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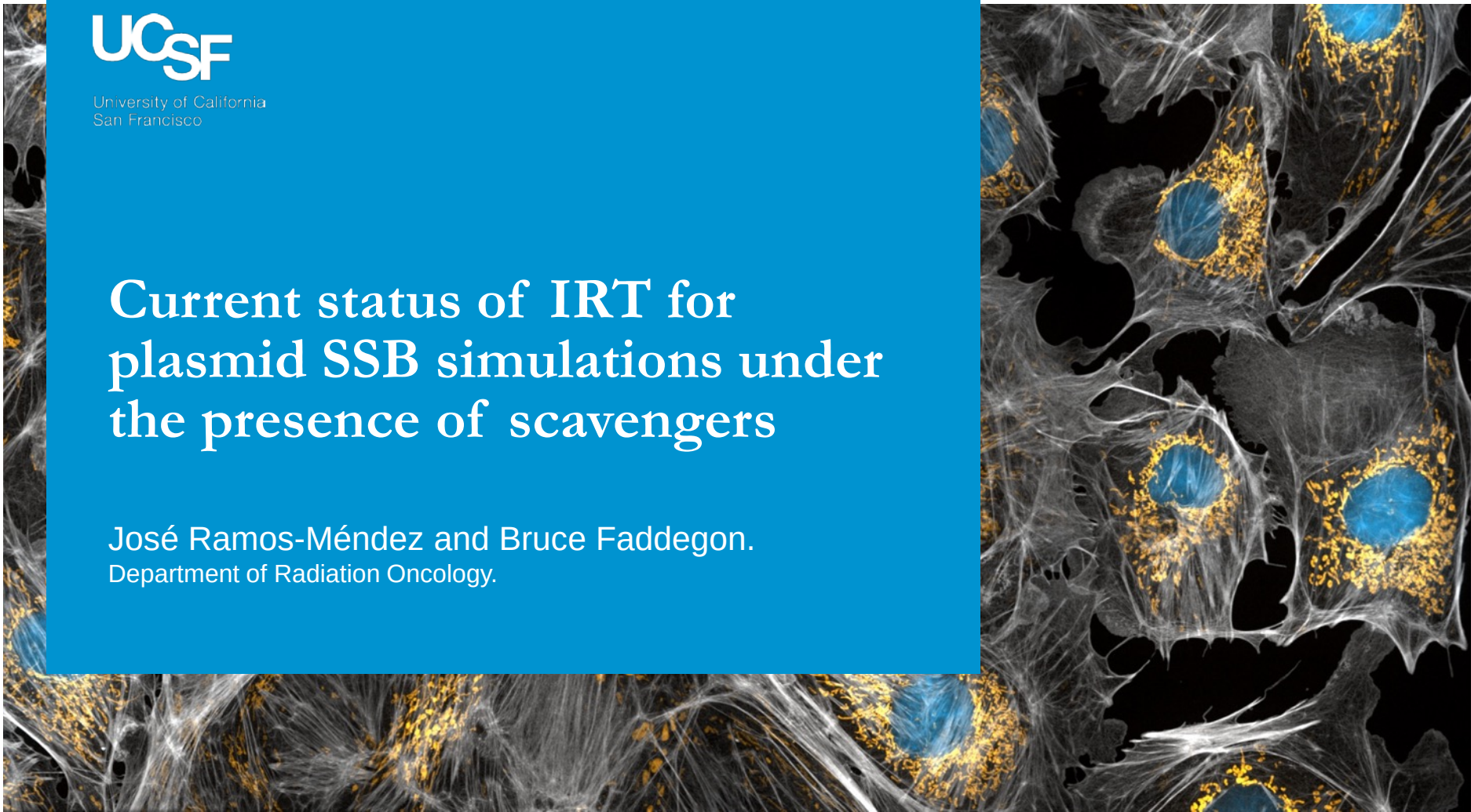
Current status of IRT for plasmid SSB simulations under the presence of scavengers

José Ramos-Méndez and Bruce Faddegon.
Department of Radiation Oncology.



In collaboration with:

- Carmen Villagrasa, Hoang Tran and Yann Perrot.
- Sebastien Incerti and Wook-Geun Shin.
- Shogo Okada.
- Václav Štěpán
- Naoki Domínguez-Kondo.

Outline.

- Independent Reaction Times.
- (Preliminary) Performance.
- Plasmid’s SSB: simulation setup.
- (Preliminary) Results.
- Future directions.

Independent Reaction Times.

IRT implementation into GEANT4

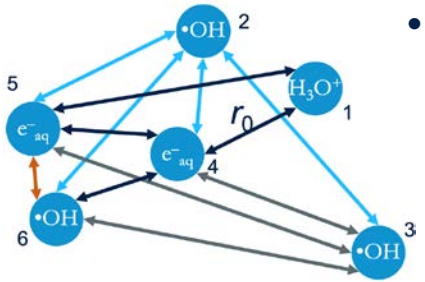
IRT approaches are currently being implemented by a dedicated working group within Geant4-DNA collaboration

- **The implementation will be compatible with the current chemistry "interface" (basic chemistry functionalities) to facilitate development and maintenance**
- Easy-to-use for the user: swapping between SBS to IRT changing the chemistry list via constructors or UI.
- E.g. chemistry constructors are in new examples: *chem5* and *dnadamage1* (session Parallel3B) and new example *chem6* (WG Shin et al., 2019 JAP. *In press*)

Two alternative IRT models are being developed

- IRT using the position approach (Clifford et al., 1986):
  - Faster approach, suitable for comparison with radiochemistry's experimental data: yields, scavengers, etc.
- Time-by-time – IRT position approach.
  - Facilitate interaction with geometry boundaries, parallel navigation, magnetic fields, etc.

Independent Reaction Times.



- The probability of reaction, $P(t \mid r_0)$, is given by the radial Green's function of the interparticle diffusion equation.

Reactive pair	Sampled time	Product (if any)
1+4	3 ps	7
4+5	6 ps	X
2+6	9 ps	8
2+4	12 ps	X
3+6	14 ps	X
5+6	47 ps	X
…	…	…
2+3	7564 ps	X

- By assigning random numbers U to the probability of reaction, random time values can be sampled after solving for t.

Classification of reactions

- Totally diffusion controlled (10 reactions)
  - $P_I(t \mid r_0) = \frac{\sigma}{r_0}\mathrm{erfc}\left(\frac{r_0-\sigma}{\sqrt{4Dt}}\right)$
  - $P_{III} = \frac{\sigma_{eff}}{r_{eff}}\mathrm{erfc}\left(\frac{r_{eff}-\sigma_{eff}}{\sqrt{4Dt}}\right)$
- Partially diffusion controlled (42 reactions)
  - $P_{II}(t \mid r_0) = \frac{\sigma\alpha+1}{r_0\alpha}\left[\mathrm{erfc}\left(\frac{r_0-\sigma}{\sqrt{4Dt}}\right) - W\left(\frac{r_0-\sigma}{\sqrt{4Dt}}, -\alpha\sqrt{Dt}\right)\right]$
  - $P_{IV} = \frac{\sigma''_{eff}}{r_{eff}}\left[\mathrm{erfc}(b) - W(a,b)\right]$
- First order (19 reactions)
  - $P_{VI} = 1 - \exp\left(-k[B]\Delta t\right)$

- Up to 72 reactions are available from the literature.
- However, between 14-22 (low and high LET) are recommended for water at neutral pH and ambient temperature.

Clifford et al., *J. Chem. Soc.*, Faraday Trans 1, 1986
Green, et al., *J. Chem. Phys.* 1990

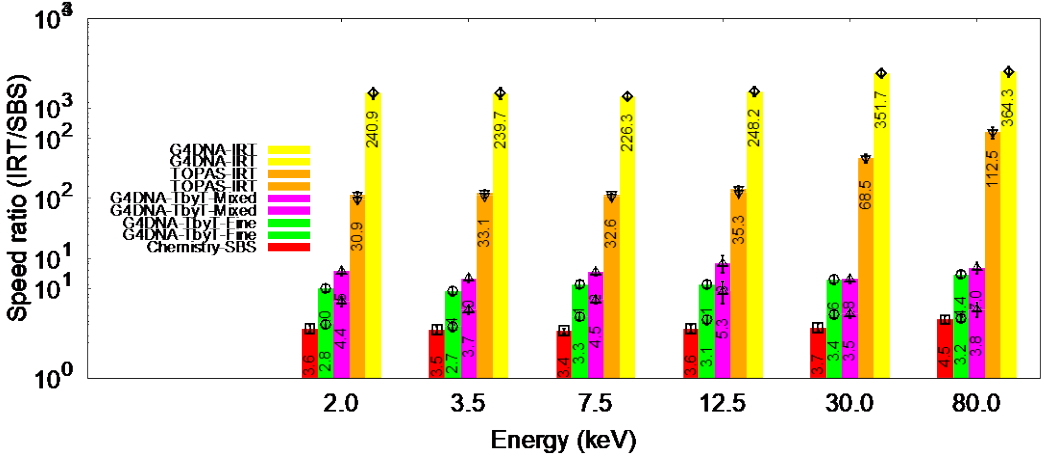
(Preliminary) Performance.

Performance (preliminary implementations)

- In all simulations G4EmDNAChemistry_option1 and G4EmDNAPhysics_option8 were used.
- G-values were calculated for electrons: 2, 3.5, 7.5, 12.5, 30 and 80 keV[1,2].

Time interval (s)	Δt (ps)
Until 10^{-11}	0.1
$10^{-11} - 10^{-10}$	1
$10^{-10} - 10^{-9}$	3
$10^{-9} - 10^{-8}$	10
Above 10^{-8}	100

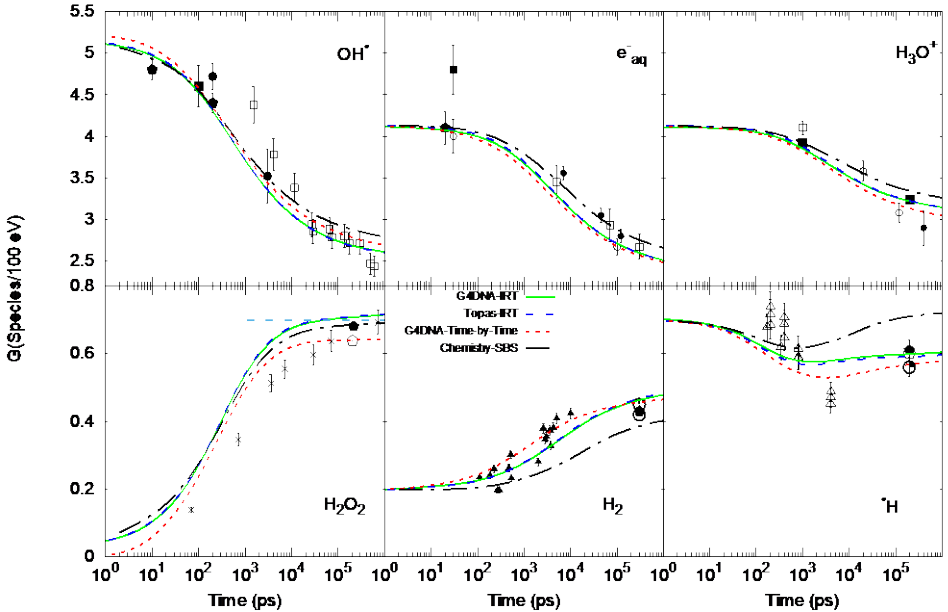
Average $LET_{100\,eV}$ (keV μm^{-1})
8.53 ± 0.32
4.91 ± 0.15
2.48 ± 0.07
1.82 ± 0.13
0.76 ± 0.06
0.42 ± 0.07
0.08 ± 0.01



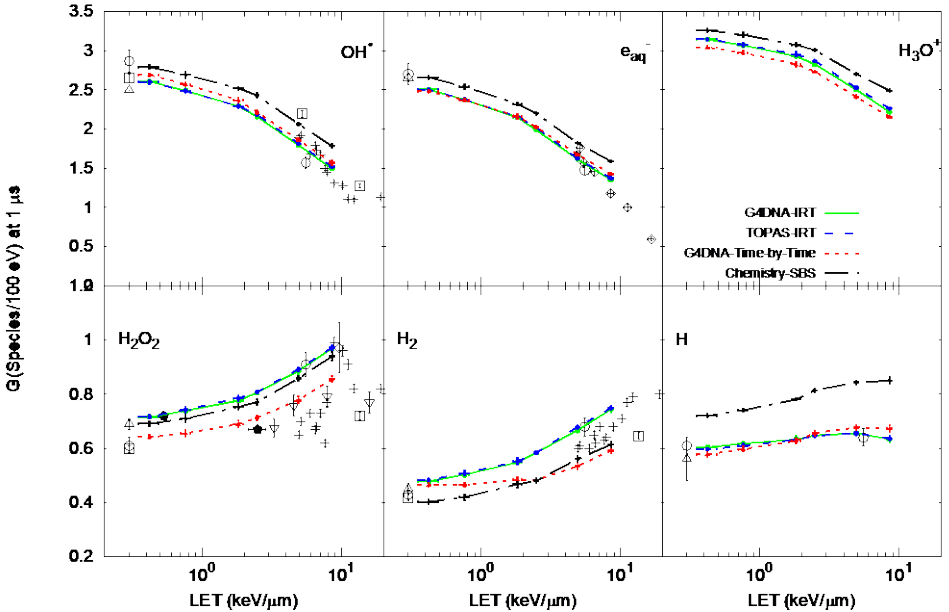
Speed ratio with respect to step-by-step simulations using the default time step resolution. Error bars represent 1 standard deviation for TbyT-style simulations. TbyT stands for Time-by-Time.

[1] WG Shin, et al., JAP, In press, 2019.
[2] Ramos-Mendez et al., Phys. Med. Biol, 63 105014-12pp 2018.
[3] Karamitros et al., *Prog. Nucl. Sci. Technol.* **2** 503–8, 2011

Performance (preliminary implementations)



Time-dependent G-values.



LET-dependent G-values.

For collected experimental data:

- Ramos-Mendez, et al., 2018 Phys. Med. Biol.
- Shin WG, et al., 2019 J. Applied Phys, In press.

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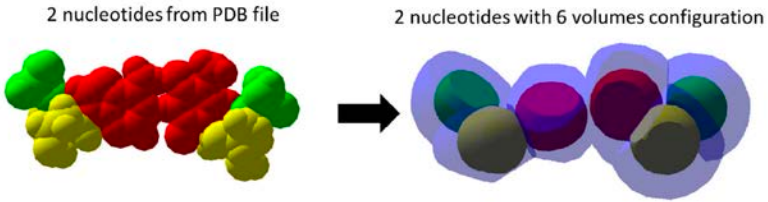
Plasmid's SSB: simulation setup.

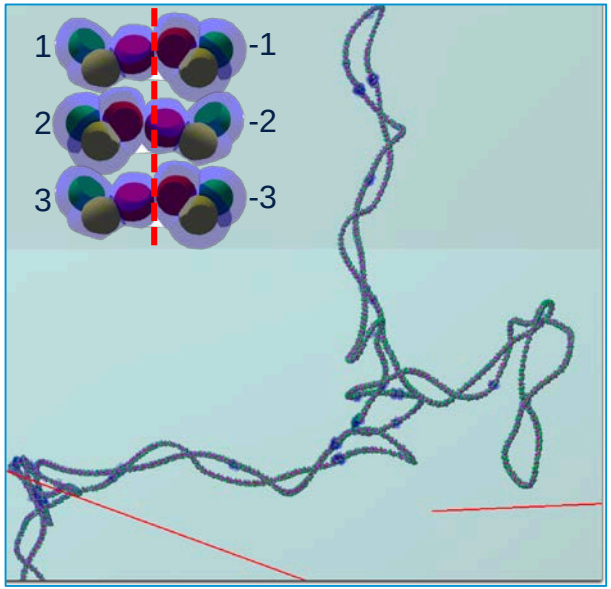
Integration of DNA components.

Reaction rates used between radicals and DNA components (x10^9 L/mol/s), from Buxton G, et al., 1988 *J. Phys. Chem. Ref. Data* **17** 513–886

	$^{\bullet}OH$	$H^{\bullet}$	e^-_{aq}
$C_6H_5O_6P$	1.8	0.029	0.01
Adenine	6.1	0.10	9.0
Thymine	6.4	0.57	18.0
Guanine	9.2	-	14.0
Cytosine	6.1	0.092	13.0



Phosphoric acid
2-Desoxyribose
Adenine, guanine,
cytosine and thymine
Hydration shell

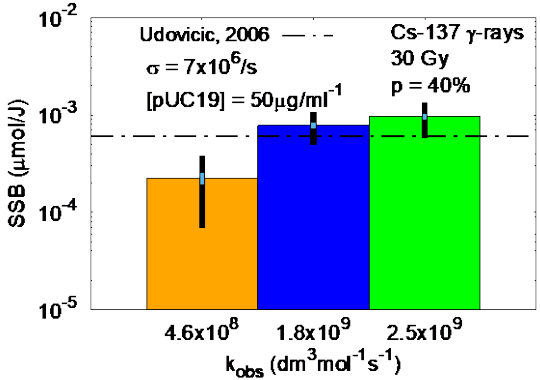


Plasmid pUC19
Václav Štěpán, at Nuclear Physics Institute
Czech Academy of Sciences

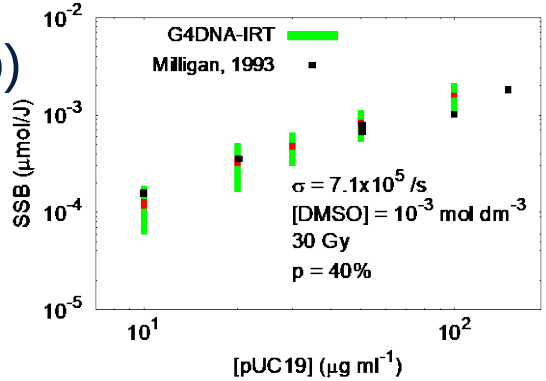
Image adapted from Meylan S, et al., **2015** *Comput. Phys. Commun.* 204:159-169

Results.

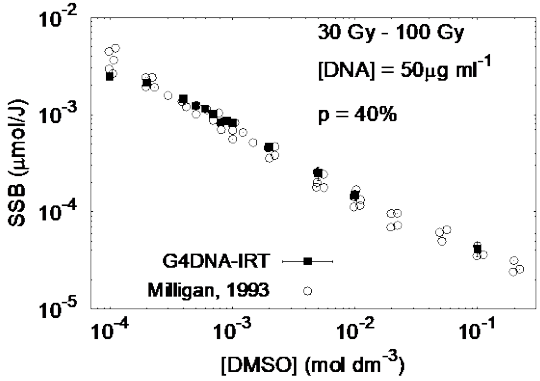
a)



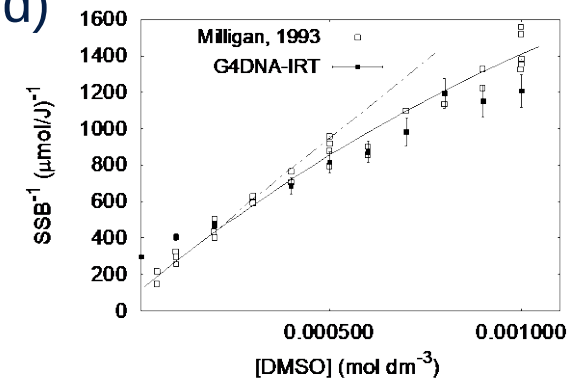
b)



c)



d)



Results with Cs-137 gamma-rays.

a) SSB yields for three published reaction rates. b) SSB as a function of pU18 DNA concentration (1ug/ml = ca. 10 plasmids in a sphere of 1 μm diameter). c) SSB as a function of DMSO concentration. d) 1/SSB as a function of DMSO concentration. Simulation setup in c) and d) is the same. 100 Gy for the highest concentration of DMSO.

Future directions.

Ongoing/Future work

- Performance evaluation are planned for LET-dependent G-values with protons, alpha and carbon ions. This will be performed with recently published physics and chemistry lists (Shin WG et al, JAP, 2019, *In Press*)
- Integration via a dedicated chemistry constructor.
- Integration via G4Scheduler.
- Limitations in performance was observed with different approaches.
  - Different applications should be used to test them, then we need also extent/add some examples, e.g. incorporating GNP.

Tentative release on next year's December release.

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