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**Irene Pala,
Executive Editor,
BMC Bioinformatics**

Bergen, July 11th, 2014

Dear Madam,

Please find enclosed a manuscript entitled “**WEBnm@ v2.0: web server and web services for comparing protein flexibility**” by Sandhya P. Tiwari, Edvin Fuglebakk, Siv M. Hollup, Tristan Cragolini, Lars Skjaerven, Sverre H. Grindhaug, Kidane Tekle and myself, Nathalie Reuter. We would like to submit this manuscript for publication to *BMC Bioinformatics*.

We have developed the first automated method allowing for the comparative analysis of a set of pre-aligned protein structures using Elastic Network Model (ENM) based Normal mode analysis (NMA). It has been implemented within the recently upgraded version of our early web server, WEBnm@¹, where our regular users can access both applications in one common framework. It has now been renamed as WEBnm@ v2.0. The concept behind this automated method lies in the fact that the function of a protein depends not only on its structure but also on its dynamics. NMA using ENMs has been shown to be a reliable and cost-effective computational method to characterise intrinsic dynamics of proteins that can be extended to studying larger datasets. Further insight into the dynamics–function relationship can be gained by studying the evolutionary divergence of protein motions, for example, and we provide the possibility for this type of analysis in our tool.

Although several web servers offering ENM NMA analysis of protein structures exist, to our best knowledge, none of them provide access to comparative NMA measures as in WEBnm@ v2.0.

WEBnm@ v2.0 has the added facility of programmable access via web services. This will enable the interested user to integrate the analyses developed for our web server with Workflow Management Systems, an emerging trend in bioinformatics. The beta version of WEBnm@ v2.0 has been available since 2012, and has had a steady stream of users (nearly 2500 unique users outside of Norway in two years²). We released the first version of WEBnm@ in 2005 and have continuously maintained and upgraded it, using state-of-the-art infrastructures. The current web server/services will be supported by the Norwegian bioinformatics platform through its Elixir.no infrastructure grant from the Research Council of Norway, thus ensuring its sustainability for the years to come.

We thank you in advance for your handling of this manuscript.

On behalf of all the authors,
Yours sincerely,

Nathalie REUTER, PhD

¹ Hollup et al., *BMC Bioinformatics* (2005) 6:52 [doi: 10.1186/1471-2105-6-52], cited 79 times according to Google scholar and 50 times according to ISI

² Source: Google analytics, number of unique visitors excluding users from Norway, and those sessions lasting for less than 5 minutes