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BIOSTATISTICS NOW

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1. 1901. THE ORIGIN

This Special Issue gives me the opportunity to resume the ongoing debate on the definition of biostatistics and its current evolution. A debate which has continued over a century in respected specialist journals. When in 1901, Galton, Weldon and Pearson presented the first issue of a new magazine, in its title *Biometrika* coined a term to which at the time did not correspond to any established meaning and nor did they concern themselves with providing content which was not simply the objective of the magazine itself.

In the opening lines of the editorial, (Biometrika, vol. I, No. 1, 1901) Karl Person wrote: "It is intended that *Biometrika* shall serve as a means not only of collecting under one title biological data of a kind not systematically collected or published in any other periodical, but also of spreading a knowledge of such statistical theory as may be requisite for their scientific treatment".

This objective enabled all the currently flourishing quantitative research in systematic biology on the revolutionary theories of Darwinian evolution by natural selection to be gathered into a single, unified body (I. Scardovi, 2009). The idea of creating a newspaper entirely devoted to quantitative studies of the theory of evolution by natural selection that would collect all types of naturalistic research had long been in the thoughts of scholars of the time. In a letter dated 1900 to Pearson, Weldon writes: "The contention 'that numbers mean nothing and do not exist in Nature' is a very serious thing, which will have to be fought. Most other people have got beyond it but most biologists have not. Do you think it would be too hopelessly expensive to start a journal of some kind?" (D.R. Cox, 2001).

Pearson also wrote about the need of addressing the observation of biological phenomena through quantitative methods: "These, and many other problems, involve the collection of statistical data on a large scale. That such data may be rendered intelligible to the mind, it is necessary to find some way of expressing them by a formula, the meaning of which can be readily understood, while its simplicity makes it easy to remember. The recent development of statistical theory, dealing with biological data on the lines suggested by Mr. Francis Galton, has rendered it possible to deal with statistical data of very various kinds in a simple

and intelligible way, and the results already achieved permit the hope that simple formulae, capable of still wider application, may soon be found". He then added: "The number of biologists interested in this question, and willing to undertake laborious statistical enquiries, is already considerable, and is increasing. It seems, therefore, that a useful purpose will be served by a journal especially devoted to the publication of statistical data, and of papers dealing with statistical theory. (…) Further, *Biometrika* will endeavour to introduce a uniformity of statistical treatment, terminology, and notation, so that results obtained by different investigators on different types of life may be easily and effectively compared".

Over time the word "biometry" was enriched in meaning and purpose and has finally restrained its area of expertise to statistical methods for the analysis of biological phenomena, somewhat betraying the unified vision of science that had so animated its creators. The evolution of editorial line has created a rift between those who know the methods and those who know phenomena. So, after a century it is no longer clear whether there is still a united disciplinary body that is recognized in the terms biometrics or biostatistics.

A discipline cannot be just a collection of techniques, many of which are communal assets to the most varied areas of phenomena and can all be essentially reduced to the great body of statistical methodology. It is more constructive to speak of biostatistics disciplines as being under a broad umbrella, including medical, biological and natural research, which cannot fully be expressed without statistical language (G. Molenberghs, 2005). With this, it is not suggested that we simply understand the research that makes extensive use of classificatory or inferential statistical techniques for data analysis, we mean above all, to unite all the phenomena of life that can only be expressed with the language of probability and statistics under a single conceptual category.

In this sense, biostatistical methodology has its roots in a line of thought that English empiricism has evolved into an autonomous body of research through the contributions of probability and statistical methodology. The convergence of biology and statistics, successfully begun in the last century when the unity of the sciences itself became the undisputed principle of natural and social research, today finds new inspiration from the influence of a strong methodological unity.

In scientific research one truly needs to have a multidisciplinary and interdisciplinary approach to create more effective synergies in the various fields of knowledge and at the same time we are expected to be highly specialized in order not to waste resources on divergent lines of interest that can distance the research from the expected result. Exasperated specializations, typical of these times, have confined scientists on independently evolved linguistic islands, in a type of cultural drift which is very similar to the processes of genetic drift that has differentiated the species.

To overcome this increasing inability to communicate, we believe that the language of biostatistics can provide an effective synthesis of scientific knowledge and investigative techniques.

2. THE TROUBLES OF INTERDISCIPLINARY

The evolution of the biomedical sciences calls for a careful and specific critical analysis. From early anatomical studies to current computerized diagnostic techniques, the need has been suggested for an authentic scientific reassessment of medical research. This is especially true for someone who, having shown a preference for the bio-statistic disciplines, repeatedly found herself involved, not without profound disillusionment, in joint research groups. Above all, the problems relate to the current unsatisfactory situation which seems to be characterized by the uncritical and repetitive use of statistical techniques, more inspired by the need to appear methodologically up-to-date rather than being an authentic, phenomenally motivated choice. Unfortunately this seems to be a common attitude within all sectors of research, and not only those medical or naturalistic.

This is evident not so much from the scarcity of a statistical culture but more from the lack of experimental spirit, of scientific curiosity, of that methodological rigour, which should always lead to the search for the most appropriate criterion for providing rational and coherent answers to the individual questions posed (J.H. Ellenberg, 1990).

Nowadays too many researchers seem to prefer to withdraw into their own self-sufficiency, without making any attempt to initiate authentic interdisciplinary teaching involving experienced statisticians. This has caused alarm in the more advanced scientific fields provoking the concerned intervention of illustrious scientists.

Precisely from the pages of one of the most prestigious international journals, *Biometrics* (1983), in an animated discussion about the bio-statistical disciplines, a group of scholars, including physicians, biologists and methodologists, feared the diffusion of a continually less rigorous mode of operating, which depended only upon contingencies (M. Zelen, 1983). The lack of an accurate research plan shows the rare practice of the so-called "statistical design of experiments": a scientific way of thinking which also offers the technical instruments for a coherent analysis of the data. In fact, statistics are more frequently used to resolve the irremediable inconsistencies of an inadequately organized investigation, rather than to design a well-structured research plan.

This lack of integration, continually enlarging the cultural gap which renders the various languages irreconcilable, is a characteristic of medical culture where the incomprehension of statistical experimental questions may even become a reason for boasting in the false conviction that intuition is the only winning arm in medical practice. But one should not confuse the ability to hit upon the correct diagnosis with the ability to carry out research. The greatest discoveries in medicine have virtually never come from professional clinicians, who are more concerned with curing the symptoms rather than finding the causes. Just consider the fundamental contributions to human knowledge and to medical health made by genetics, biochemistry, microbiology, pharmacology and bioengineering which modern medicine uses, often without having collaborated in any way.

One of the greatest dangers of current biomedical investigation derives more from the scatterbrained use of computer software with the abuse of pre-packaged statistical tools rather than the difficulty in expressing a hypothesis for working within the rigorous methodological practices of quantitative research. The erroneous conviction that a marketed computer program can automatically process any set of observations leads to the treatment of different problems in a standardized and often improper manner, leveling out the results. This inevitably ends up in an avoidance of the essential step of defining the requirements of the research itself, or the working hypothesis.

Only an incompetent or an idiot - it has been written - could delegate a diagnosis to a computer, because automated diagnostics represent only one of many pieces of information used to associate the most probable causes with given symptoms. To believe that an "expert system" or a "statistical package", however wide ranging, could offer a coherent solution to any concrete problem of quantitative analysis in the real world means suffocating any incentive towards innovation, any element of creativity. If the researcher suddenly ceased to invent methodological criteria adequate for controlling his own working hypotheses, scientific research would lose its instruments for supplying different answers to different problems, and statistical method itself would be reduced to being a sterile apparatus, incapable of renewing itself, and therefore destined to failure. Standardization of methods suffocates speculative thought.

The incumbent danger of delivering oneself to automatic data management, neglecting the conceptual step of statistical analysis of the phenomena, often ignored by statisticians themselves, more oriented towards the computing aspect rather than methodological questions, is clear to the most illuminated scientists. "The concentration by statisticians on improving computer hardware and especially software sometimes tends to inhibit creative thinking in statistical methodology" is the point of view of Bernard Greenberg (1983). Peter Armitage (1985) warns physicians and biologists against using computing tools without the rigid control of a statistician, who is invited not to be too complacent. The statistician, according to Armitage, should not only cooperate with the identification of the statistical aspects of the problem and with the search for the most coherent solutions, but should also convince whoever uses statistics that it is "an important discipline which can not be left wholly to the amateur".

3. THE STRENGTH OF INTERDISCIPLINARY

In spite of the trivial use of statistical techniques in so much biostatistics research, I am certain that many original contributions lie hidden in the redundant heap of scientific literature and only time can be the judge of what will really represent methodological conquest. On a more optimistic note, it should not be forgotten that the most important contributions to statistical method even today, as in the past, still come from the most advanced biological research. The ingenious attempts of the late-nineteenth century biometricians searching for quantitative

confirmation of the theory evolution of the species by natural selection, from which the origins of studies on the transmission of characters came, were responsible for suggesting the mathematical solutions which led to the composition of correlation theory and laid the first foundation stones of multivariate statistical analysis. It was precisely upon these themes that Fisher found his inspiration to attempt his splendid statistical systemisation of Darwinism and Mendelism by a rigorous theorematic formalization which already contained the methodological seeds of the design of experiments, the analysis of variance and discriminant analysis, later widely developed with the theory for testing statistical hypotheses and statistical estimation.

Precisely for this reason Fisher was asked in 1947 to chair the International Biometric Society, and to give life to Biometrics, the new journal which would become a true competitor for *Biometrika*, which again brought about the opposition, although ideal, between Karl Pearson and Ronald Fisher (S.M. Stigler, 2007).

Over time many sources have been enriching the methodological body of biostatistics. For example, the requirements of psychologists at the beginning of the twentieth century, who were faced with the variability of answers given to intelligence/ability tests and the attempts to distinguish between the components to be attributed to the intelligence levels of the subjects (specific ability or accidental factors) led to the definition of the methodological characteristics of factor analysis, principal components, latent factor analysis and correspondence analysis.

Even in more recent times statistical techniques have been enhanced by original proposals founded in the midst of modern biology. In the second half of the last century, the theory of stochastic processes found new results in genetic studies, while cluster analysis exacted new solutions from biological research. For example, partitioning techniques in terms of variance decomposition or dissimilarities measurements are now the basis of statistical methods for genetic studies. To mention some of the more recent methodologies useful for psychological studies, statistical catastrophe theory itself has its origins in the modeling of psychophysical behavior. In a similar manner the recent, and very fashionable, fractals theory, in the graphical description of anatomical microstructure seems to be a fruitful field of investigation.

In these few but emblematic references and in the many that could be might have been cited, the essential role played by a well-educated experimental aptitude systematically emerges (A. Mead, 2009).

During the last century a strong consciousness of the close links between phenomenal variability and observation tools, working hypotheses and testing rules, models and empirical data has been emerging. From this consciousness a technical and methodological apparatus has been generated in which the statistical *modus operandi* has found a natural extension in the Galilean experimental method and has offered an operating system to decompose statistical phenomena into its components, to recognize constants in variability and to distinguish the different kinds of variability.

Grosenbaugh's words in 1947 could become a real warning to all of us: "The advances in biometry have developed through the close cooperation of biologists

confronted with problems and of statisticians who develop methods for solving them. Both have gained from this collaboration".

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SUMMARY

Biostatistics now

This paper offers reflections on the biostatistic sciences, from their origin to the present, following the path of two historic and prestigious journals: *Biometrika* and *Biometrics*.