Title:

I am not very proud of the title. I think we could do better. The current version is “*i-DNA stability: confronting in vitro experiments with models and in cell data*” Feel free to propose alternatives!

i-DNA vs i-motif:

Both terms are fine, but I (JLM) agreed with the suggestion to mostly use i-DNA. I just left “i-motif” in the keywords, as i-DNA is not a convenient expression for text search (you will get Topoisomerase I-DNA for example). Just note that you can write “The i-motif” but would almost never write “The i-DNA” (same for B-DNA, or Z-DNA), except if you write “The i-DNA structure” (or topology, etc).

**Journal**:

We are considering PNAS. PNAS policy is 10 Proof pages, 7000 words in the main text, 10 Figures and Tables, 85 References.

Our main manuscript now has 8 Figures + 1 Table (OK then) but we may need to further condense the text. However, these limits are not very stringent, as some published PNAS papers are 11 page-long with 10000+ words.

**Suggested reviewers: (other names welcome !)**

* Cynthia Burrows
* Jonathan B. Chaires
* Ahn Tuan Phan
* Michaela Vorlickova ?
* Antonio Randazzo
* Avoid Zoe Waller ? Laurence Hurley ?

**Keywords:**

We selected more than five, only the first 5 will be used for online submission if there is a limit. There is no need to put i-DNA again here as it already appears in the title.

**Bullet points:**

* Lukas: I don’t think the sentence “i-DNA formation in human cells is established by *in vivo* NMR” gives proper credit to NMR. I added “relative in cell i-DNA stabilities parallel those found *in vitro”*... but suggestions welcome.

**About the different conformations**:

There is a misunderstanding between Laurent’s comments and Mingpan’s answer. There are four conformations possible for a given sequence. Refer to our 1994 paper on telomeric repeats. Figure 1 only shows two of them – you would have to add the cases where the external CC+ base pairs are the 5’ or 3’ ones.

**Eureka §:**

Alexandr, note that I tried to rewrite the last sentences of the § page 9. Check if OK: “Furthermore, the other Eureqa solutions found show comparable performance, due to the internal restrictions on the spacer lengths in the used experimental dataset (in most cases, two spacers being equal in length, hence some candidate solutions eliminating some of the spacers). The equations are consistent with our observations in the explored i-DNA subspace, and capture the stabilizing role of the lengthy middle spacer length (T2) within a given overall length of i-motifs.”

**Figure modification**:

* Mingpan:
  + Check my definition of 53E and give a reference in Figure 1 legend
  + may be change i-motif to i-DNA in Figure 2
* Lukas: I proposed to merge figures 7 and 8, this would require relabelling panels 7A / 7B / 7C.
* Aleksandr: for your figure (now figure 8), can you please
  + Delete the upper and right border lines, same to all other figures
  + Delete the 2x and 7348 at the down-right corner of panel B.

**About T111**:

Alex wrote: “Would be great to explicitly mention/emphasize here, whether (or not) pHt is high also as compared to T111? I.e. is longer central loop actually preferred in general, or is it the case that only if one long loop has to be present by definition, then it would be preferred to be at the centre.”

JLM: Note that T111 is perhaps not the best example / may be problematic as it can be intermolecular – I would avoid making this comparison.