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Automated oligopeptide formation under simple programmable conditions

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Introduction: Biopolymer formation (including nucleic acids and proteins) is one of the most relevant process towards origin of life. However, polymeric reactions include condensation processes which are thermodynamically constrained in an aqueous environment. Traditionally, in the case of peptides, many high-yielding reactions have been developed, but these are complex and use activated amino-acid precursors or heterogeneous supports [1].

Prebiotic chemistry has usually investigated the formation of life's precursors and their polymerization under very specific conditions. In contrast, we have explored the effect of several parameters at once on a model oligomerization reaction. We used a high-throughput automated platform – the 'abiotic peptide synthesiser' (APS) – that allowed us to run several reactions in parallel and automatically vary both the input and process variables. Herein, we show peptide bond formation from hydration/de-hydration cycles of unactivated amino acids, achieving yields of up to 50%, in which the majority of products are longer oligomers ($n \geq 3$) [2].

[1] Jakschitz TAE, Rode BM (2012) *Chem.Soc.Rev.* 41:5484. [2] Rodriguez-Garcia M, Surman AJ, Cooper GJT, Suarez-Marina I, Hosni Z, Lee MP, Cronin L (2015) *Nature Communications*, 6:8385, DOI: 10.1038.

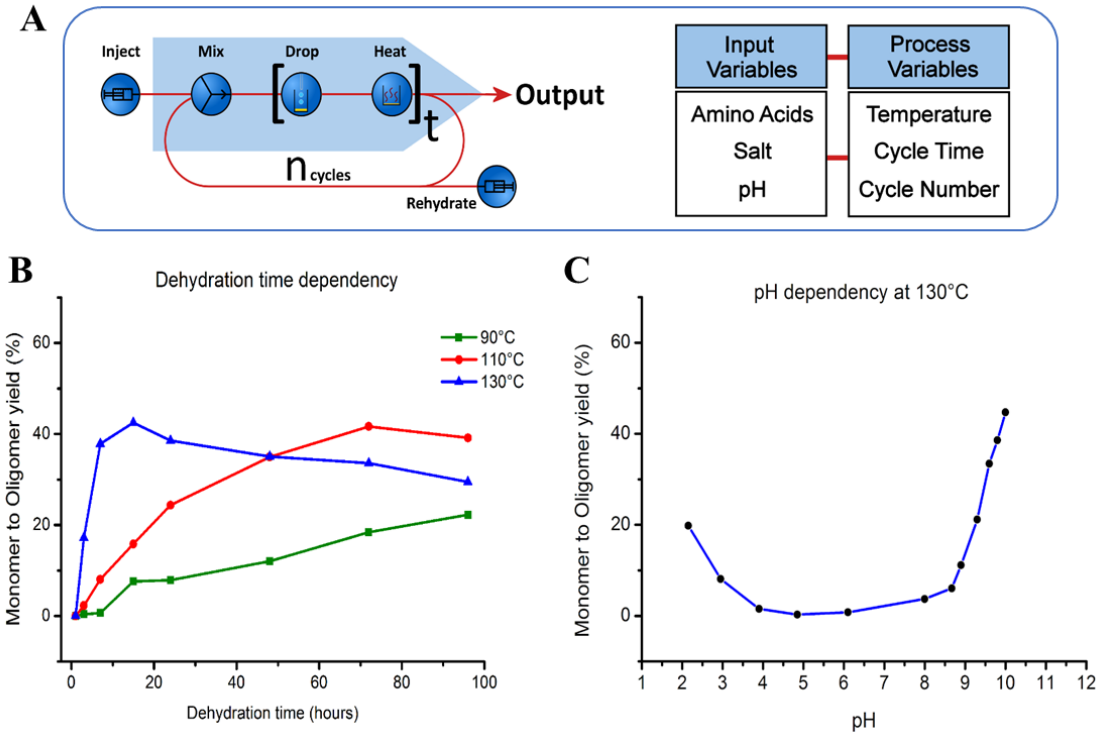

Figure 1 – **A.** Process flow diagram for the 'Abiotic Peptide Synthesiser' (APS) system. Reaction outcome is controlled by selection of input variables and process variables. **B.** Graph showing glycine oligomer yield from a single cycle as a function of dehydration time. **C.** Graph showing glycine oligomer yield from a single cycle as a function of pH (at 130ºC for 24 h).