aq})

Differential yields: LET = 3.01 ± 0.75 eV/nm

Hydroxyl radical $HO^{\bullet}$



Very similar yields between probes
Constant with dose-rate

No dose-rate effect on probe mechanisms

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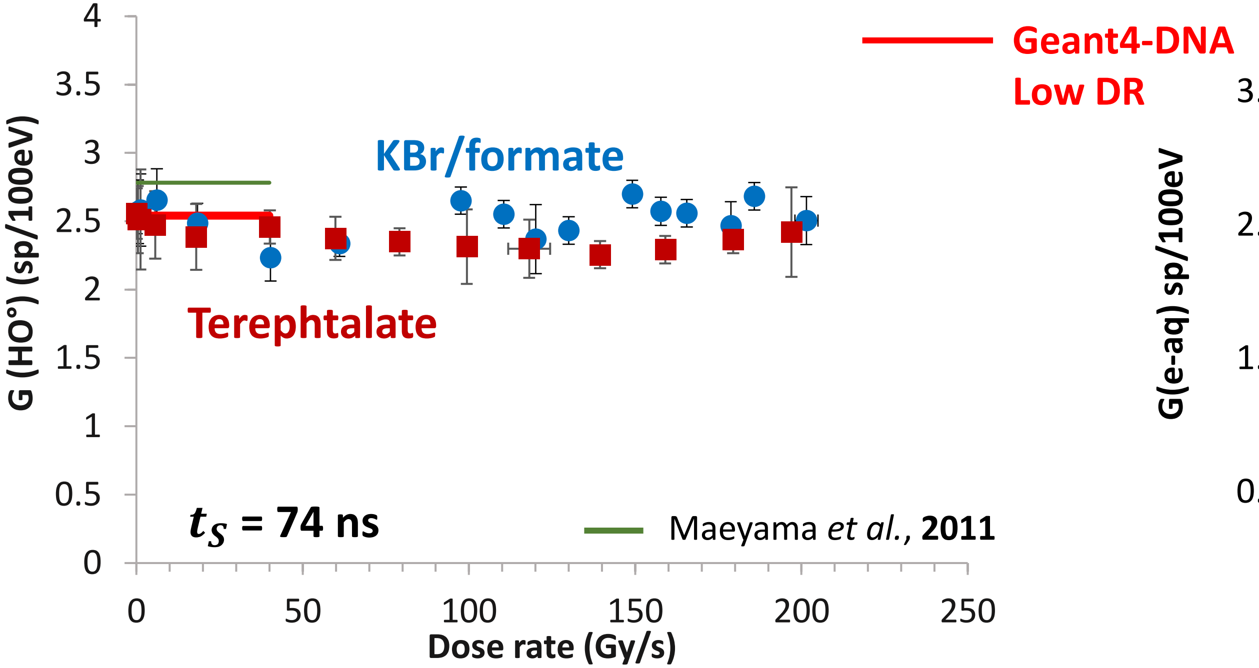

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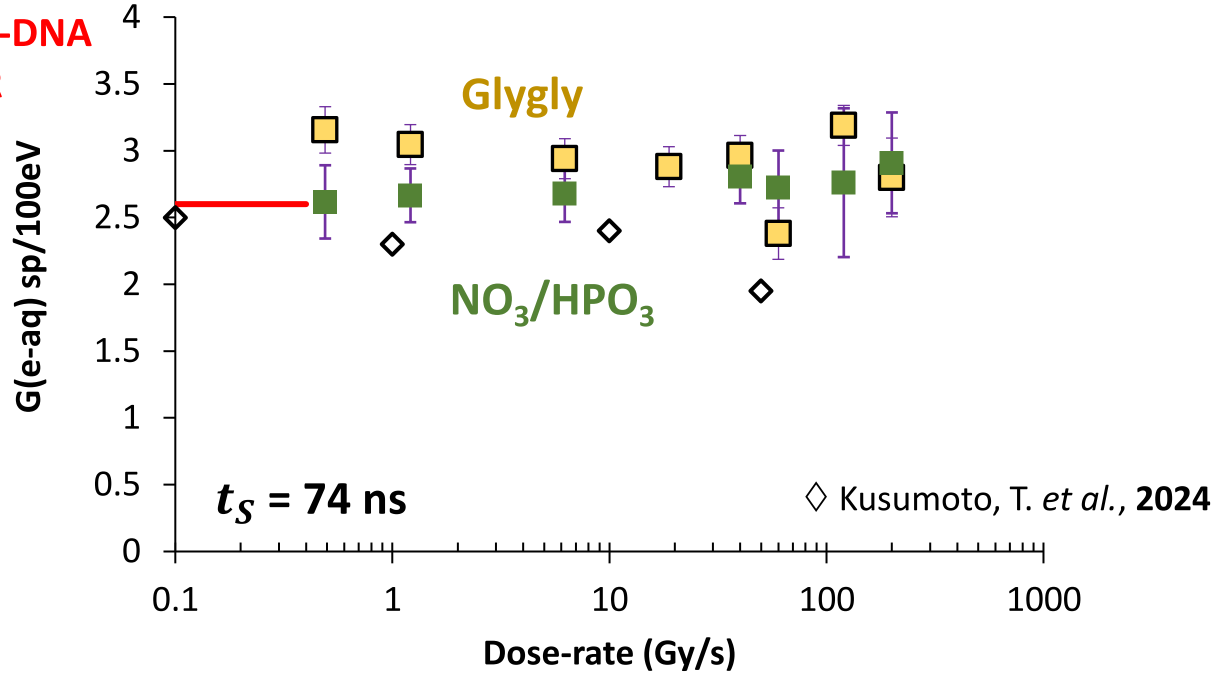

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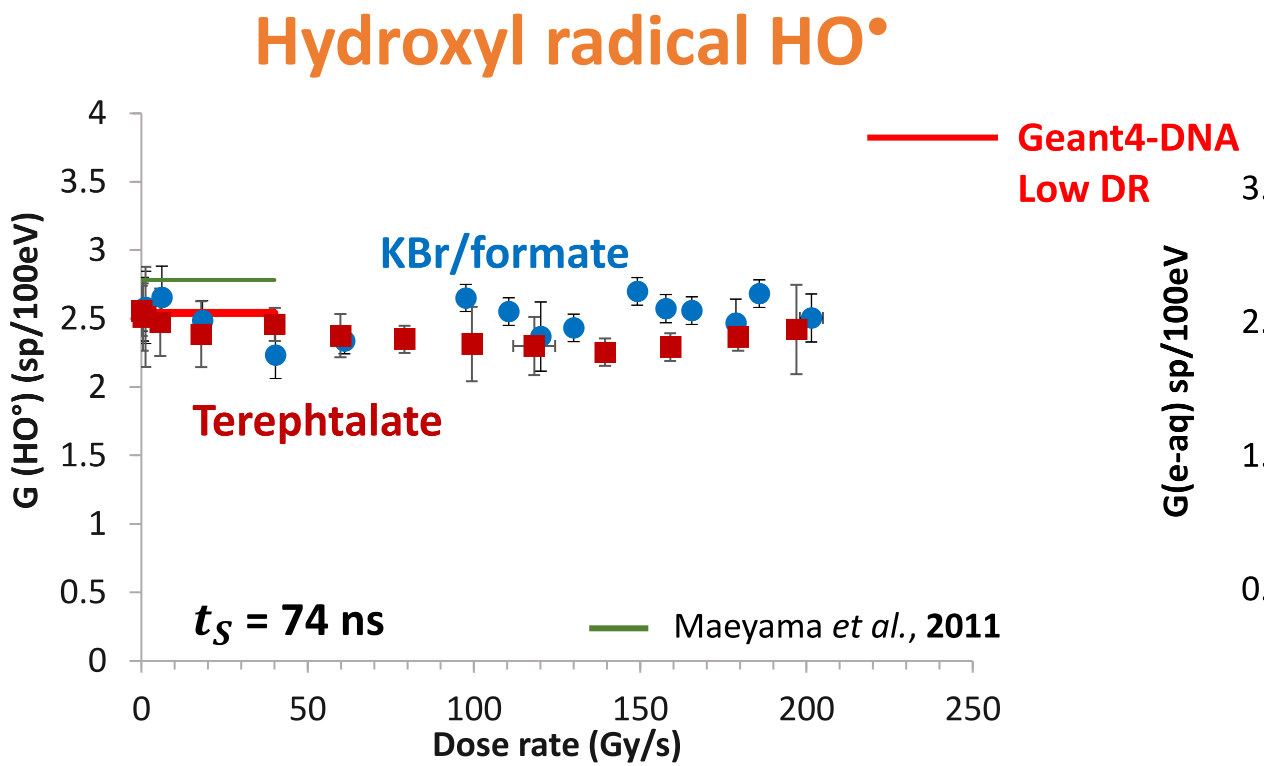
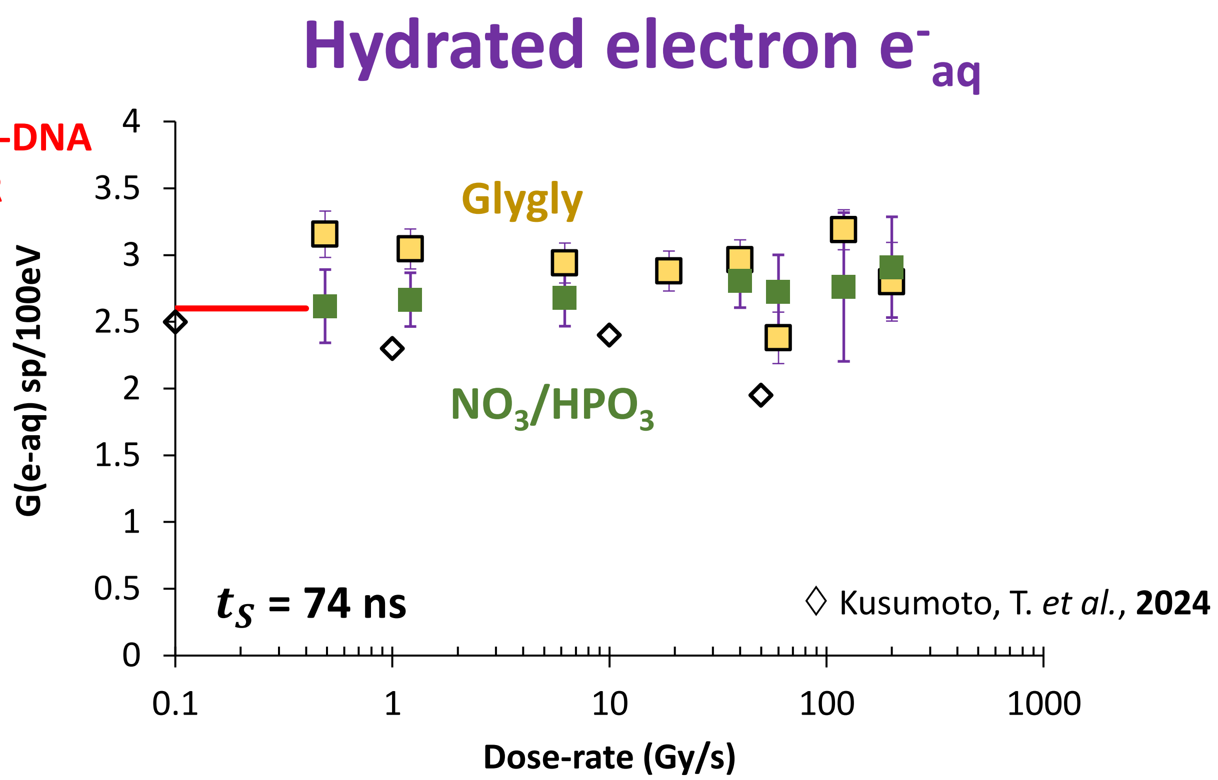




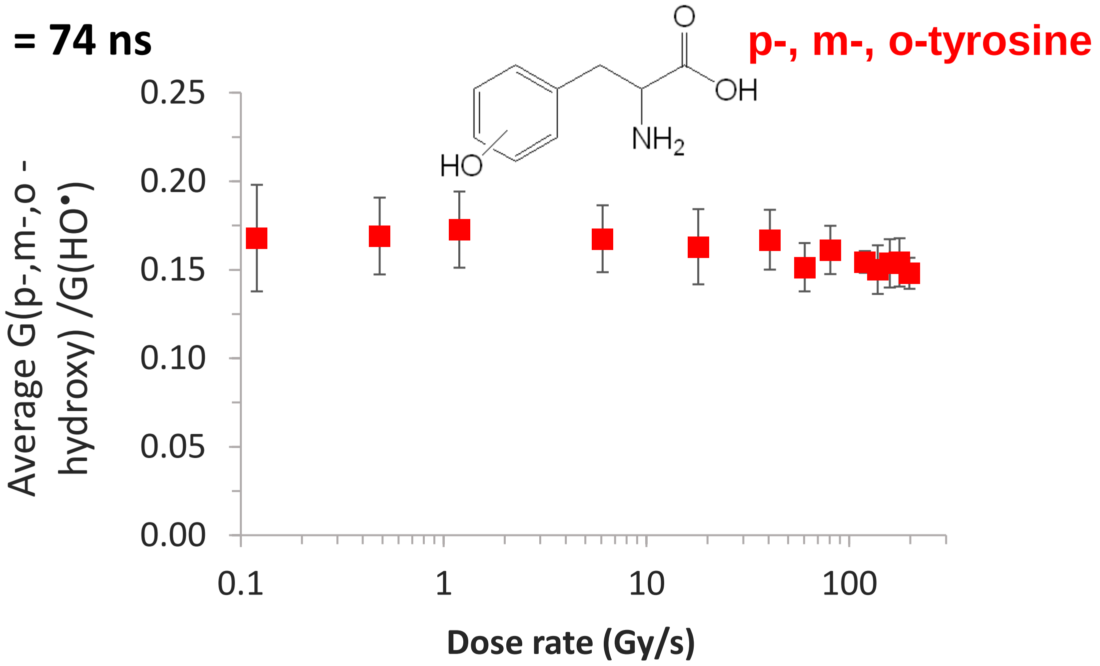
Very similar yields between probes
Constant with dose-rate

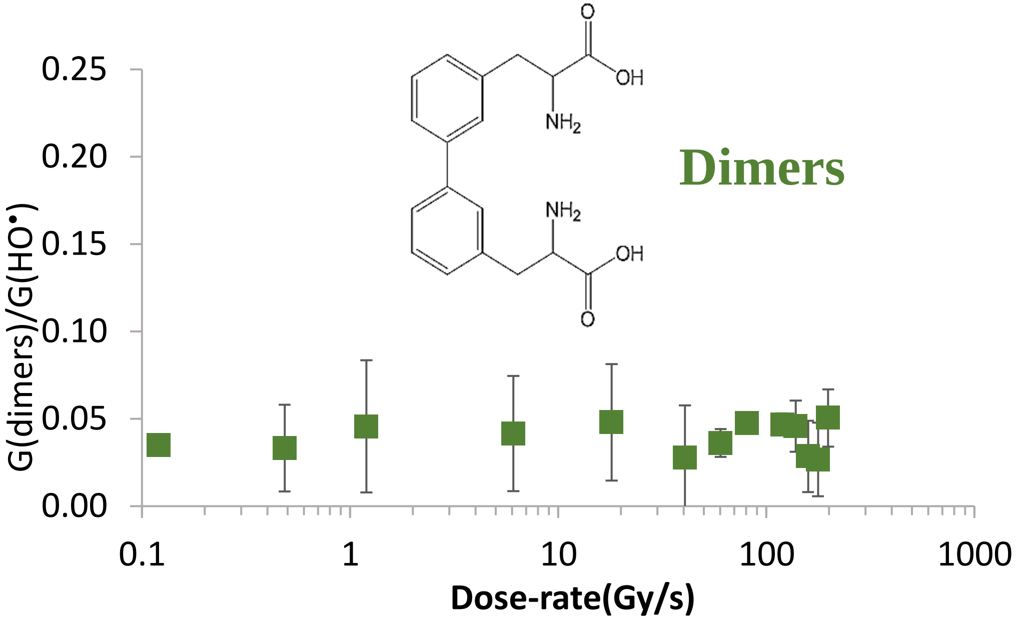
No dose-rate effect on probe mechanisms

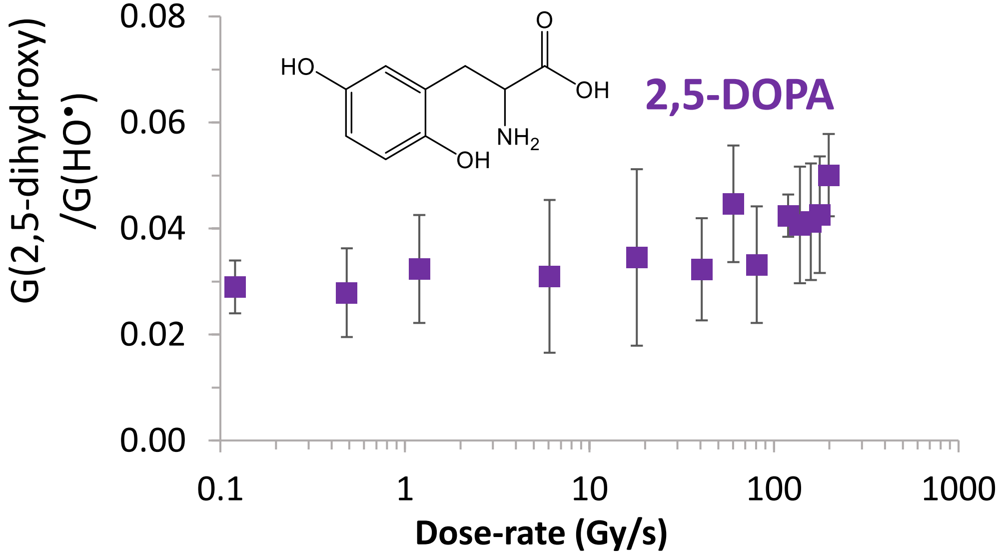
No dose-rate effect on $G(HO^{\bullet})$ and $G(e^{-}_{aq})$

24 MeV protons - Biomolecule radiolysis

t_S = 74 ns







G(product)/G(HO•) → independant of any effect on HO•

No DR effect on mono-OH products or dimers

Significant DR effect on G 2,5-DOPA

24 MeV protons - Biomolecule radiolysis

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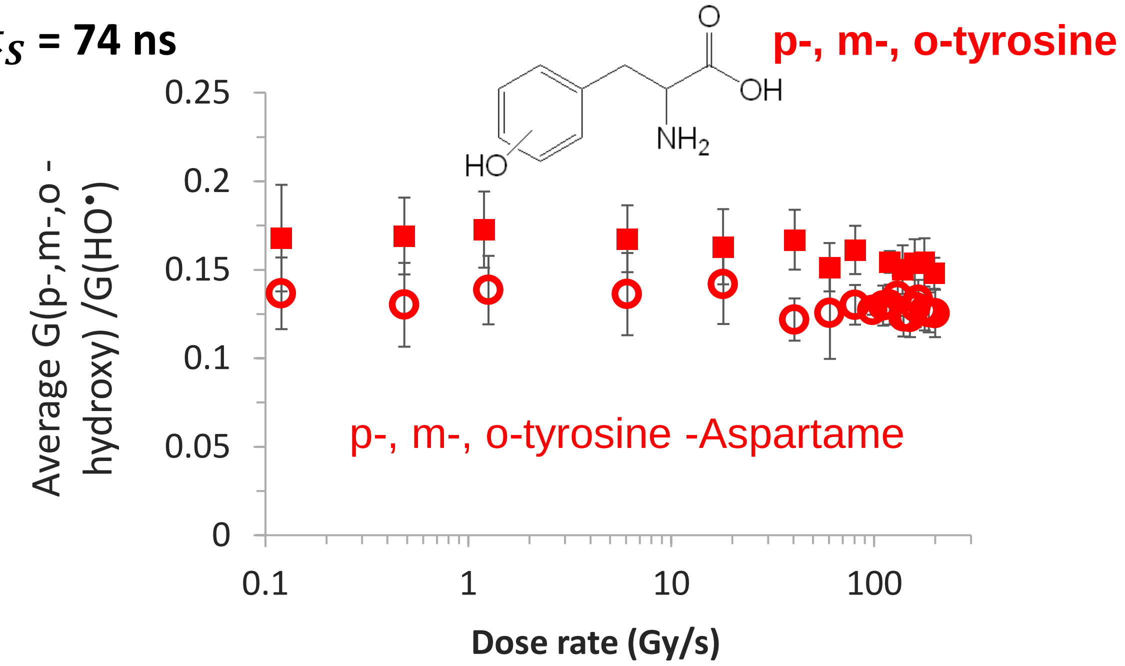

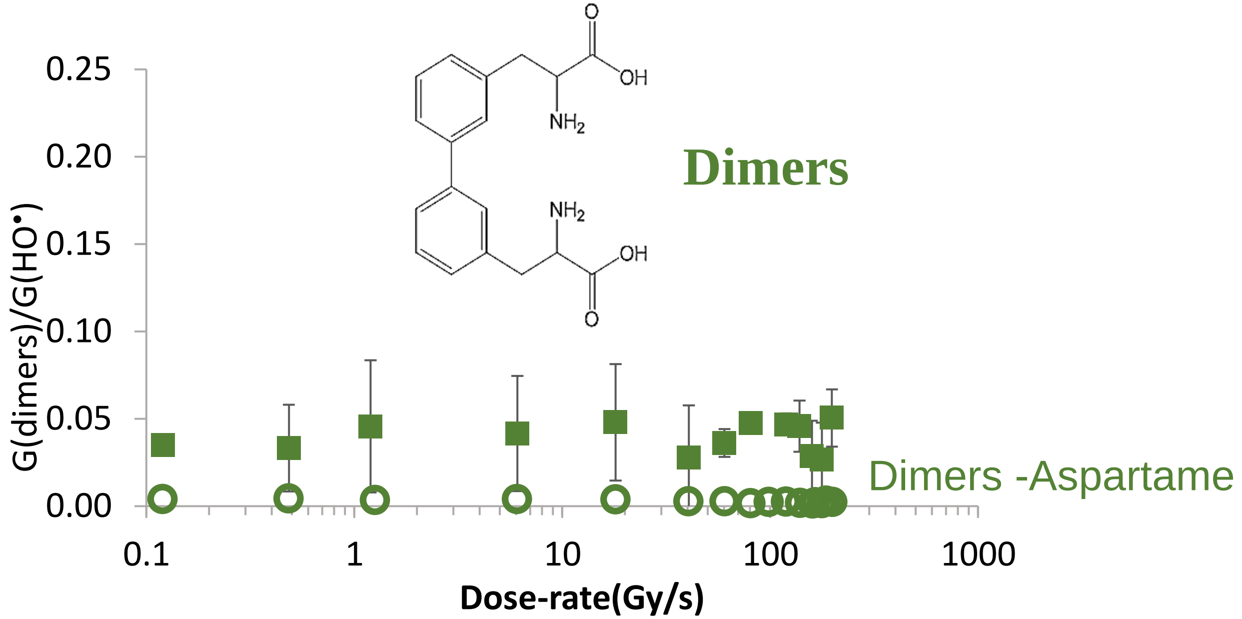

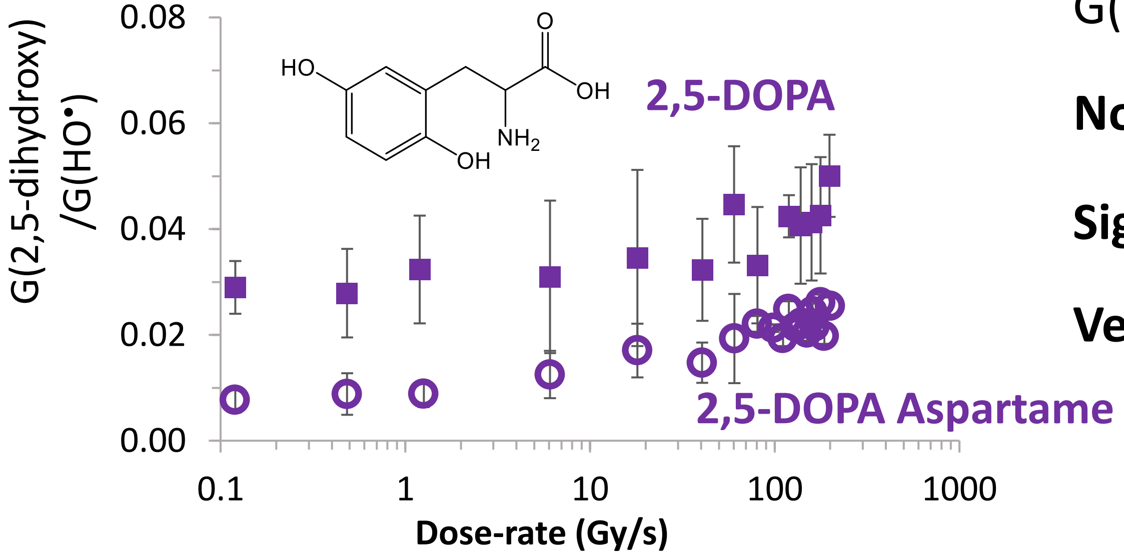

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No DR effect on mono-OH products or dimers

Significant DR effect on G 2,5-DOPA

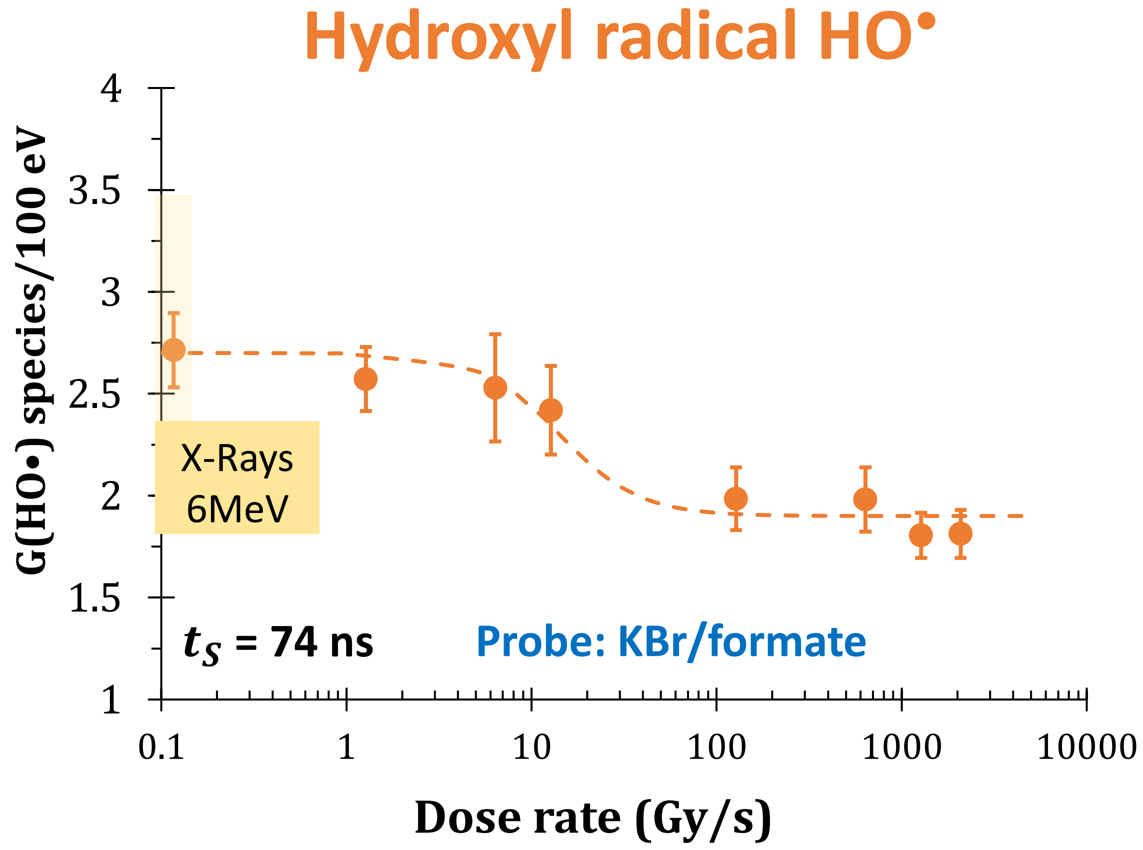
Very similar effects on peptide

Lower yields dimers/2,5-DOPA.

Lower diffusion in solution?

XR / 1 MeV electrons - Water radiolysis (HO•) / Biomolecules

LET = 0.2 eV/nm



- **DR effect on G(HO•)** with electrons

XR / 1 MeV electrons - Water radiolysis (HO•) / Biomolecules

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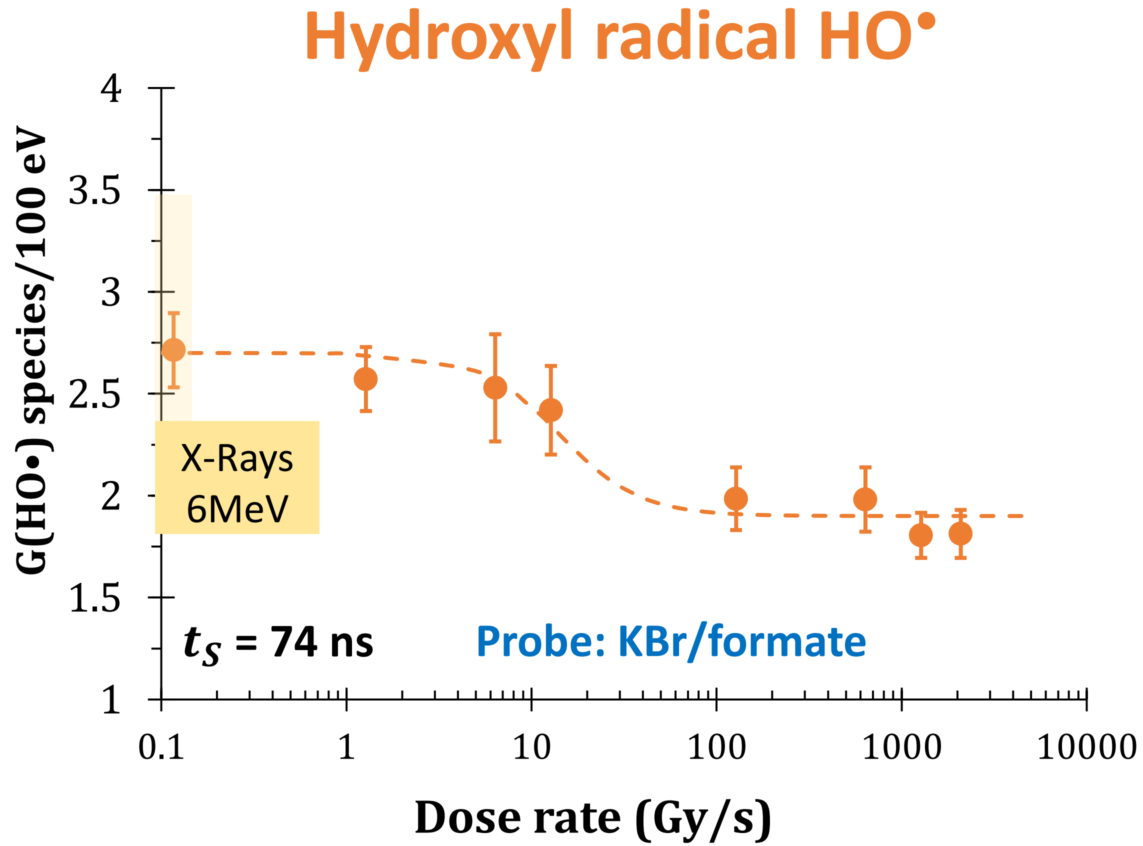
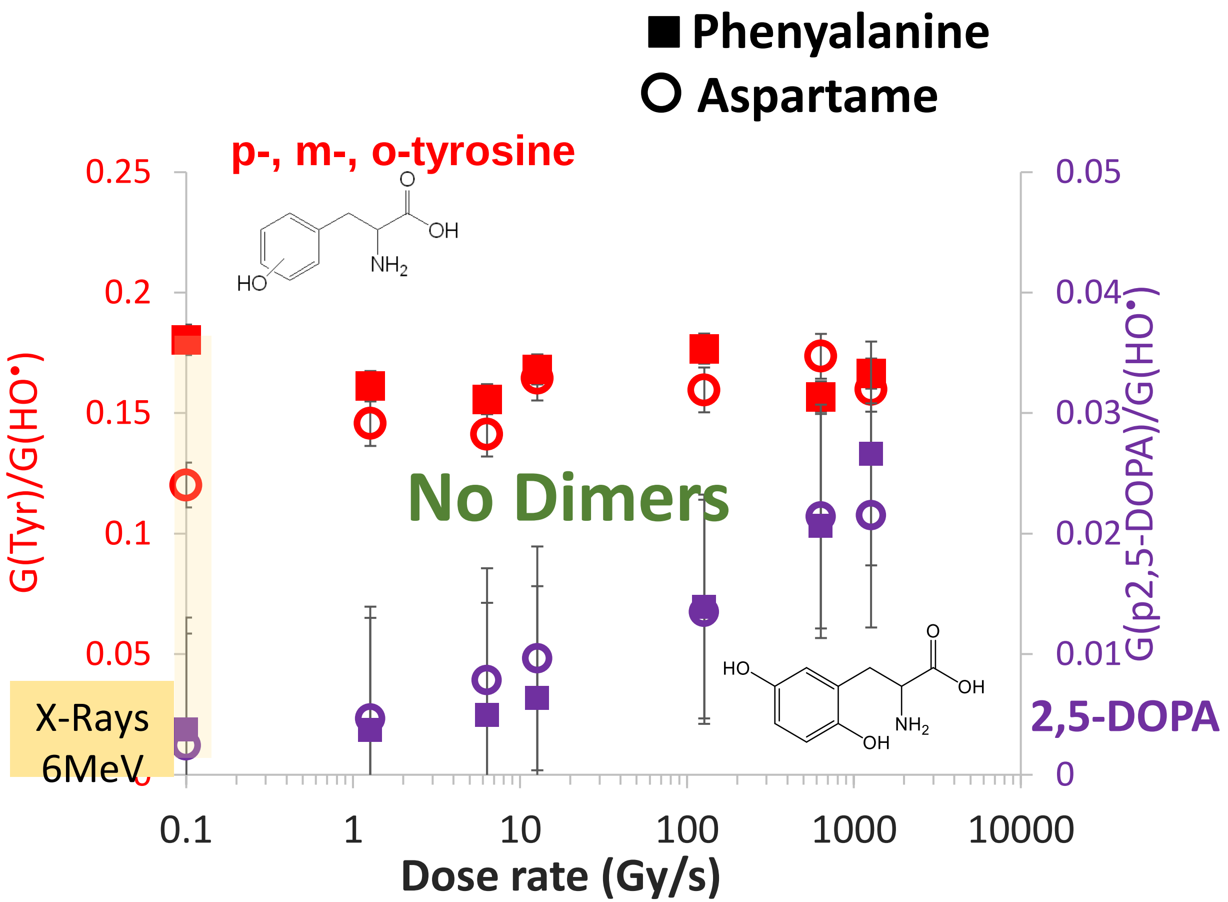




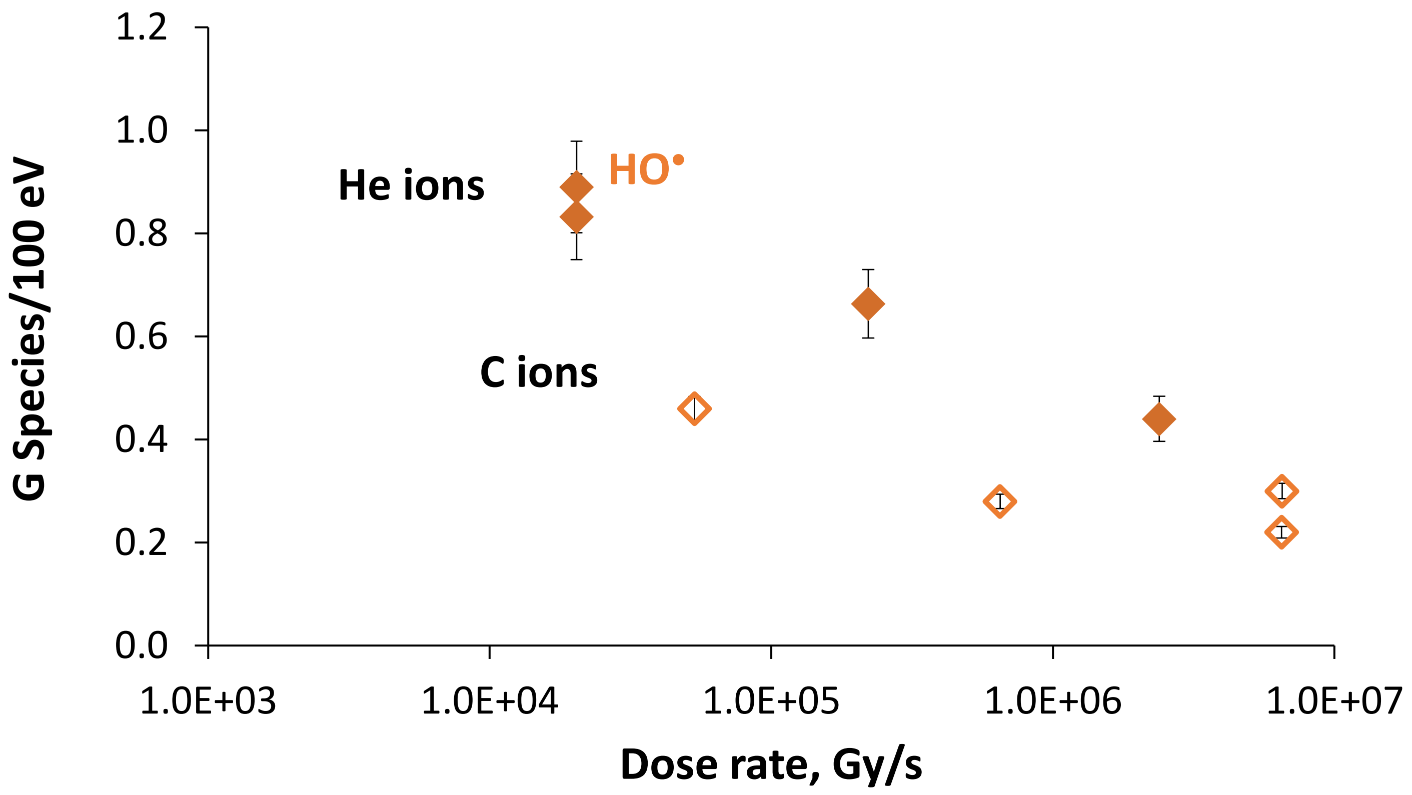
- **DR effect on G(HO•)** with electrons

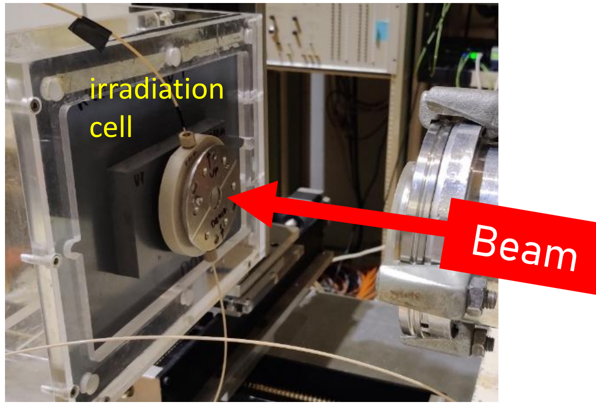
- No DR effect on G(mono-OH products)
- **Strong DR effect** on 2,5-DOPA
- **No dimers**, even at high DR

Low energy C and He ions - Water radiolysis ($HO^{\bullet}$, e^-_{aq})

Integral yields. LET_0: C ions 380 eV/nm He ions 31 eV/nm
Pulsed beam, µm depth → UHDR

Probes used
KBr/formate
Gly gly





6 MeV/u ions

- Dose-rate effect on G($HO^{\bullet}$) and G(e^-_{aq})

Low energy C and He ions - Water radiolysis (HO$^\bullet$, e^-_{aq})

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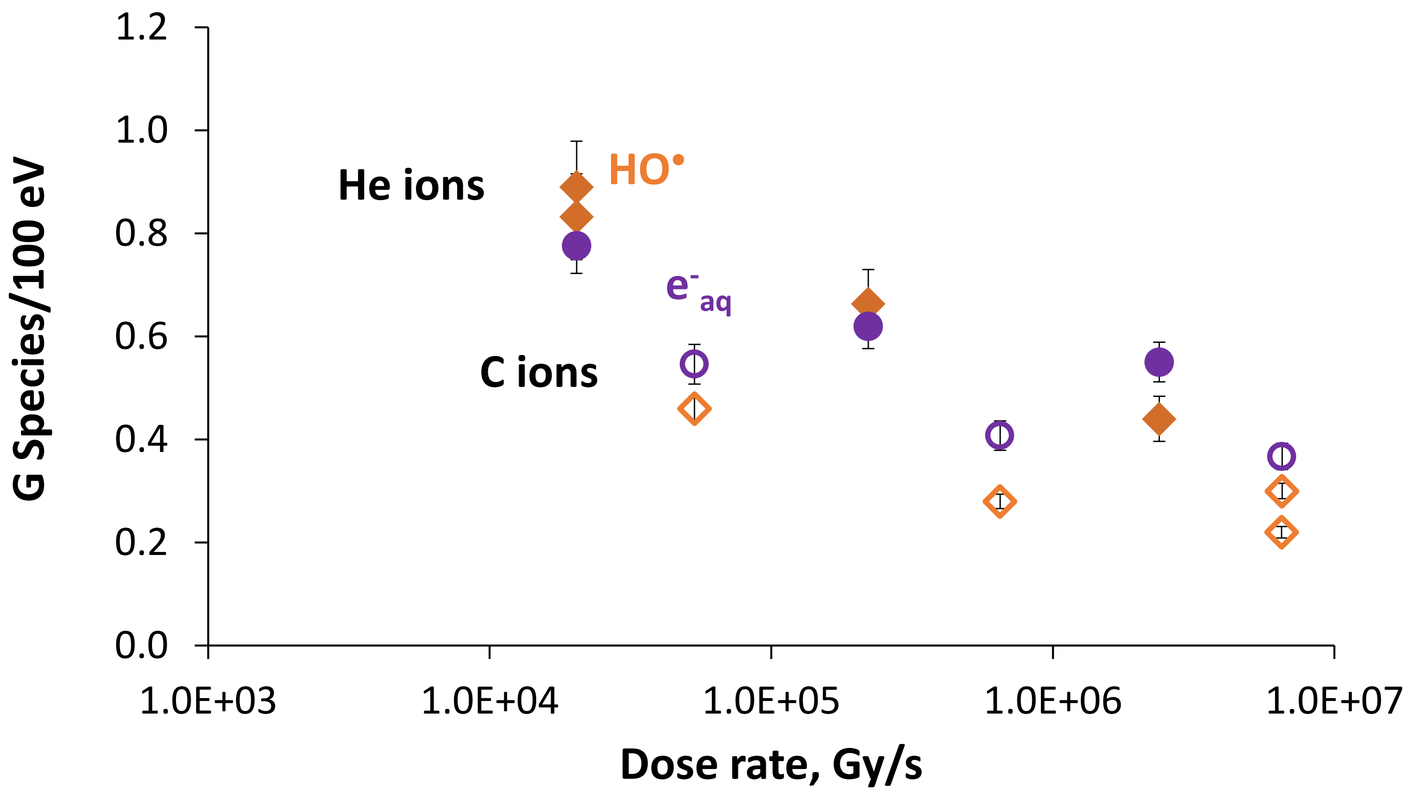
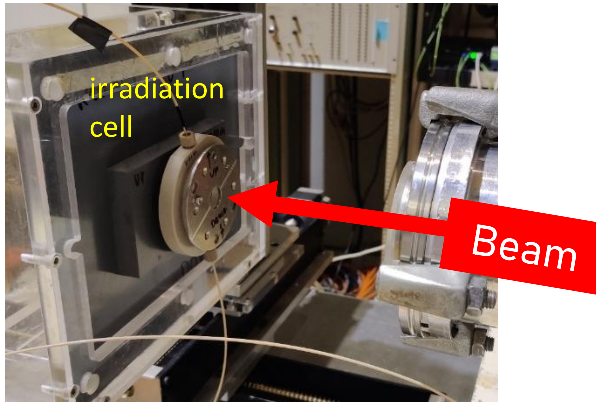
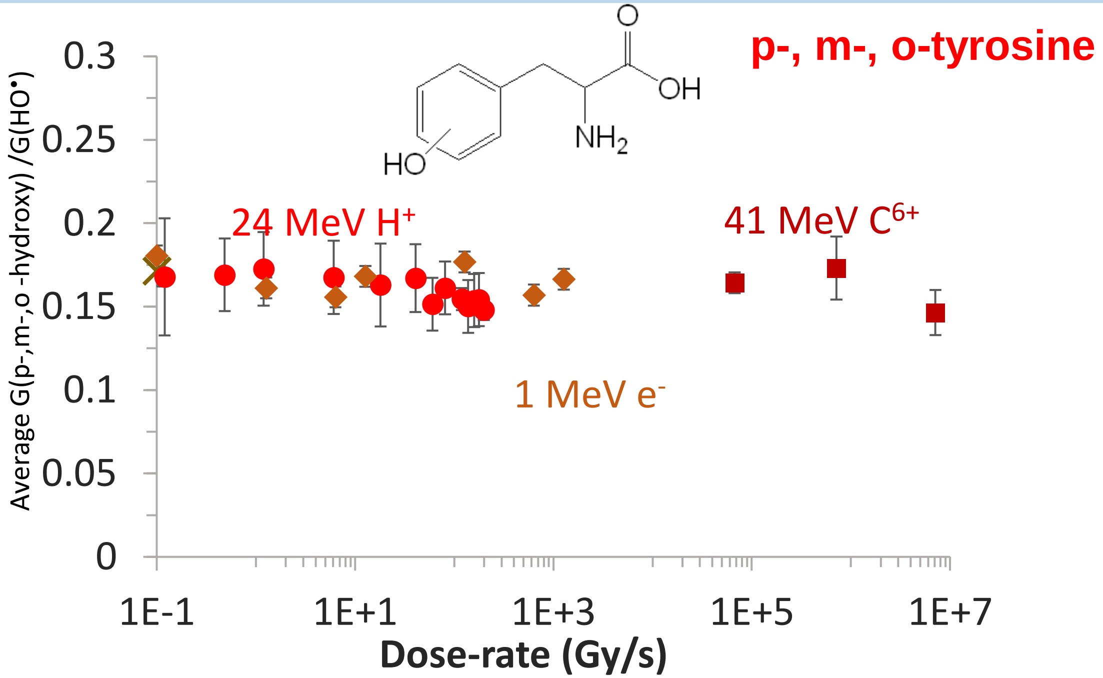


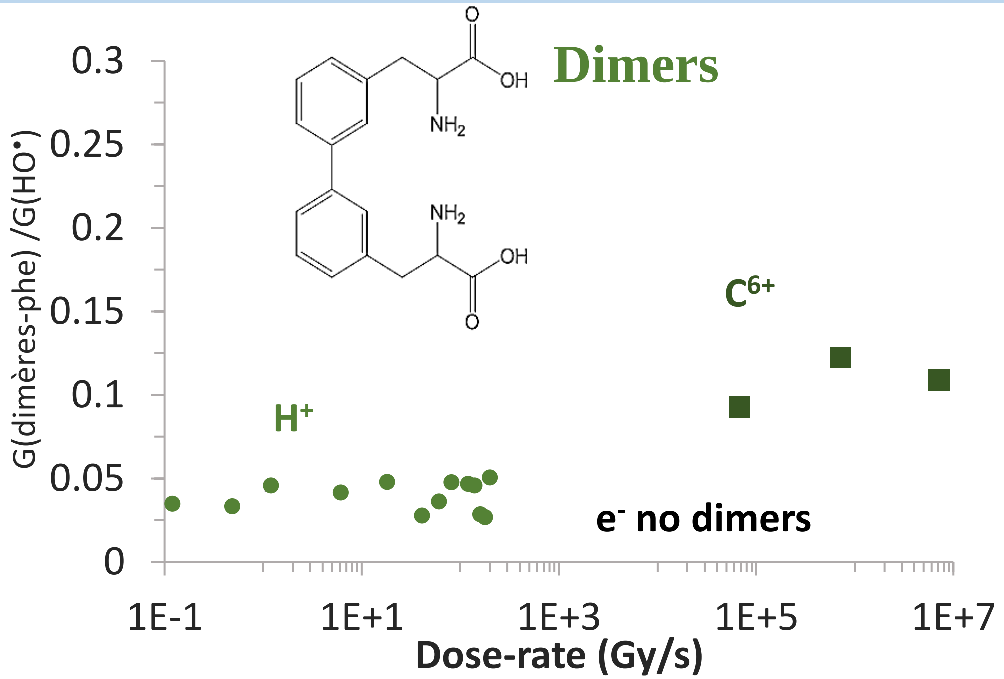


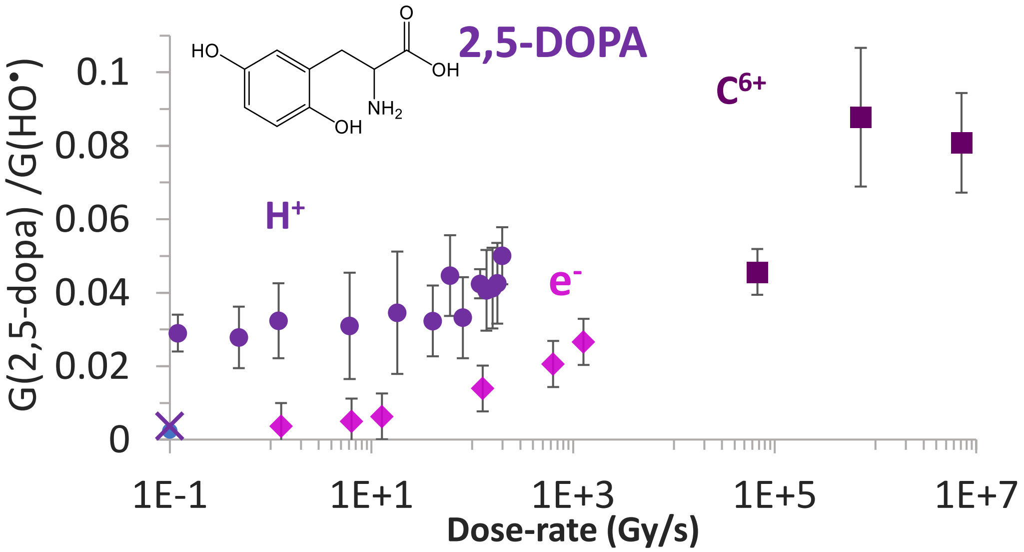
6 MeV/u ions

- Dose-rate effect on G(HO$^\bullet$) and G(e^-_{aq})

Biomolecule radiolysis: global evolution







Effects on formation mechanisms :

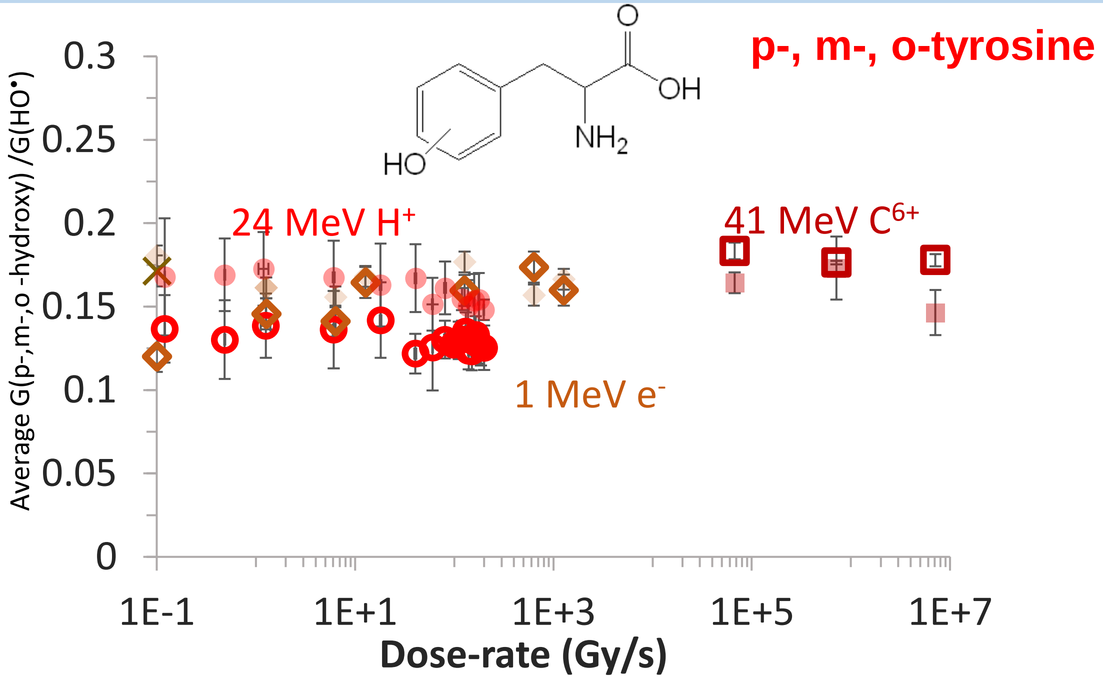
-No DR or LET effect on mono-OH products

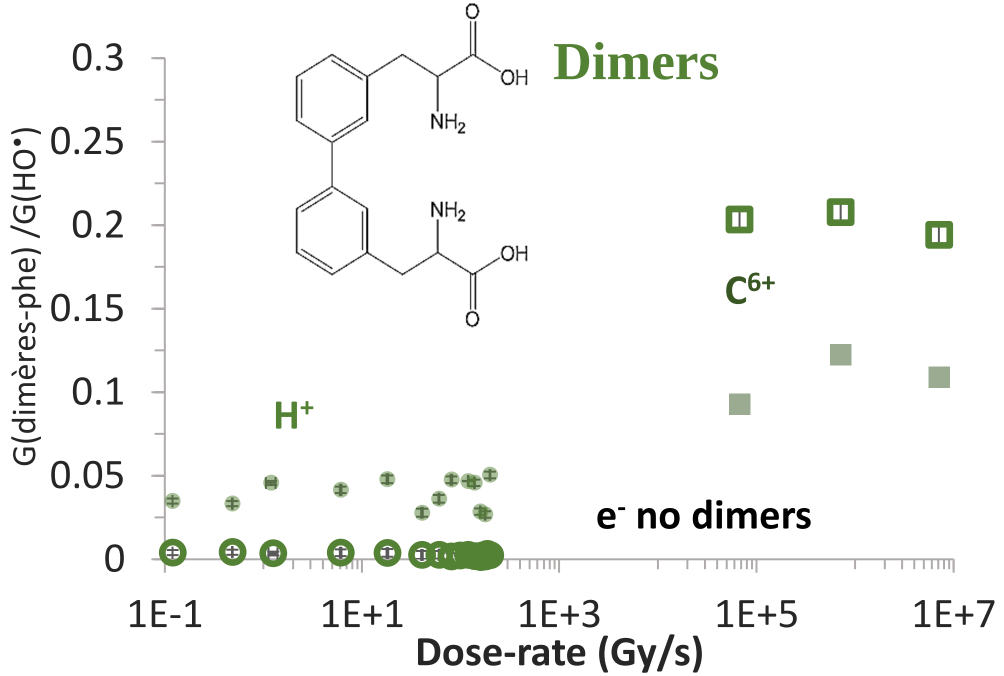
-LET effect on dimers, no DR effect → intra-track reactions

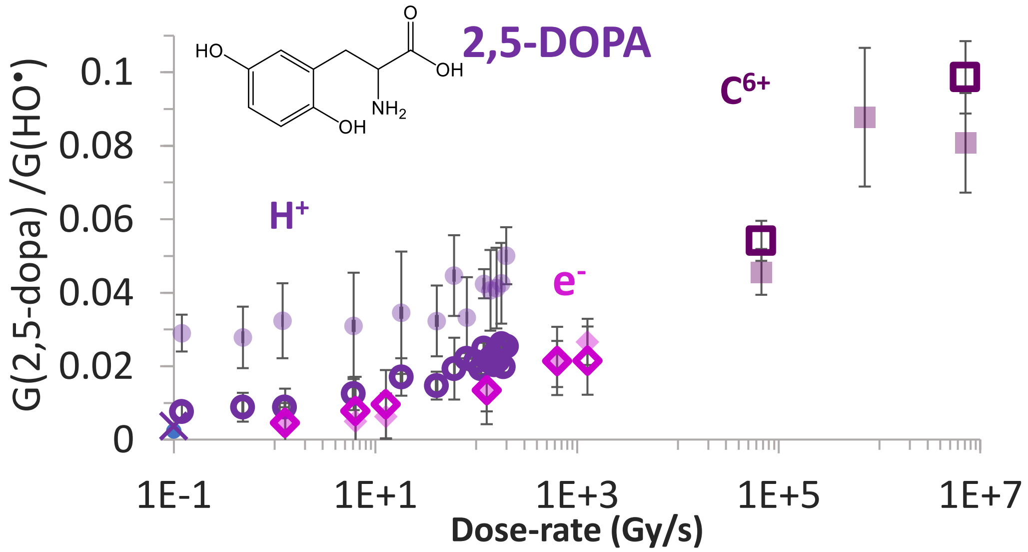
-Strong dose-rate and LET effect on 2,5-DOPA

→ Inter and intra-track reactions

Biomolecule radiolysis: global evolution







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-Strong dose-rate and LET effect on 2,5-DOPA

→ Inter and intra-track reactions

Aspartame: same mechanisms, lower yields

Conclusions

Water radiolysis

H^+ 24 MeV 0.1 – 200 Gy/s	No dose-rate effect observed,
X-Rays/e^- 1 MeV 0.1 – 2 kGy/s	Decrease of $G(HO^\bullet)$
	Effect on $G(e^-_{aq})$?
UHDR / High LET 10^4-10^6 Gy/s	Decrease of $G(HO^\bullet)$ and $G(e^-_{aq})$

Amino acid / peptide

Peptide: similar mechanisms as amino acid

Dose-rate effects on 2,5-DOPA → one step after water radiolysis

Role of O_2 in dose-rate effects?

Aurélia Arnone (PhD Student)
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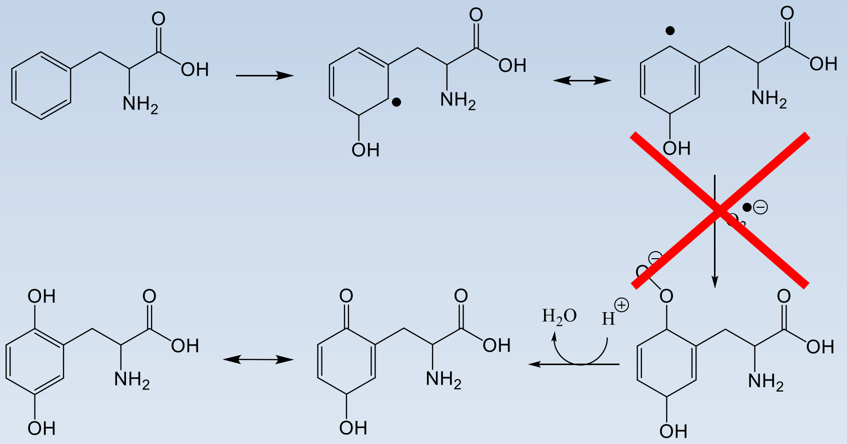
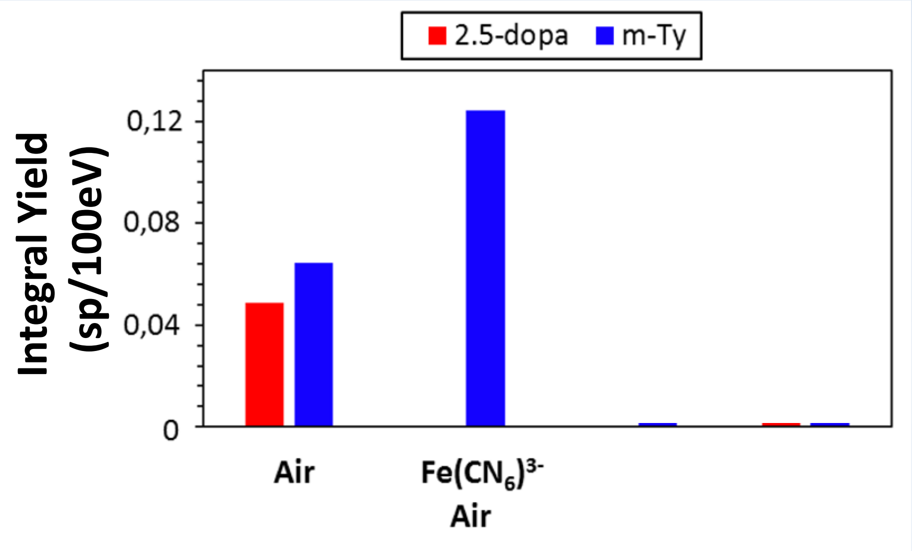
Production of 2,5-DOPA



Observation of the peroxyde by ESI-MS

$Fe(CN_6)^{4-}$ fast oxidant of radical to tyrosines

-> no more 2,5-dopa



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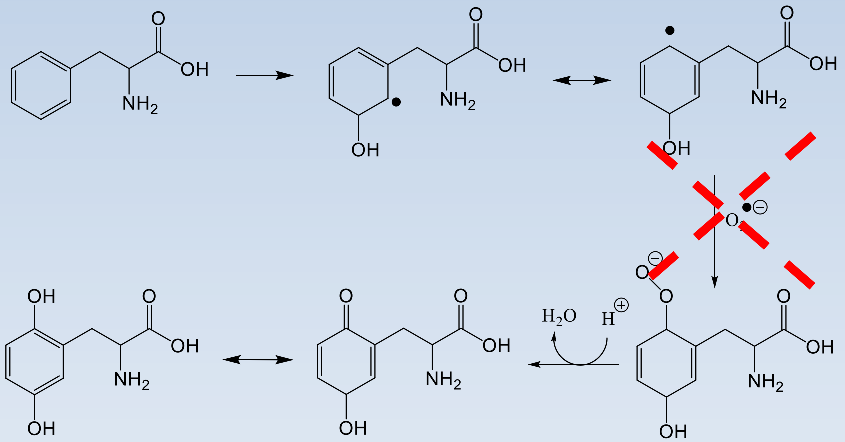

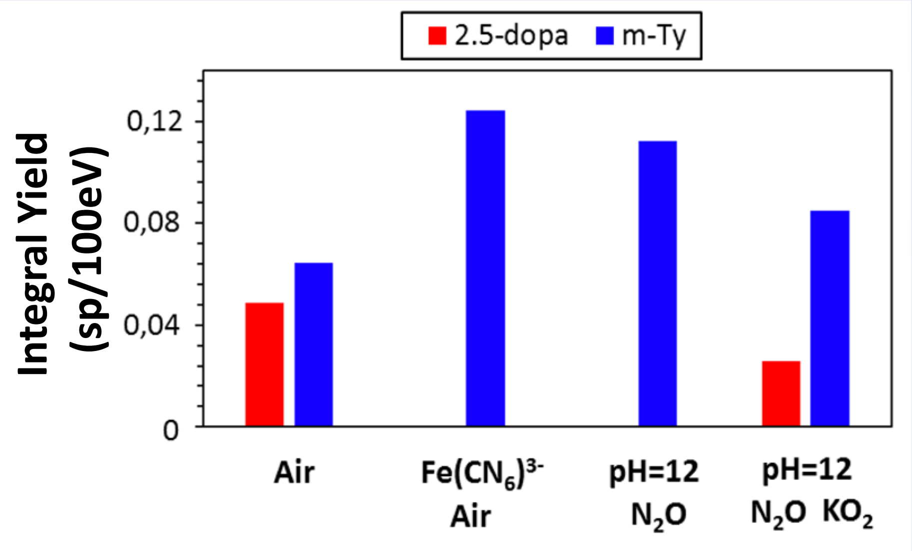

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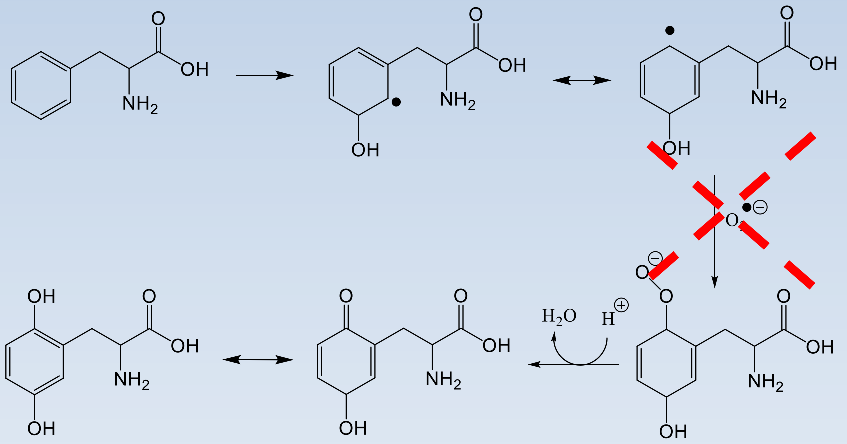
N_2O medium pH =12
-> no 2,5-dopa

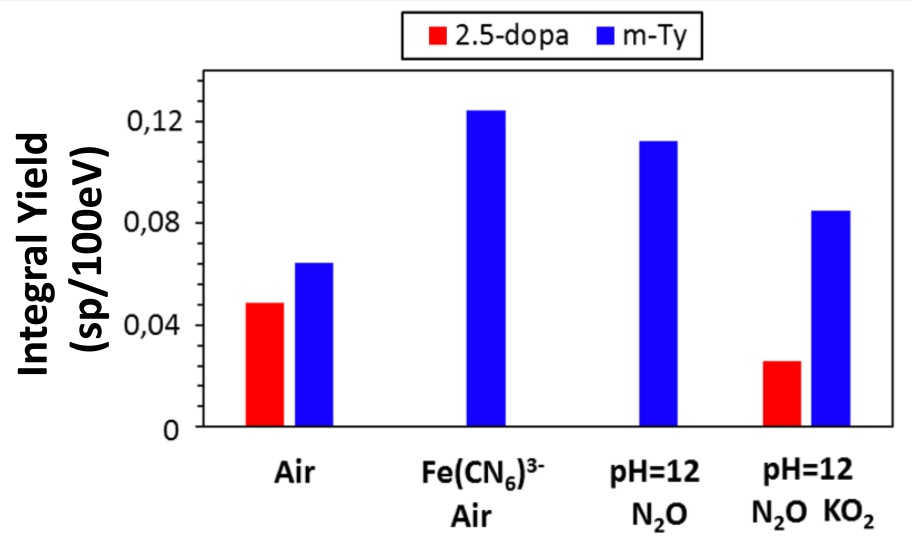
N_2O medium, pH =12 + K^+ $O_2^{\bullet -}$
-> formation of 2,5-dopa

$$e_{aq}^- + N_2O + H_2O \longrightarrow HO^\bullet + HO^- + N_2$$

$$e_{aq}^- + O_2 \longrightarrow O_2^{\bullet -}$$

Production of 2,5-DOPA





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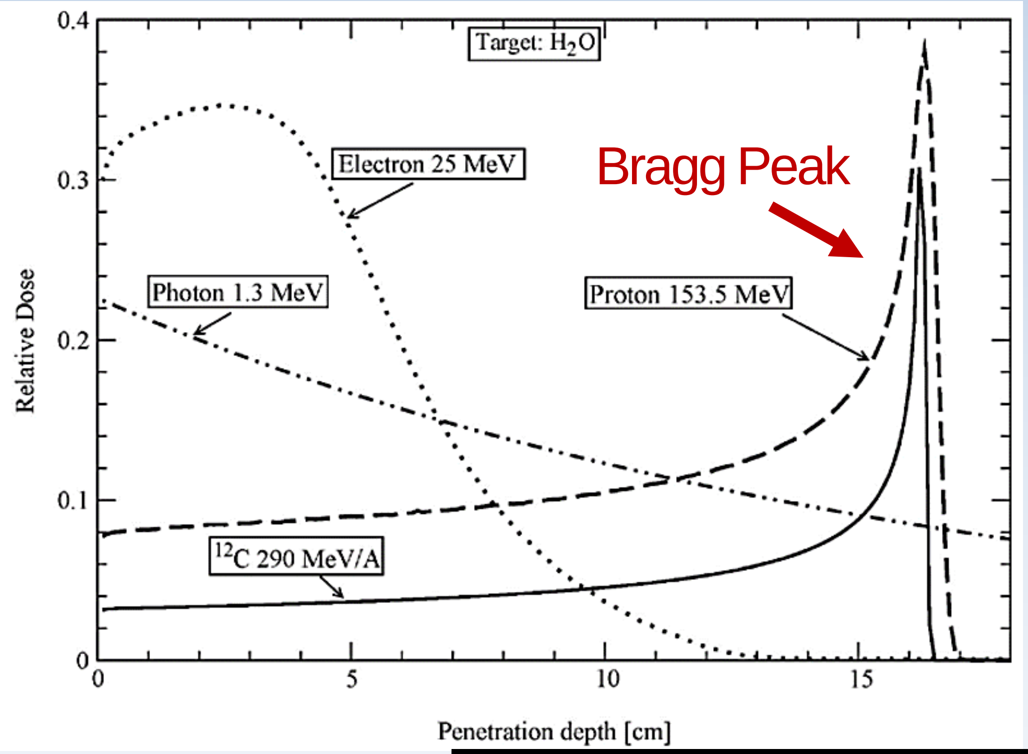
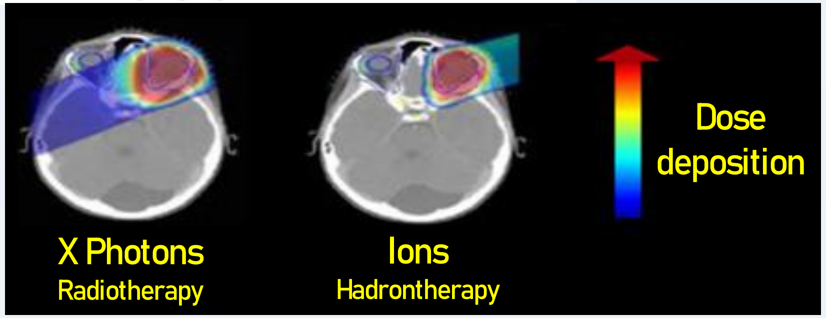
Irradiation in $H_2{}^{18}\mathbf{O}$ / Air $^{16}O_2$
-> One ^{18}O / One ^{16}O in 2,5-dopa
-> ^{16}O from $^{16}O_2$ via $O_2^{\bullet-}$

Context





Hadrontherapy: **Accelerated Ions**

- Better localized dose deposition in the tumor
- High LET → Higher density of energy deposition
- Superior biological efficiency

FLASH therapy : High dose rate (>40 Gy/s)

→ FLASH effect

Reduced damage to healthy tissue while maintaining a strong impact on tumors

Soltani, J.; Cata-Danil, G. Monte Carlo Computation of the Energy Deposited by Heavy Charged Particles in Soft and Hard Tissues. UPB Sci. Bull. Ser. Appl. Math. Phys. 2008, 70.