## "Control(led) experiments" in historical and philosophical perspective

By: Jutta Schickore

Arguably, the introduction of controls is a key methodological tool in scientific experimentation. Yet there are surprisingly few historical and philosophical studies of the concept of experimental control, and what little there is does not form a coherent picture. There is some work specifically on the emergence and career of randomized controlled trials, focusing on 20th century psychological and medical research (Hacking 1988, Keating and Cambrosio 2012). Often R. A. Fisher's agricultural experiments from the early 20th century are presented as a milestone in the discussion (e.g. Hall 2007) Some historians have hinted at a connection between controlled experiments and the process of industrialization and have argued that the concept of experimental control emerged in the mid- or late 19th century (Figlio 1977, Pauly 1987). Other scholars have suggested that controlled experiments were already performed in the late 18th century (Dunn 1997); yet others date their origin back to the Middle Ages (Crombie 1952) and even to Antiquity (Knoefel 1988, Stigler 1974).

The historiographical conundrum has not been tackled; and broader systematic analyses of the concept, the epistemological significance of the practice of controlling, or the conditions of the emergence of the methodological idea behind experimental controls do not exist. In this paper, I seek to prepare the ground for such a broader analysis. I offer a historical and philosophical interpretation of control(led) experiments in the biomedical sciences, focusing on the second half of the 19th century. I disentangle different strands of the history of control(led) experiments, draw some crucial conceptual distinctions among different meanings of the concept of control, and identify a number of questions that a historical and philosophical analysis of control experiments need to answer.

First of all, it is obviously important to distinguish between the emergence of the terms "control experiment," "experimental control", etc. and the history of the methods or strategies of experimentation that these terms refer to. Based on this distinction, a simple solution to the historiographical conundrum suggests itself: Perhaps the experimental strategies that came to be called "controls" had been applied long before the introduction of the term – maybe already in Antiquity – even though the methodological terms "controlling", "control experiment," "(experimental) control", etc. emerged in the second half of the 19th century? However, it seems to me that if we adopt this solution, we overstate the similarities between experimental strategies, and we downplay differences in the different contexts and historical settings in which these strategies were applied and in the significance that past experimenters attached to them.

I begin my presentation with a survey of concepts of control in late 19th-century bacteriology, immunology, and experimental embryology. I pay particular attention to the works of influential and methodologically reflective investigators, especially William Henry Welch, Paul Ehrlich and his co-workers, and Jacques Loeb. The concept of control plays an important role in all of these works. But it is used in at least three ways: to refer to a strategy that "controls for"

the impact of specific factors on the outcome of experiments, to refer to a practice that corrects for unknown variables in the experiment, and to refer to the calculated design of new forms of organic life.

In the second part of my paper, I consider several 19th-century methodologies of experimentation that had an impact on methodological thought in late 19th-century biomedicine, namely the methodologies advocated by the French clinician Pierre Louis, John Stuart Mill, Claude Bernard, and the German embryologist Wilhelm Roux. While none of these methodologies mentioned the concept of control, each of them introduced strategies of securing experimental results that involved elements of comparison. But there are significant differences with regard to what was compared and for what purposes. According to Louis, experiments could be made more secure by comparing two populations, one of which receives treatment. According to Mill and Roux, causal factors can best be identified if two experimental situations are compared in which all conditions are held constant except the one under study. According to Bernard, experiments could be made more secure if a specimen is compared to a second, which is subjected to the same treatment except for a change in the variable under study.

In the third part of my paper, I bring the first two parts together and draw out a number of implications for a historically and philosophically informed account of control(led) experiments. Obviously, "the" history of experimental controls does not exist. Rather, we need to distinguish at least two traditions in the discussion about controls, the comparison of populations and the comparison of individual experiments. The works of Louis and Fisher are part of the first tradition, but during the 19th century there was little discussion about the problem of comparing populations (Coleman 1987). The second tradition – the most relevant for methodological thought in late 19th-century biomedicine – includes works by Mill, Bernard, Roux, Welch, Ehrlich, and others. In this tradition, the introduction of the term "control" came together with a loss of trust in the practical applicability of Mill's method of difference. We find criticisms of Mill's method in the writings of both Bernard and Roux. The concept of control came to be used after these experimenters had advanced the view that Mill's methodology of experimentation expressed an unattainable ideal, and that Mill's method could not address the most pressing problems of scientific experimentation in the life sciences – the complexity of living things. Finally, Jacques Loeb's notion of "control" is the only concept that can be traced to an engineering context (Pauly 1987). But if we read Loeb's work against the background of contemporaneous methodologies, it becomes immediately clear that he did not use the term "control" in a methodological sense.

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