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Characterization of radiation quality based on nanodosimetry

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Motivation

- Biological effectiveness of ionizing radiation depends on radiation quality

- Radiation quality is ...

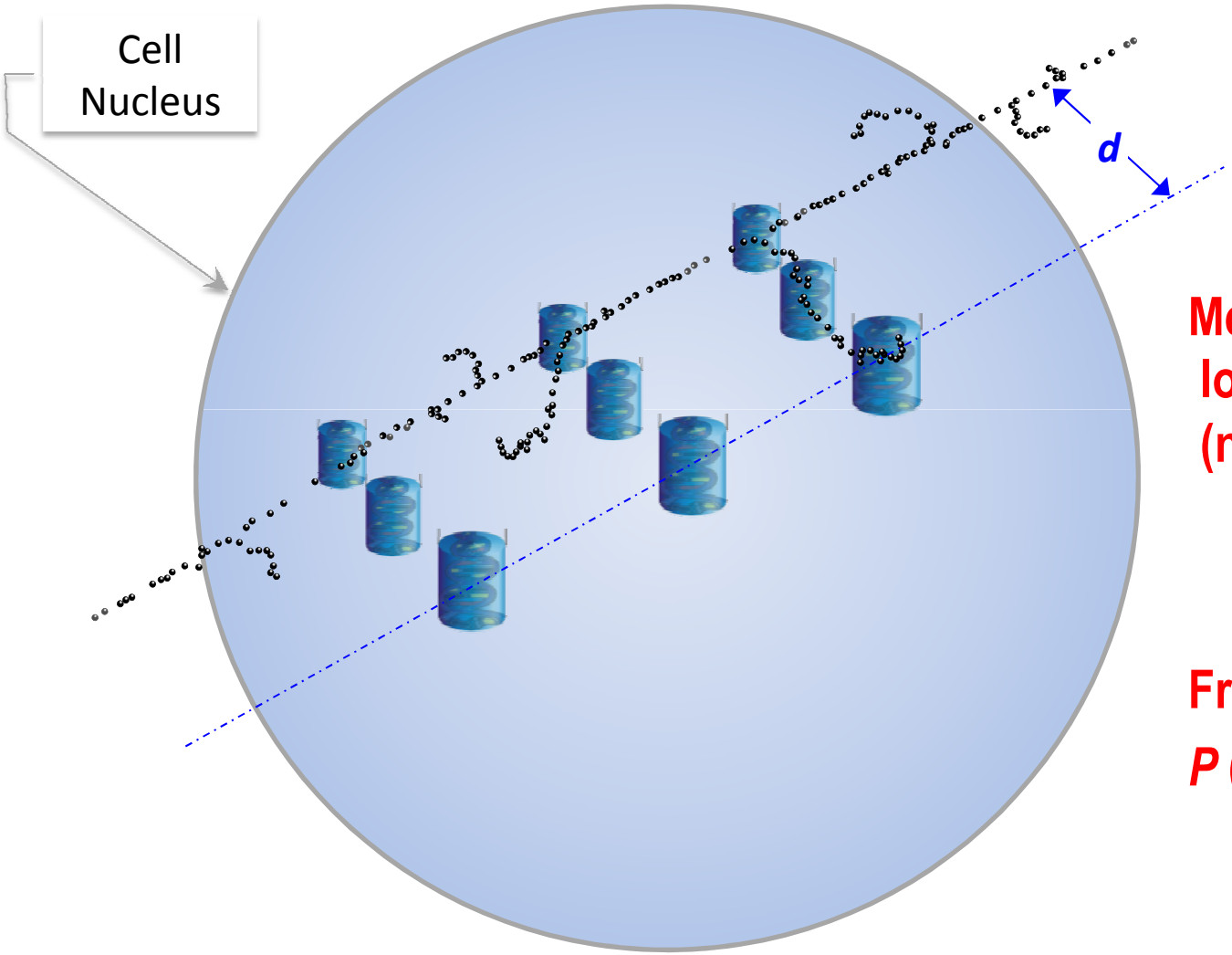
  ... defined as the spectrum of particles and their energies

  .... related to the microscopic particle track structure
  (and DNA is believed to be the critical target)

- Defining radiation quality in terms of measurable physical quantities related to particle track structure would enable a ***unified approach*** for risk assessment and radiotherapy ...

  .... and the realisation of a ***measurand***

Nanodosimetry versus Microdosimetry



Measurement quantity:
Ionization cluster size ν
(number of ionizations)

Frequency distribution

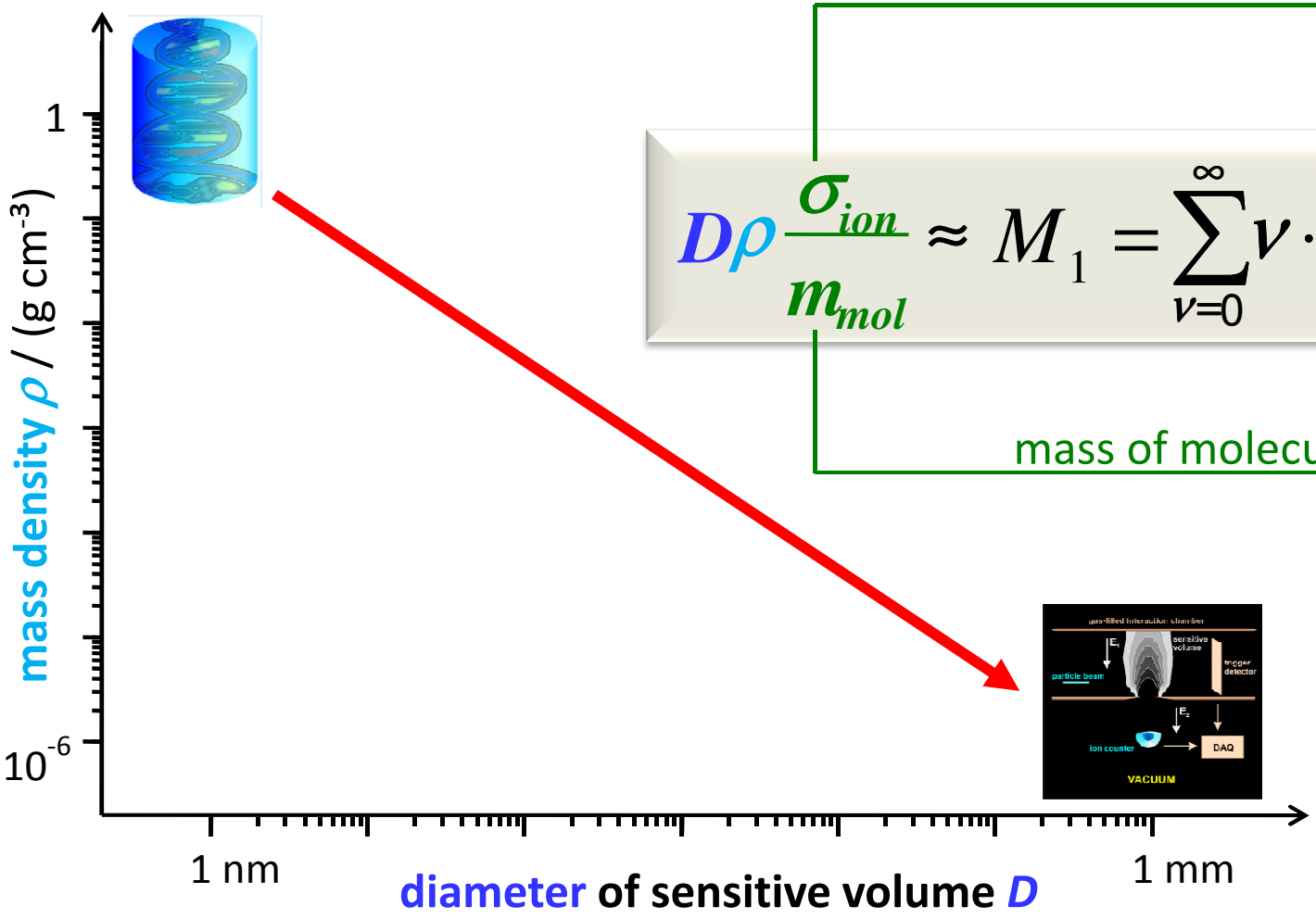
$P(\nu \mid d\,;\,Q)$

Scaling relation for ionization cluster size distributions

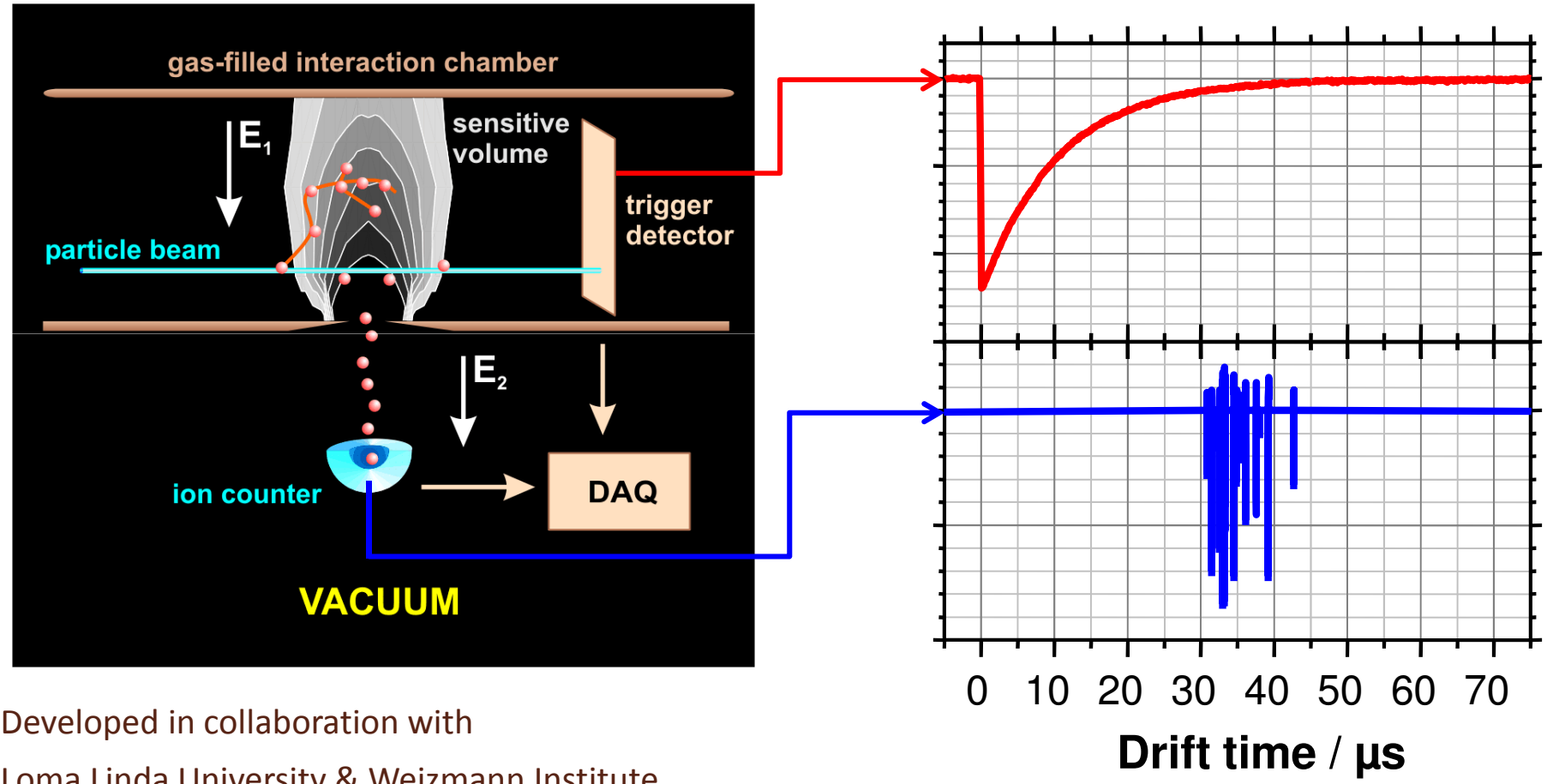
ionization cross section

$$D\rho \frac{\sigma_{ion}}{m_{mol}} \approx M_1 = \sum_{\nu=0}^{\infty} \nu \cdot P(\nu)$$

mass of molecule



Ion-counting nanodosimeter for measuring ionisation cluster size distributions



Developed in collaboration with

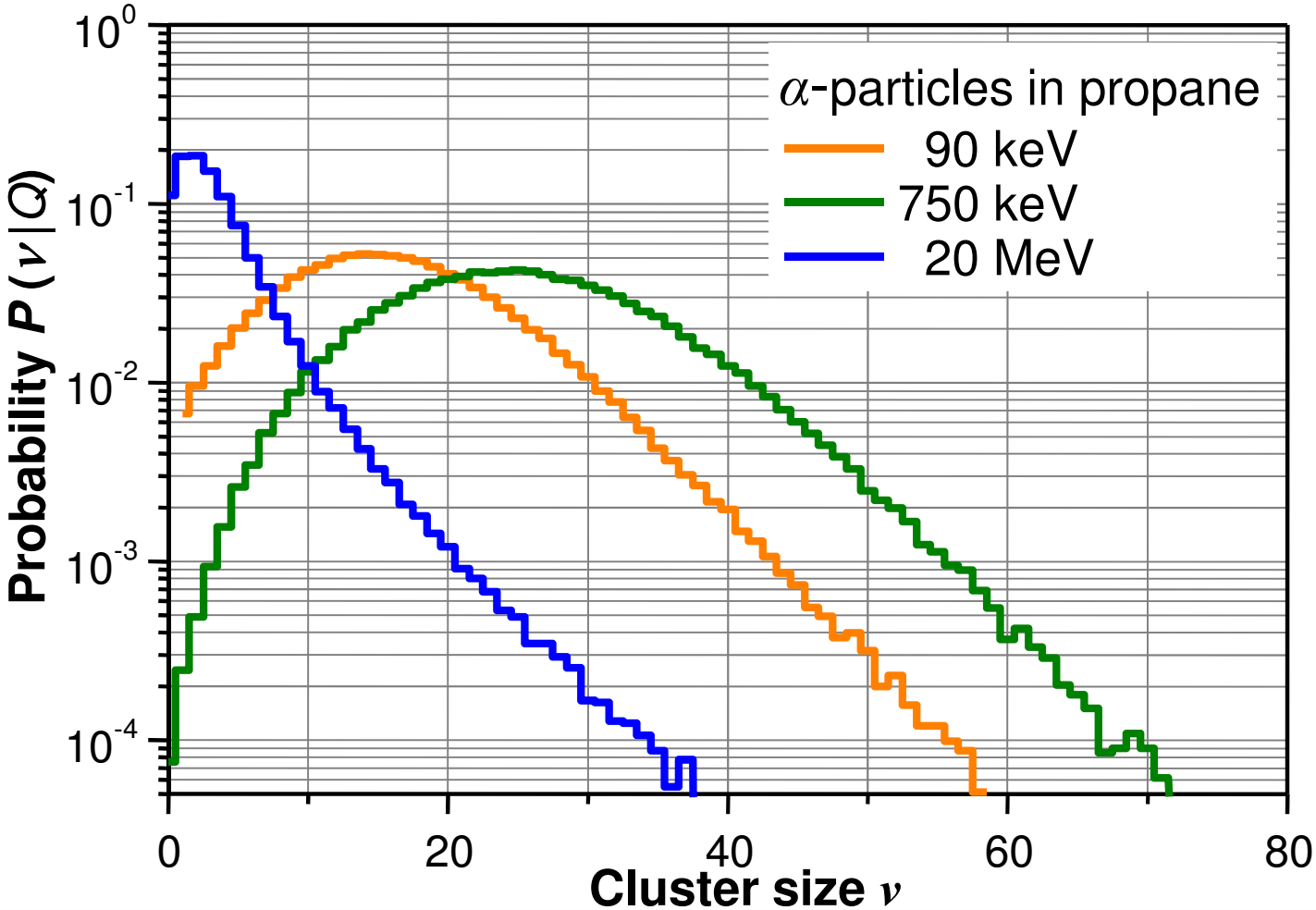
Loma Linda University & Weizmann Institute

Source: B. Grosswendt

Source: G. Hilgers

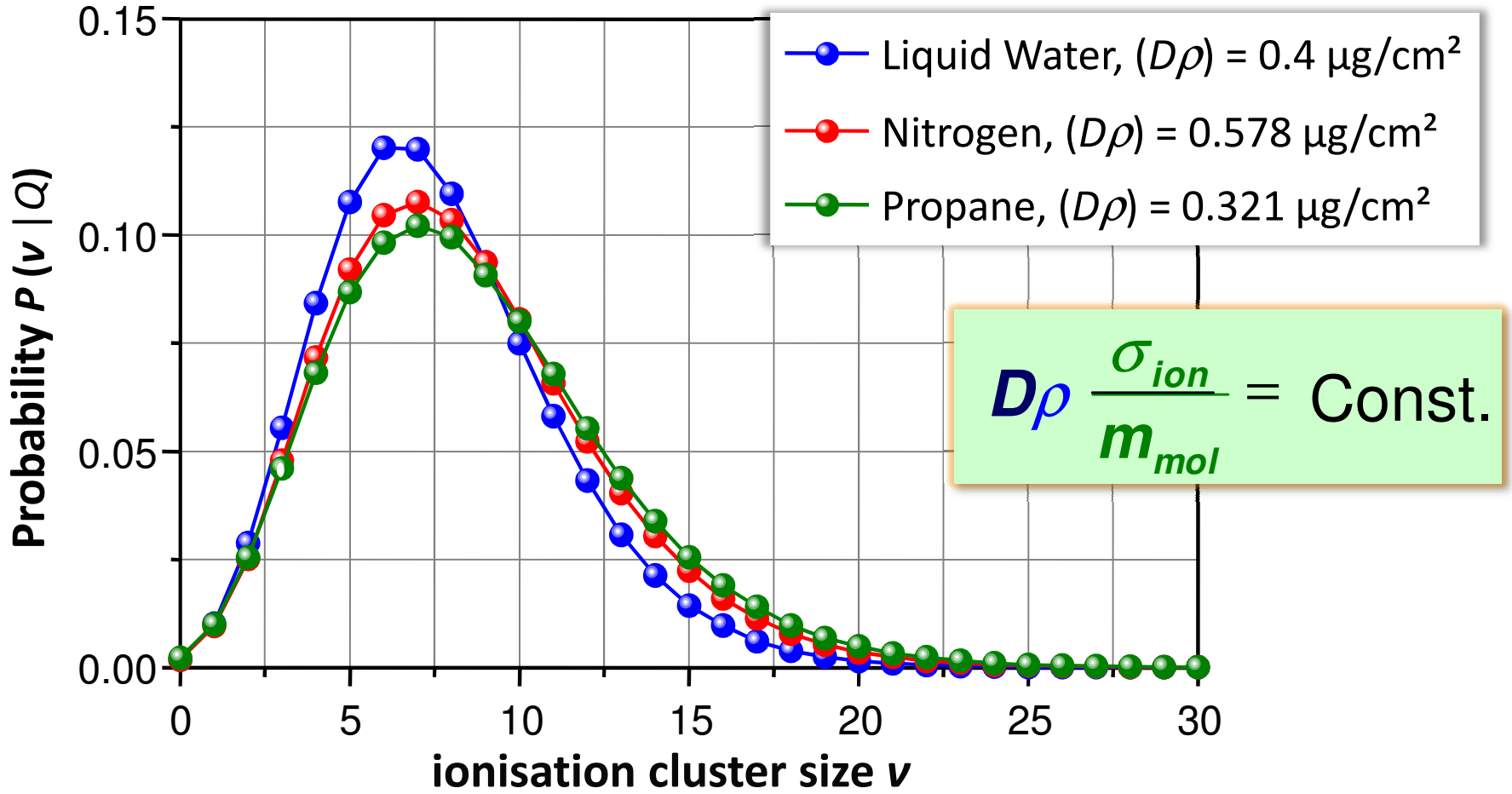
Ionization cluster-size distributions

Measurement in a gas target equivalent to a DNA segment



Ionisation cluster-size distributions

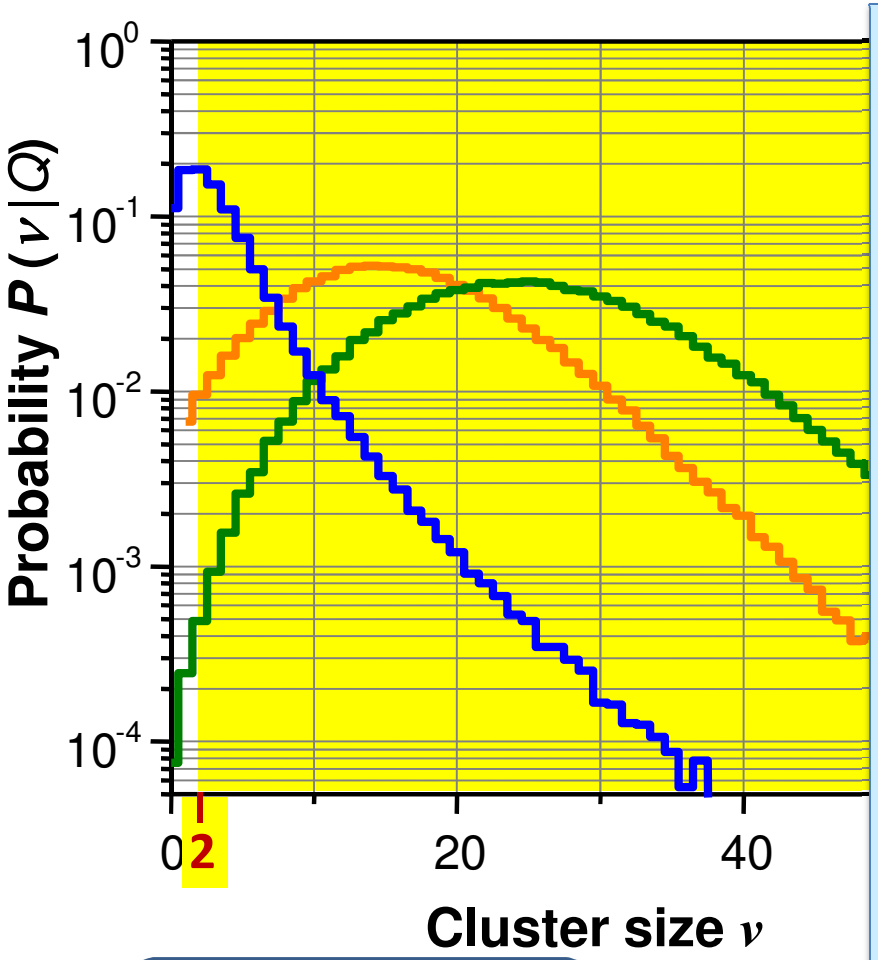
(Monte-Carlo simulations for 4.6 MeV α-particles)



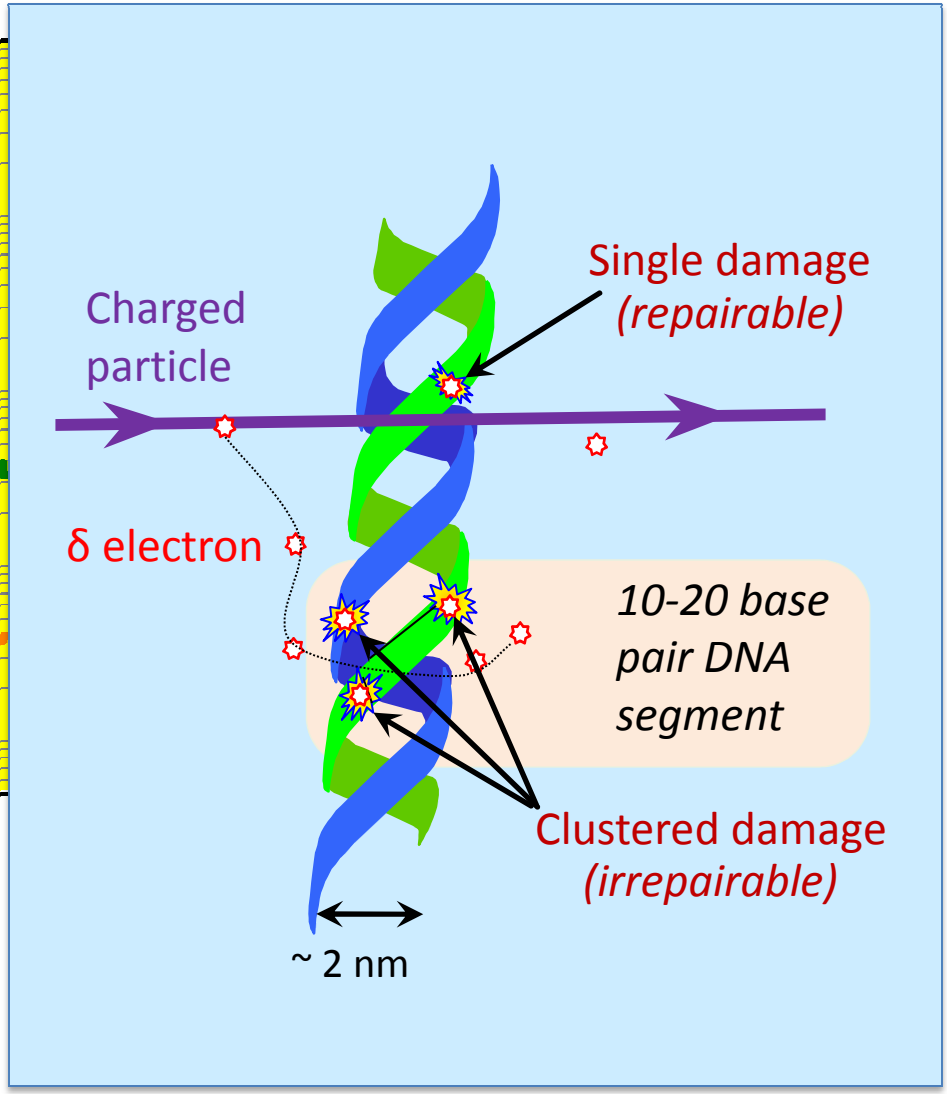
$$D\rho \frac{\sigma_{ion}}{m_{mol}} = \text{Const.}$$

Adapted from Grosswendt, RPD 110, 789 (2004)

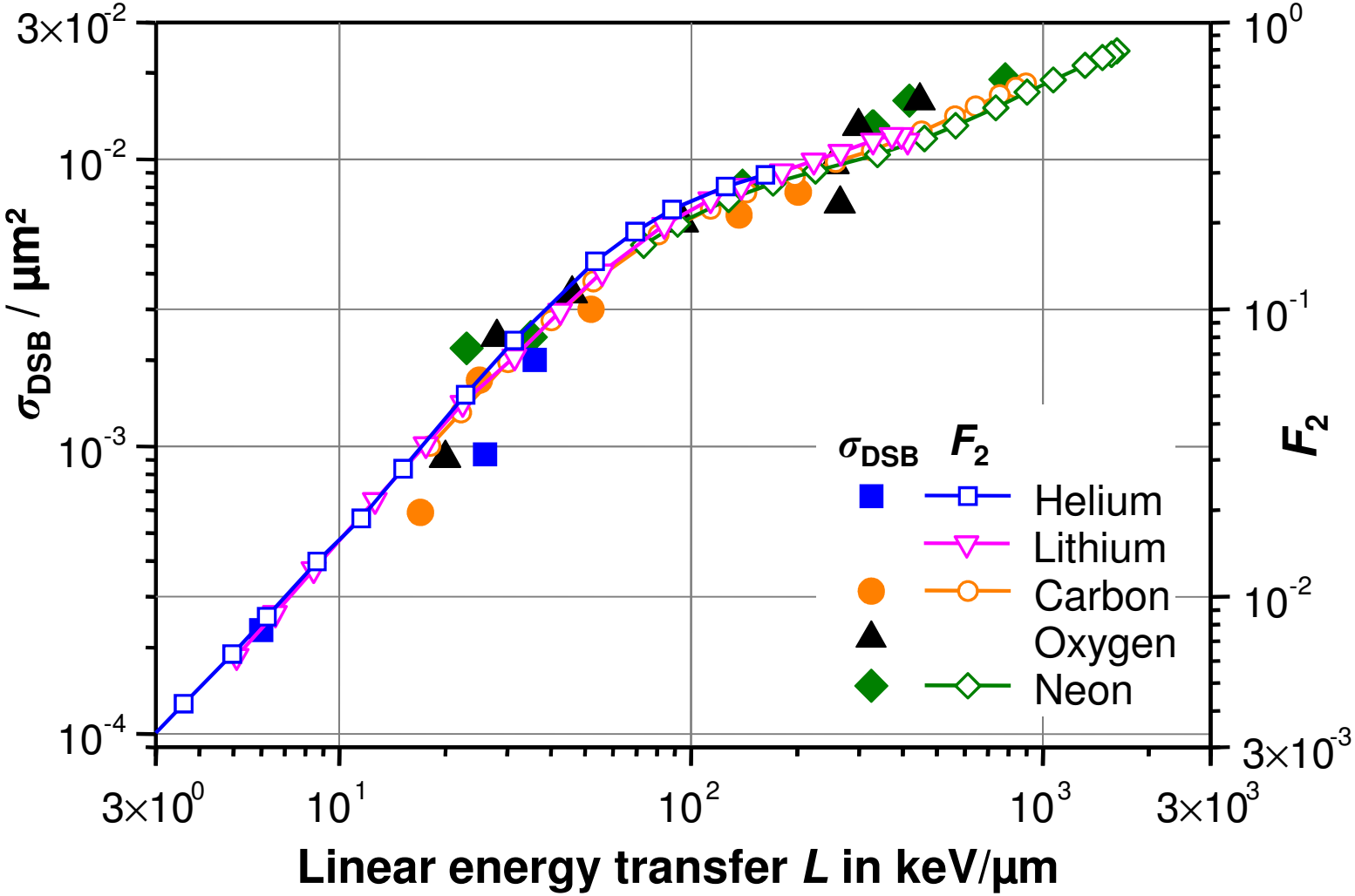
Track structure parameters and biological effectiveness



$$F_2(Q) = \sum_{\nu=2}^{\infty} P(\nu \mid Q)$$



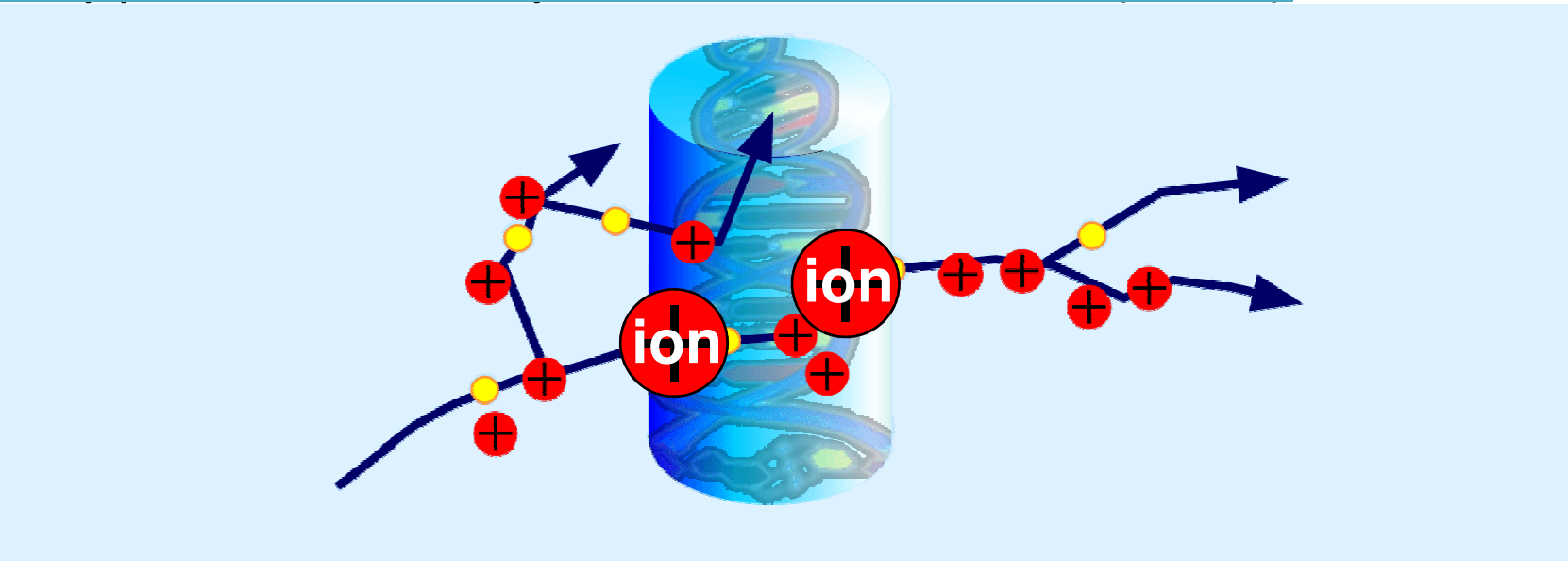
F_2 *vs.* double strand breaks (DSB) in plasmid DNA

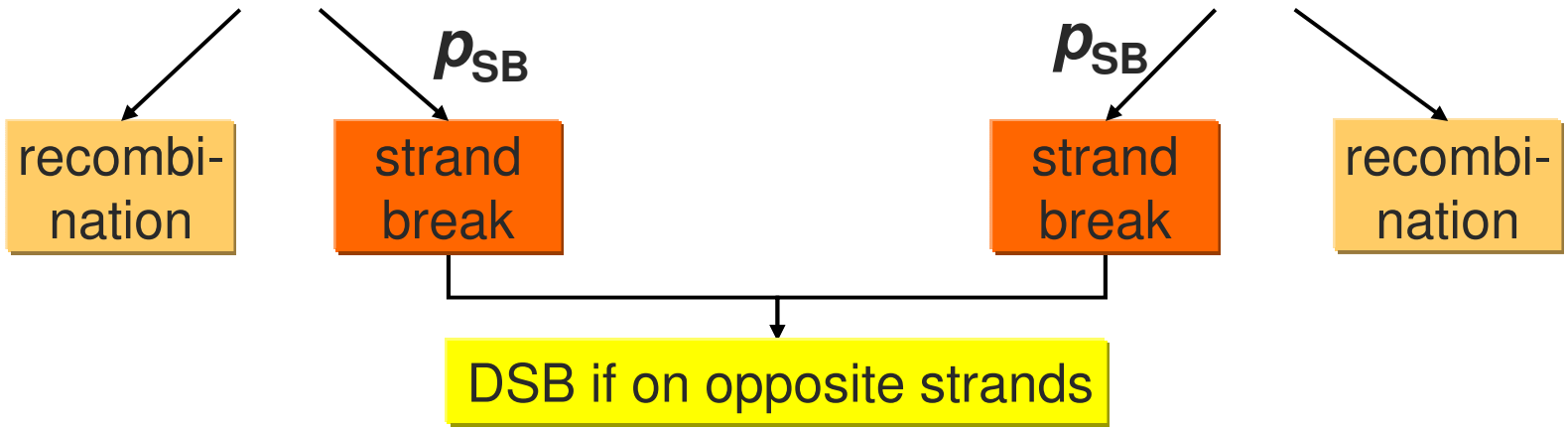


Exp. data from Taucher-Scholz and Kraft, Radiat. Res. 151 (1999), simulations by Bernd Grosswendt

Linking nanodosimetry and radiobiology

The approach of *Garty et al., PMB 55, 761 (2010)*





Linking nanodosimetry and radiobiology

The approach of *Garty et al., PMB 55, 761 (2010)*

$$P(DSB \mid Q) = \sum_{\nu=2}^{\infty}\left[1+(1-p_{SB})^{\nu}-2(1-p_{SB}/2)^{\nu}\right]\times P(\nu \mid Q)$$

Probability for double strand break

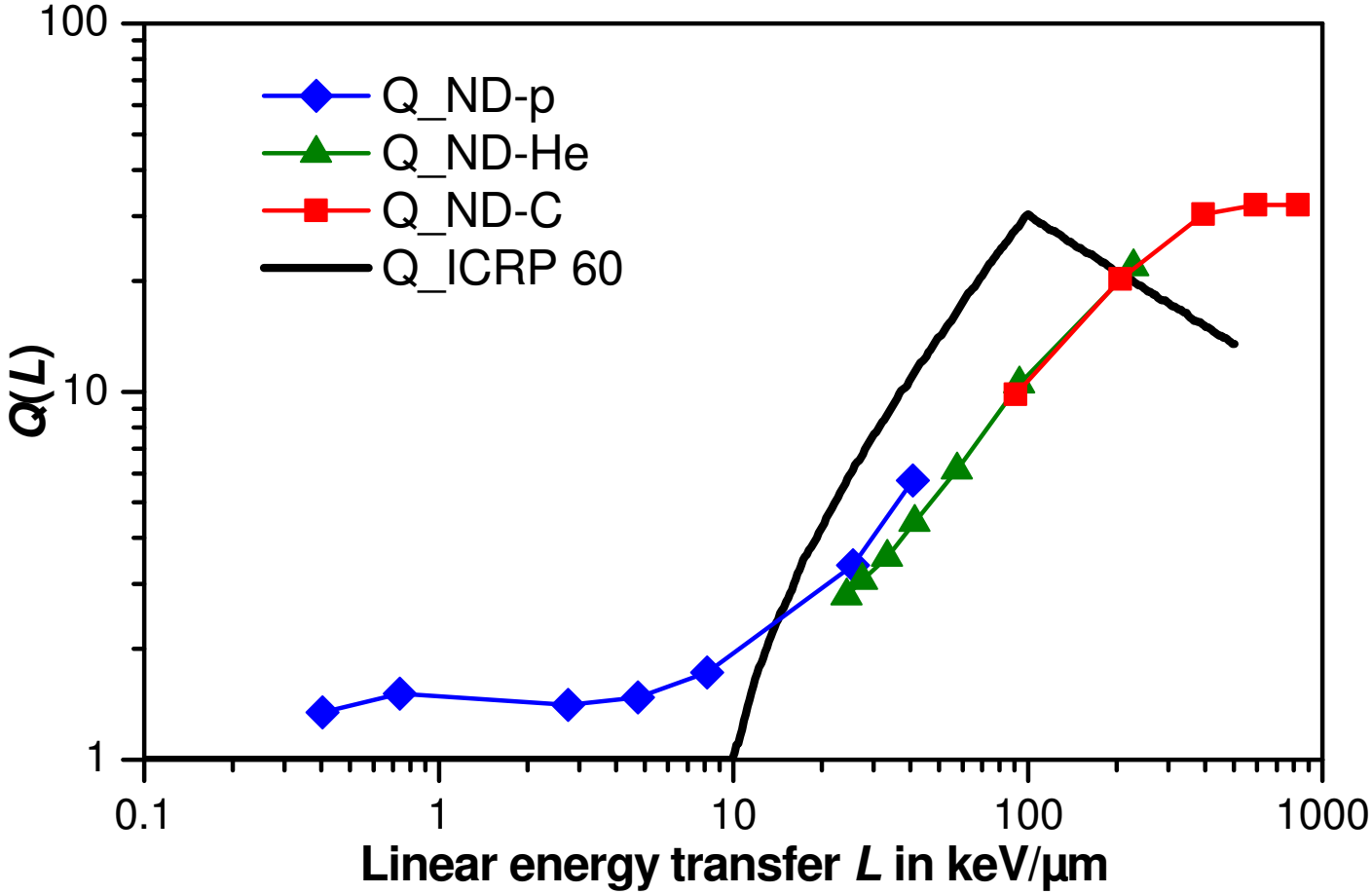
From data fitting to radiobiological assay

ionisation cluster size distribution

Nanodosimetric rad. quality factor

$$Q_{ndos} = \frac{P(DSB \mid Q)}{P(DSB \mid Q_{ref})}$$

Radiation quality factors derived from nanodosimetric track structure characteristics



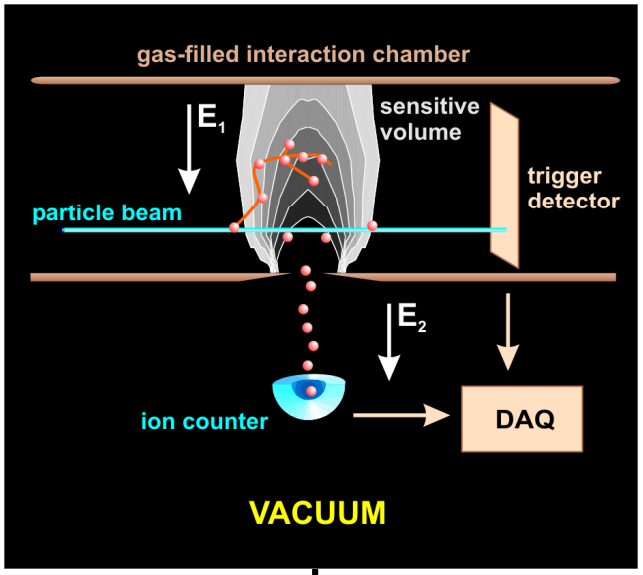
R. Schulte et al. Z. Med. Phys. 18, 286-296, 2008

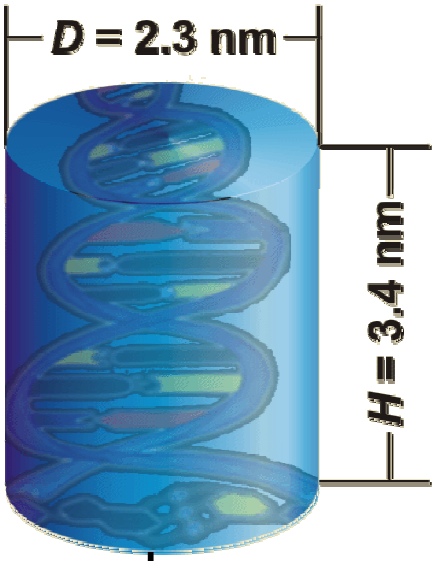
Summary: R&D strategy for nanodosimetry

Concerted development of techniques to

measure ionisation cluster sizes in macroscopic (mm) gas targets

simulate ionisation cluster sizes in nano-volumes (nm)





'Biophysical' models for linking ionisation cluster size distribution and DNA damage probability

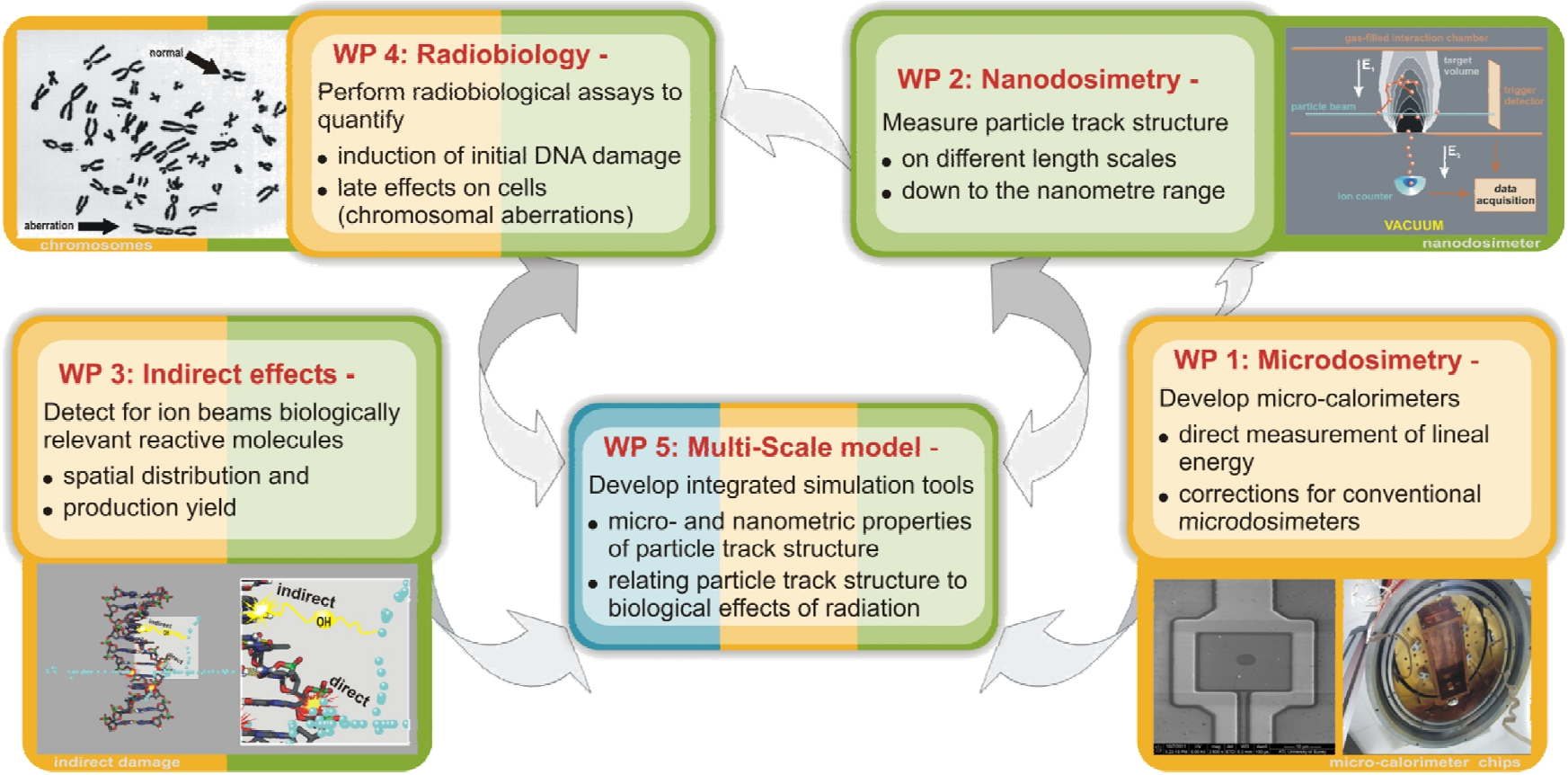
Challenges and open issues

- Relevant target size? (DNA segment, histone, cell nucleus)
- Multi-scale characterisation of track structure?
- Relevance of DNA cross sections?
- Relevance of condensed-phase effects?

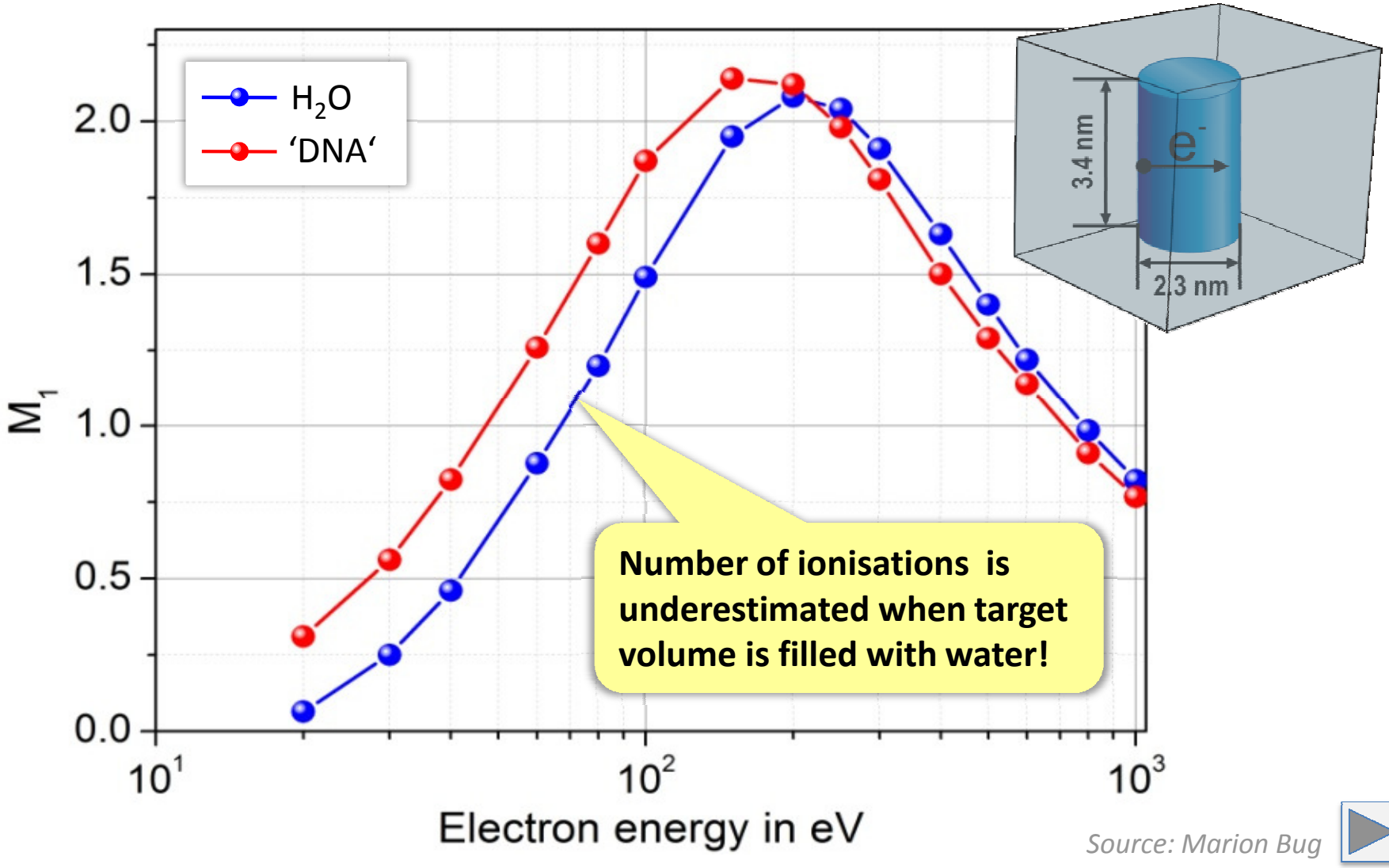
⇨ Joint Research Project within the European Metrology Programme

http://www.ptb.de/emrp/**BioQuaRT**.html

EMRP Project "Biologically Weighted Quantities in Radiotherapy" (2012-2015)



Mean ionisation cluster size for DNA-segment target



Source: Marion Bug

Nanodosimetry - take home messages

- Different radiation qualities are distinct by the microscopic interaction pattern of the particle track structure.
- Nanodosimetry characterises radiation quality by measurable physical properties of track structure.
- Nanodosimetry is based on a density scaling principle that has been verified by simulations and experimentally .
- Nanodosimetric track structure parameters correlate with yield of early biological endpoints.
- The EMRP joint research project BioQuaRT studies the relation of nanodosimetry and track structure in a multi-scale approach. http://www.ptb.de/emrp/bioquart.html

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Thank you for your attention!

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