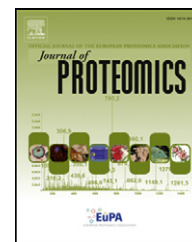


Available online at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/jprot

Review

The Monkey King: A personal view of the long journey towards a proteomic Nirvana☆☆☆

Pier Giorgio Righetti

Politecnico di Milano, Department of Chemistry, Materials and Chemical Engineering “Giulio Natta”, Via Mancinelli 7, Milano 20131, Italy

ARTICLE INFO

Keywords:

Proteomics
Two-dimensional maps
Immobilized pH gradients
Mass spectrometry
Combinatorial peptide
ligand libraries

ABSTRACT

The review covers about fifty years of progress in “proteome” analysis, starting from primitive two-dimensional (2D) map attempts in the early sixties of last century. The polar star in 2D mapping arose in 1975 with the classic paper by O’Farrell in *J Biol. Chem.* It became the compass for all proteome navigators. Perfection came, though, only with the introduction of immobilized pH gradients, which fixed the polypeptide spots in the 2D plane. Great impetus in proteome analysis came with the introduction of informatic tools and creating databases, among which Swiss Prot remains the site of excellence. Towards the end of the nineties, 2D chromatography, epitomized by coupling strong cation exchangers with C₁₈ resins, began to be a serious challenge to electrophoretic 2D mapping, although up to the present both techniques are still much in vogue and appear to give complementary results. Yet the migration of “proteomics” into the third millennium was made possible only by mass spectrometry (MS), which today represents the standard analytical tool in any lab dealing with proteomic analysis. Another major improvement has been the introduction of combinatorial peptide ligand libraries (CPLL), which, when properly used, enhance the visibility of low-abundance species by 3 to 4 orders of magnitude. Coupling MS to CPLLs permits the exploration of at least 8 orders of magnitude in dynamic range on any proteome.

Biological significance

The present review is a personal recollection highlighting the developments that led to present-day proteomics on a long march that lasted about 50 years. It is meant to give to young scientists an overview on how science grows, which ones are the quantum jumps in science and which research is of particular significance in general and in the field of proteomics in particular. It also gives some real-life episodes of greater-than-life figures. As such, it can be viewed as a tutorial to stimulate the young generation to be creative (and use their imagination too!).

This article is part of a Special Issue entitled: 20 years of Proteomics.

© 2013 Elsevier B.V. All rights reserved.

☆ This article is part of a Special Issue entitled: 20 years of Proteomics.

☆☆ A review for the Siena meeting, August/September 2014.

E-mail address: piergio.righetti@polimi.it.

Contents

1. Introduction	0
2. The early days	0
3. The polar star	0
4. The Mid-west Tornado	0
5. Mapping a star-studded sky	0
6. A firmament of fixed stars	0
7. 2D maps or 2D chromatography?	0
8. The proteome of the third millennium and the Monkey King	0
9. What about Pigsy, then?	0
References	0

1. Introduction

My first encounter with the Monkey King took place in April 1983 upon my first visit to China, in Shanghai. One evening a Chinese tovarish took me to a theater for a puppet show of this endless saga of the deeds of Sun Wukong (popularly known as the Monkey King). I had no idea what this was all about and the tovarish patiently gave me a résumé of the story. The saga, by the title *Journey to the West*, was written in the 16th century during the Ming Dynasty and attributed to Wu Cheng'en and seems to be one of the Four Great Classic Novels of Chinese literature. It is a fictionalized account of a legendary pilgrimage to India of the Buddhist monk Xuanzang (also known as Tripitaka) to retrieve and bring back to China the sacred Buddhist texts (the sutras). The novel is based on real events, though. Xuanzang, a monk in the early Tang Dynasty, left Chang'an in 629 bound for India to retrieve the original sutras via today's Kyrgyzstan, Uzbekistan and Afghanistan, via Gandhara, reaching his destination in 630 (interestingly, he traveled on the Silk Road East to West, whereas Marco Polo moved in the year 1271 in the opposite direction). He made a pilgrimage in the Indian subcontinent, visiting important Buddhist sites, which lasted 13 years. Xuanzang left India in the year 643 and in 646 arrived back in Chang'an, where he built the Big Wild Goose Pagoda in order to store the scriptures and icons he had brought back from India. In the fictional novel, though, things did not go so smoothly. Poor Xuanzang in his trip was constantly under threat from demons and other supernatural beings, as well as from bandits assaulting caravans on the Silk Road and had to have free access to the powers of Heaven to survive those ordeals (which amounted to no less than eighty-one tribulations). Heaven courteously furnished him with four super-natural creatures, of which two, the Monkey King and Pigsy, were the two most important characters providing help in dire straits (the other two, Sandy, a sort of marine deity, and Yulong, a dragon king transformed into the white horse the monk rode upon, being secondary figures in the plot). The super-hero, though, was the Monkey King, a creature endowed with extraordinary super-powers, always appearing, as the *deus ex machina* in the Greek tragedies, to save the monk when in peril and risking life. The puppet show was so extraordinary that at the end I wanted to visit the two artists back-stage and see vis-à-vis those artistically carved wooden puppets. That is not the end of the story, though. In December 2012 I attended a meeting in Singapore and I learned about the Haw Par-Villa, a theme park

located along Pasir Panjang Road, also known as the Tiger Balm Garden, since the two Haw-Par brothers who built it in 1937 had become extremely rich via the sales of this popular herbal medicine (Tiger Balm), supposed to be endowed with healing properties and soothing relief for aches and pains and giving a sense of wellness to body and mind. One of the major attractions there includes dioramas of scenes from *Journey to the West*, represented by life-size gypsum statues. There, of course, the Monkey King is the main character, as you will see depicted in Fig. 1, battling against the Scarlet Child (the figure on the right, a demon transvestite as a young and charming person). I confess, my guide (Lonely Planet) did not recommend its visit but, upon suggestion from a local friend, I visited it and it was most amusing!

What such a strange introduction has to do with the celebration of the 20th anniversary of proteomics I hope will become clear as this tale unfolds and if you are patient enough to read through it.

2. The early days

In 1971, upon returning home after four years as a post doc at MIT and Harvard, I was hired at the State University of Milano at the Faculty of Agriculture. Soon I was engaged in plant research, in particular in the study of the storage proteins of maize, the zeins. In those days, the dogma of one-gene one-protein was still well engrained in the scientific community. Yet, via very primitive attempts at performing two-dimensional (2D) maps, we found a rather extended heterogeneity of these proteins, proven not only electrophoretically but also via short sequencing with the Edman degradation. Yet it was a rejection crisis from journal to journal and we were forced to publish our data in a not so visible journal, *Maydica*, funded by a leading authority in the field of corn genetics, Francesco Salamini [1]. Nevertheless, the idea of trying to spread a large number of components on a two-dimensional surface was not a peregrine one. Long before our less than satisfactory attempts this principle had been expounded already in 1964 by Raymond [2] in a method dubbed Orthacryl (orthogonal acrylamide gel electrophoresis). He correctly noted that if the gel and other experimental variables are identical in both directions, the ratio of migration rates in the two gels would be the same for all components. Therefore all the species in the specimen under

Download English Version:

<https://daneshyari.com/en/article/7636184>

Download Persian Version:

<https://daneshyari.com/article/7636184>

[Daneshyari.com](https://daneshyari.com)