Structural Properties of Polyglutamine Aggregates Investigated via Molecular Dynamics Simulations

Giulia Rossetti,[a,b,c] Alessandra Magistrato,[b,a*] Annalisa Pastore,[d] Francesca Persichetti [a] and Paolo Carloni[a,b,c]

[a] International School for Advanced Studies, via Beirut 2-4, Trieste, Italy
[b]CNR-INFM-Democritos National Simulation Center, Beirut 2-4, Trieste, Italy
[c]Italian Institute of Technology – SISSA Unit
[d]National Institute for Medical Research, The Ridgeway London, NW71AA, UK

Supporting Information

Calculated Properties

- *g_rms* : calculates the root mean square deviation (RMSD)

$$\mathrm{RMSD}(t_1,t_2)=\left[\frac{1}{M}\sum_{i=1}^{N} m_i \|r_i(t_1)-r_i(t_2)\|^2\right]^{1/2}$$

where $M=\sum_{i=1}^{N} m_i$ and $r_i(t)$ is the position of atom *i* at time *t*.

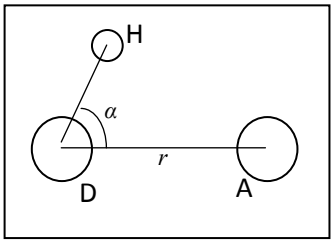
- *g_gyrate*: calculates the gyration radius (R_g)

$$R_g=\left(\frac{\sum_i \|r_i\|^2 m_i}{\sum_i m_i}\right)^{1/2}$$

where m_i is the mass of atom i and r_i is the position of atom *i* with respect to the center of mass of the molecule.

- *g_hbond*: analyzes the hydrogen bonds between all possible donors D and acceptor A. To determine if an H-bond exists, a geometrical criterion is used:

$r \leq r_{HB} = 0.35nm$; $\alpha \leq 60°$ where



r = donor-acceptor distance;
r_{HB} = the first minimum of the radial distribution function of SPC water;
α =hydrogen-donor-acceptor angle.

- *do_dssp* : analyzes the secondary structure element.
- *g_rmsf* : computes the root main square fluctuation (RMSF) of atomic positions after first fitting to a reference frame.

ADDITIONAL FIGURES FOR (I) LARGE MONOMERIC MODELS, (II) OLIGOMERS, (III) SMALL MONOMERIC MODELS

I) LARGE MONOMERIC MODELS

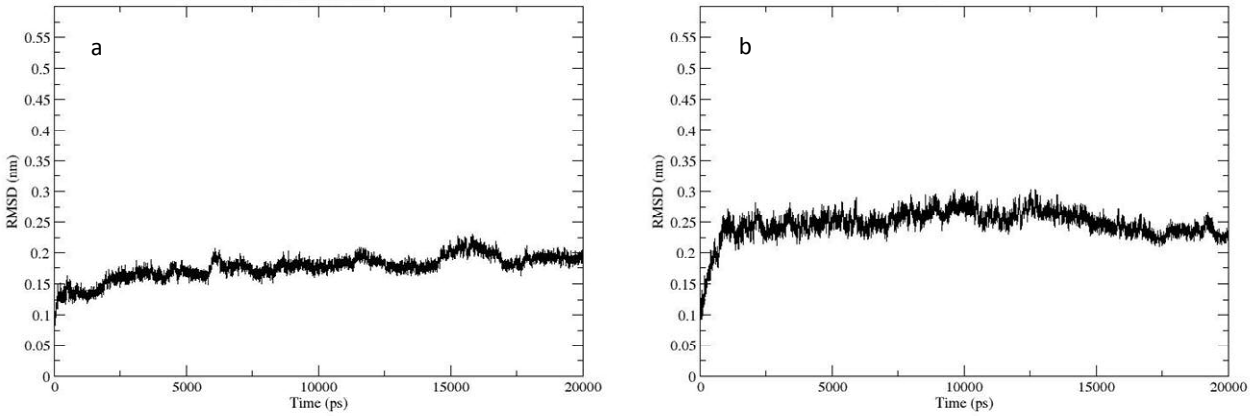


Figure SI.1: RMSD of P (a) and T (b) plotted as function of time.

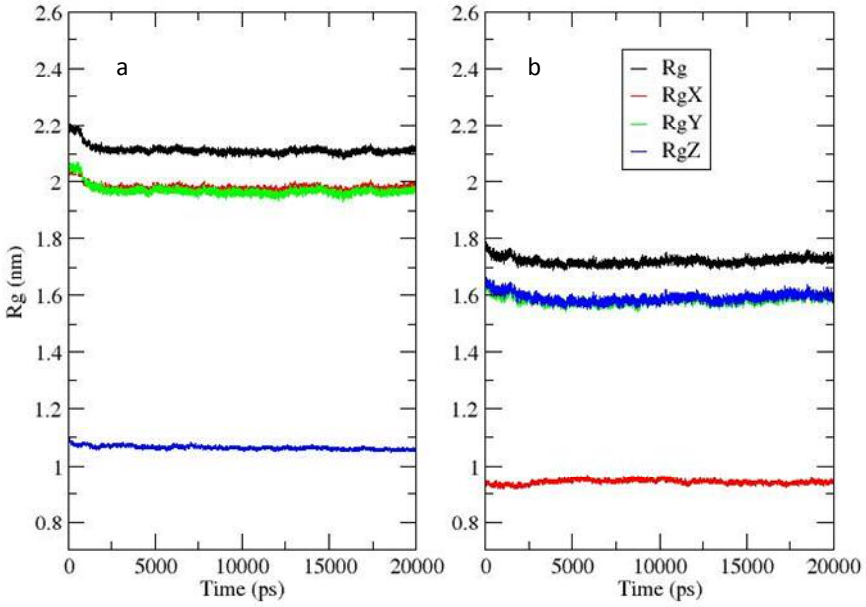


Figure SI.2: R_g of P (a) and T (b) plotted as function of time. XYZ components of R_g for both systems.

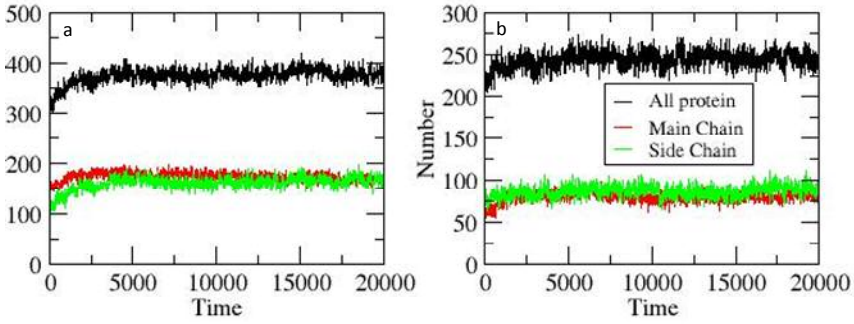


Figure SI.3: Number of HB of P (a) and T (b) plotted as function of time. The overall contribution, as well as the single contributions of the main chains and of the side chains, are also reported.

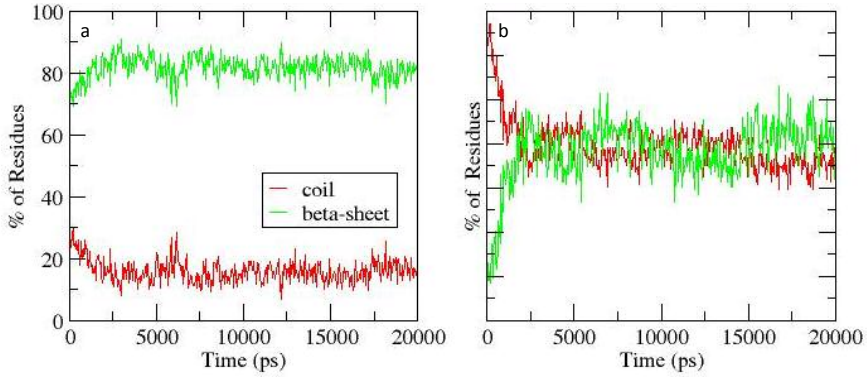


Figure SI.4: βSC and coil conformation of P (a) and T (b) plotted as a function of time.

RMSF

Flexibility. The root-mean-square fluctuations (RMSF) are relatively low, ranging between 0.05 and 0.25 for most residues (Fig. SI2). However, (i) the RMSF values of P are larger every 20 residues. This feature, which becomes even more evident in the final part of the structure, is caused by the fact that the 20th Q of each turn must be rather flexible to allow the β-helix to turn. (ii) The RMSF of T exhibits a minima every 6 residues. In this case, each turn is an equilateral triangle with 6 Qs side: the residues in the vertices – i.e. the 6th in the sequence – are the most constrained and the less flexible.

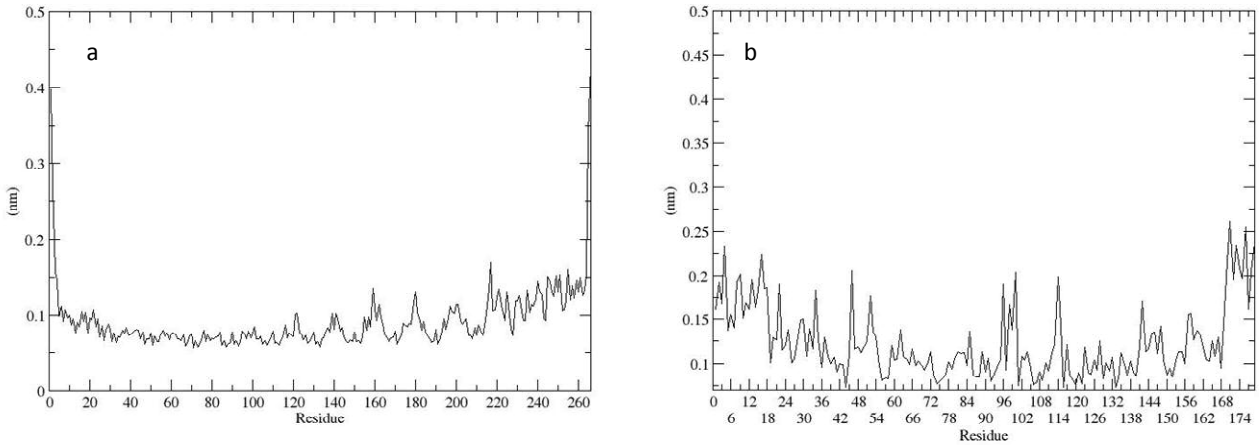


Figure SI.5: (a) RMSF of circular β-helix; (b) RMSF of triangular β-helix.

(II) OLIGOMERIC MODELS

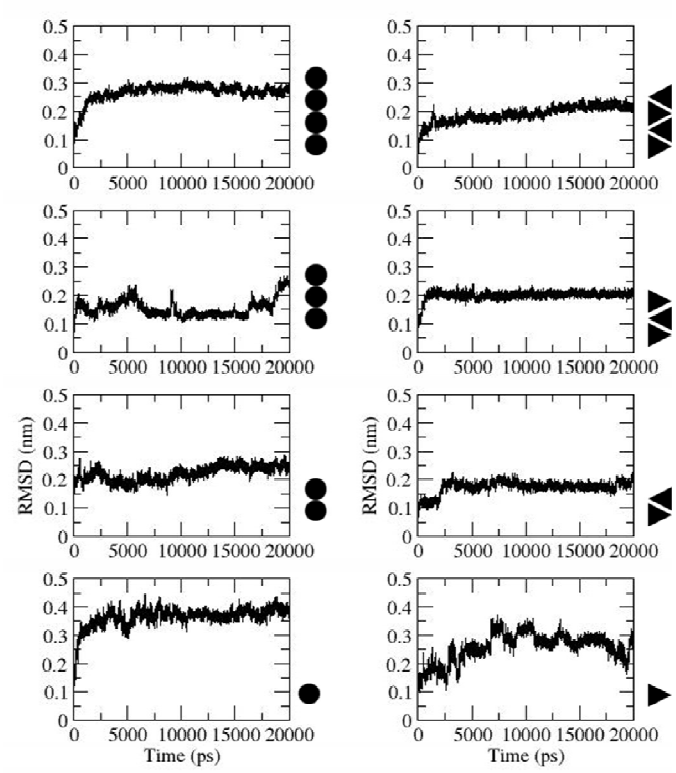


Figure SI.6: RMSD plotted as functions of time in the series of oligomers.

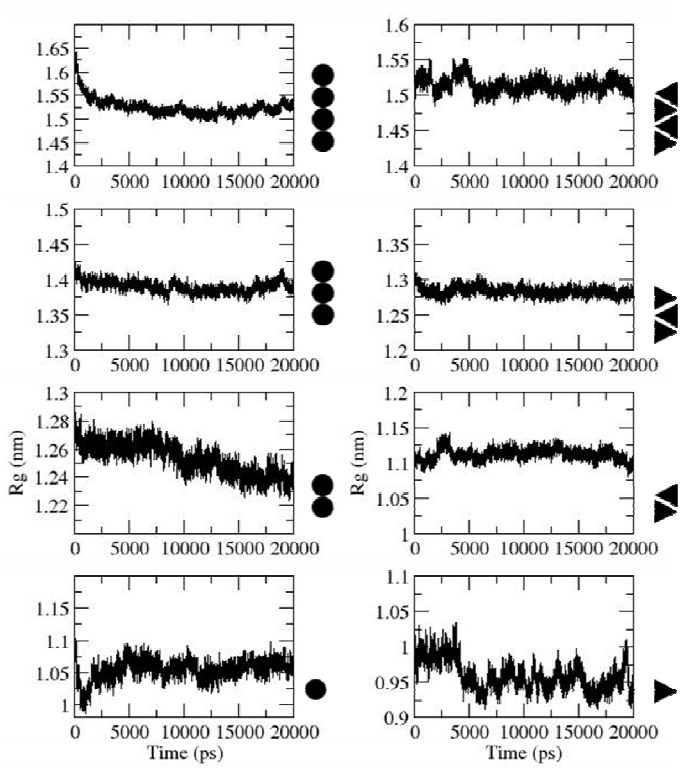


Figure SI.7: R_g plotted as functions of time in the series of oligomers.

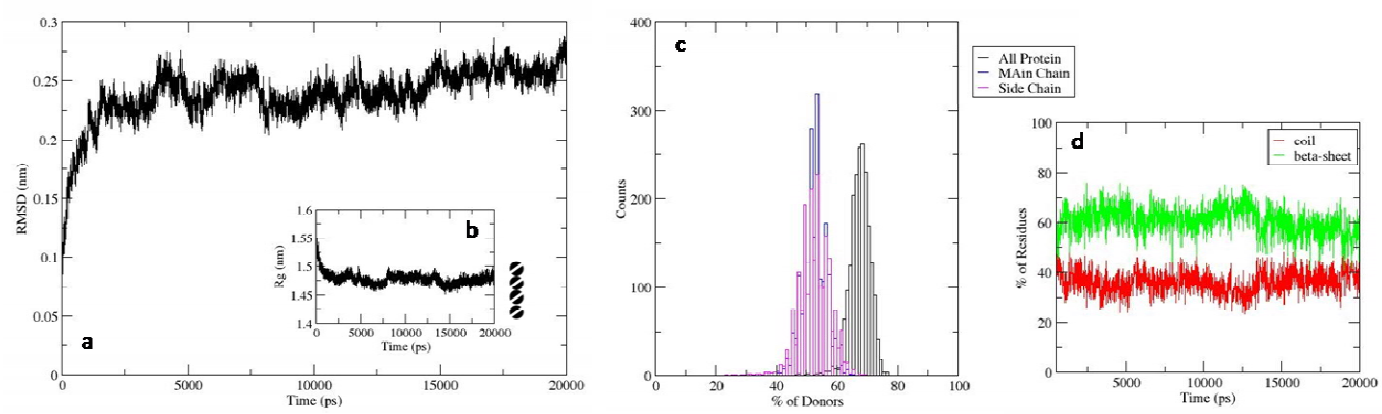


Figure SI.8: Oligomeric model built with monomers of 25 Qs (P_{AH25}): a) RMSD *vs* time; b) R_g vs time; c) hydrogen bond distribution; d) Percentage of residues in random coil (red line) and β-sheet (green line).

(III) SMALL MONOMERIC MODELS

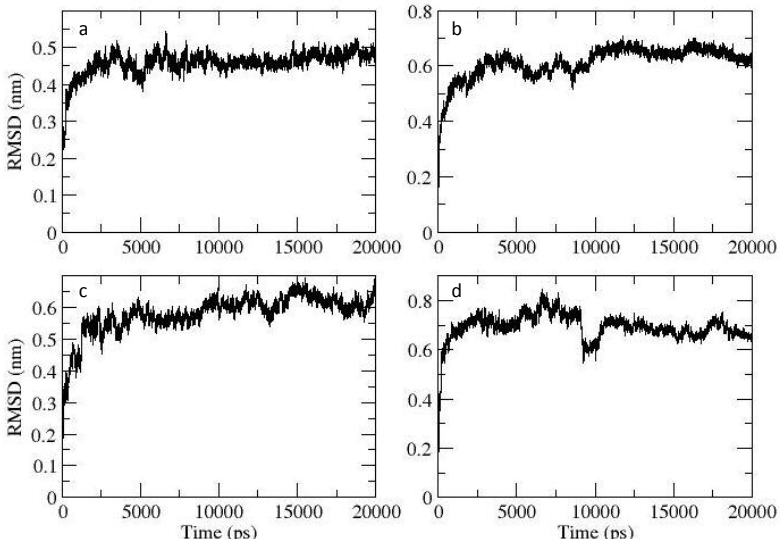


Figure SI.9: RMSD plotted as functions of time in the series of monomers: (a) monomer built with 40 Qs, (b) monomer built with 35 Qs, (c) monomer built with 30 Qs, (d) monomer built with 25 Qs.

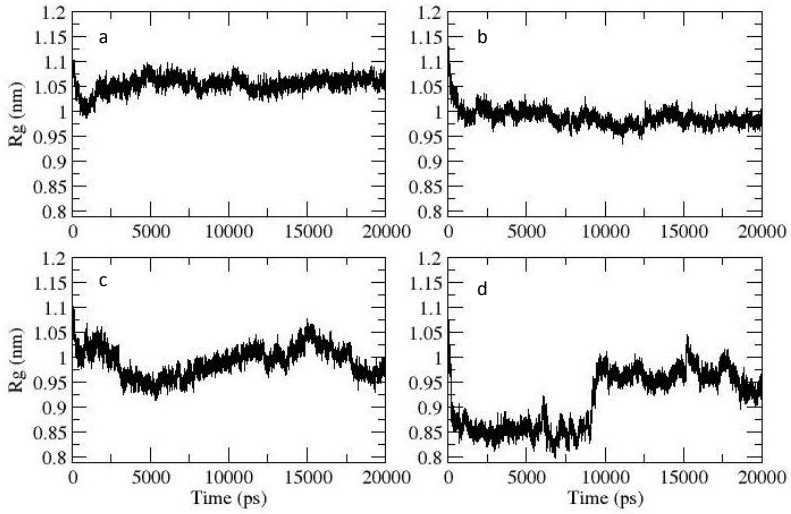


Figure SI.10: R_g plotted as functions of time for (a) monomer built with 40 Qs, (b) monomer built with 35 Qs, (c) monomer built with 30 Qs, (d) monomer built with 25 Qs.

Analysis of Hess(1, 2)

System	cosine content λ_1	cosine content λ_2	cosine content λ_2
P	0.84	0.15	0.05
T	0.31	0.19	0.66
P_{AD}	0.71	0.68	0.42
P_{AC}	0.08	0.01	0.24
P_{AB}	0.89	0.02	0.04
P_{A}	0.18	0.08	0.03
P_{AH25}	0.79	0.35	0.22
T_{AD}	0.90	0.14	0.07
T_{AC}	0.75	0.34	0.01
T_{AB}	0.35	0.15	0.44
T_{A}	0.86	0.05	0.02
40Qs	0.18	0.08	0.03
35Qs	0.76	0.08	0.02
30Qs	0.78	0.17	0.27
25Qs	0.76	0.12	0.28

Tab. SI.1: Cosine content of the first three eigenvalues for the systems studied.

1. Hess, B. 2000. Similarities between principal components of protein dynamics and random diffusion. Phys. Rev. E 62:8438.
2. Hess, B. 2002. Convergence of sampling in protein simulations. Phys. Rev. E 65:031910.