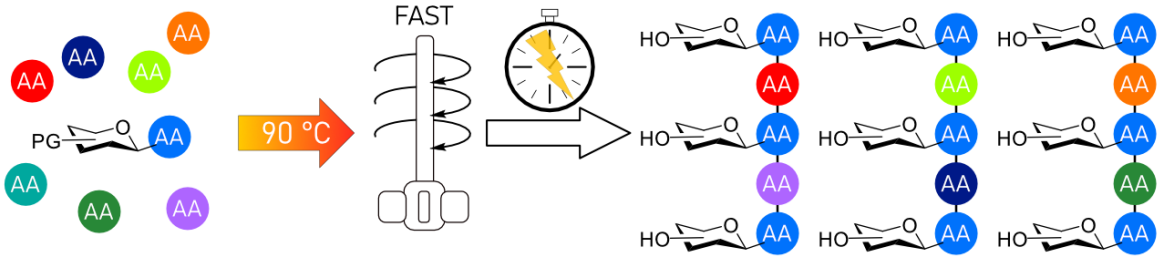
EXPEDITIOUS SYNTHESIS OF MULTIPLY GLYCOSYLATED PEPTIDES

Dror Ben Abba Amiel[a], Mattan Hurevich[b]

[a] Institute of Chemistry, The Hebrew University of Jerusalem, Edmond J. Safra Campus, Givat Ram, Jerusalem, Israel
dror.benabba@mail.huji.ac.il
[b] Institute of Chemistry, The Hebrew University of Jerusalem

Glycopeptide libraries with a high degree of purity are indispensable tools for investigating the effects of glycosylation pattern on interactions and function. Glycopeptides are prepared *via* a combination of solution- and solid-phase techniques, which require large amounts of protected glycosylated amino acids that are very difficult to obtain. The assembly of glycopeptides is very slow and inefficient due to the increased steric hindrance of glycosylated amino acids and their tendency to undergo substantial racemization. Finally, the deprotection of glycopeptides requires harsh conditions that are not compatible with the SPPS process. The above difficulties increase when peptides with multiple glycosylations are synthesized. These limitations make the state-of-the-art glycopeptide synthesis unattractive and the preparation of libraries hardly achievable.
We developed a new accelerated method for the efficient synthesis of a diverse range of peptides. The method utilizes a combination of high temperature and overhead stirring to assemble peptides within minutes [1]. Adaptation of this method provided an accelerated, racemization-free assembly of singly glycosylated peptides using equimolar quantities of glycosylated amino acids [2]. The method was further optimized to enable the rapid deprotection of the glycan on the solid support, thereby averting post-cleavage manipulations. We show that the accelerated method also prevails over the increased steric hindrance associated with multiglycosylated peptides and allows the simultaneous deprotection of multiple glycans. Thus, we are able to prepare high-purity glycoconjugates within minutes, while still using equimolar quantities of glycosylated amino acids. This presents a new path for obtaining a variety of glycopeptides in high purity and large quantities, which will allow for a better understanding of the role of glycosylation in biological systems.



References:
1. J.N. Naoum, I. Alshanski, G. Mayer, P. Strauss, M. Hurevich, *Org Process Res Dev* **2022**, *26* (1), 129–136.
2. D. Ben Abba Amiel, M. Hurevich, *European J Org Chem* **2022**, *2022* (38).