Jutta Schickore (Bloomington) REPETITION, VARIATION, & CONTROL HISTORICAL PERSPECTIVES

"Methods Discourse"

- Methods-related statements and criteria that past experimenters themselves proposed.
 - E.g.: An experimental finding should be reproducible
- I use present-day concepts and distinctions (e.g. "replication") but I also pay attention to past actors' terms (e.g. "imitation")
- I pay particular attention to the ways in which and where past scientists discuss methodological issues and whether they offer justifications for methodological views.

Snake venom research, ca. 1660-1860



- Research questions:
 - Nature and composition of venom?
 - Effects on the (human) body?
 - Antidotes?
- Research techniques:
 - Animal experimentation, post mortem dissection
 - Chemical investigations of venom



Sample episodes

- The Tuscan naturalist Francesco Redi (1626-97) and his critic, the French apothecary and chemist Moyse Charas (1619-98)
- The Tuscan naturalist and physician Felice Fontana (1730-1805)
- Their views on comparative trials, repetition, replication ("imitation"), and variation ("diversification")





Francesco Redi (1626-97)

- The "yellow liquor" causes the fatal consequences of snake bites
- Deadly when inserted into wounds, innocent when taken by mouth
- Redi's critic Charas: the viper's rage is deadly







Redi the experimentalist



- Redi demanded that experimenters see for themselves, and he stated that he could not trust the phenomena "if they are not confirmed by iterated and reiterated experience."
- Let's look beyond his general commitment to experimentalism and examine what exactly this commitment involved.



Many, many experiments

- Old fables were refuted "by experiments made many many times."
- Redi had "observed [...] very often" that the yellow liquor spurted into the wound when the viper struck.
- The effects of bile and of the yellow fluid were tested on a number of different animals (as well as on the viper catcher).
- Redi demonstrated the effects of venom taken from dead vipers in more than a hundred experiments

Comparisons



- Redi punctured the thighs of ten pigeons with broom straws sharpened like arrows and dipped in the yellow liquor collected from many dead vipers. The poisoned straws were left in the wounds. All pigeons died after two or three hours.
- He also wounded four other pigeons with straws that had not been dipped in the fluid, and these birds survived.
- The first experimenter to use experimental controls"?

Charas objected...

- In the yellow liquor but the rage of the viper that was the cause of death.
- Charas thus compared animals bitten by angry vipers and animals bitten by contented and relaxed vipers and demonstrated that only angry vipers caused death.





What's innovative about these experiments?

The practice of repetition or the practice of comparison?



Some well known comparative trials

- Galen's treatise On Theriac to Piso (ca. 200) contains the description of trials with "poisonous beasts," which are placed among wild cocks that had received theriac, and "those who have not drunk theriac die immediately, but those who have drunk it are strong and stay alive after being bitten."
- The 14th-century scholar Bernard Gordon advised that the experimenter "take two pheasants, cut off their crests, apply a poison to the wounds (or administer it orally) and wait until they begin to stagger. Then put theriac on the crest wound and in the drink of one of them: if this one lives and the other dies, the theriac is good."

Redi did not comment on comparisons, but he did discuss repetitions

- Marco Aurelio Severino, "most versed in knowledge of the viper and greatly experienced," had been convinced by "only two experiments" that the yellow liquor was not lethal when it was put into wounds.
- Image: Second Second

Charas on Redi



Redi "hath contented himself with having made some of the yellow liquor to be swallowed by one only Man, one only Duck, one only Kid, thence to know and to assure himself of its innocence when swallow'd, without making a greater number of Experiments."

"Many many" experiments

A large number of experiments (i.e. investigating a topic from many angles)
Many repetitions of a particular trial
"More than enough" trials for the purpose

- Is viper meat an antidote to viper venom?
- Charas showed that an animal bitten in the ear by a viper had been cured by eating the head of another viper.
- Redi repeated the same procedure and obtained the same (!) results.
- "A doubt arose" in Redi. He repeated the experiment without feeding the dogs viper meat. Both dogs survived, having been bitten in the ear.

- Redi proceeded to feed viper heads to a cockerel, a capon, two dogs, eight more cockerels, two kittens, two hares, and six doves. All animals had been bitten in the thigh or the tongue, not in the ear. All died.
- Redi stressed that he had done more than Charas: In some trials, the place of the bite had also been smeared with viper blood as an additional antidote.

- Charas, in turn, pointed out that Redi's first results had agreed with the evidence obtained by Charas.
- The other experiments were not proper replications. Charas had used medium-sized dogs and Redi large ones, on which "no certain judgment could be made".
- Charas presented another kind of evidence, a case history, in his favor. A young man was bitten by a viper. The young man had so much faith in the truth contained in Charas's books that he immediately decided to eat the head and neck of the perpetrator. Charas served the broiled head, neck, heart, and liver of the viper.
- Again, he did more, so that the results could be brought out more clearly. He made the young man swallow some volatile salt of vipers, too.

- Charas's group imitated Redi's experiments with the yellow liquor – and failed. Like Redi, Charas gave yellow fluid to pigeons and two kittens. Again, he did *more*. He made a point of "engaging a person whom I knew most favourable to Signor *Redi*, to make himself the incision, and intromit the yellow liquor as he should think best.
- Charas noted that this gentleman cut the wounds so deep that he, "did more than Signor Redi himself said in his Letters he had done." Yet none of the animals died, even though Charas had proceeded by "thrusting the teeth into them as deep as I could."

- Is explicitly discussed when replication attempts are unsuccessful
- The researcher who does the unsuccessful replication typically claims that *his* experiment yields the correct result; the other researcher's experiment has a flawed design or some unknown factor interfered.
- To make their point more forcefully, the critics stress that they are not doing the exact same thing but they are "doing more" (using more venom, making a bigger wound, etc.)

Fontana on variations

The "yellow liquor" from the viper's teeth affects the blood

 Volatile alkali, a commonly used antidote, is not a remedy for viper bites



TREATISE ON THE VENOM OF THE VIPER; ON THE AMERICAN POISONS: AND ON THE CHERRY LAUREL. AND SOME OTHER VEGETABLE POISONS. TO WHICH ARE ANNEXED, OBSERVATIONS ON THE PRIMITIVE STRUCTURE OF THE ANIMAL BODY; DIFFERENT EXPERIMENTS ON THE REPRODUCTION OF THE NERVES; AND A DE SCRIPTION OF A NEW CANAL OF THE EYE. WITH TEN DESCRIPTIVE PLATES. TRANSLATED FROM THE ORIGINAL FRENCH OF FELIX FONTANA,

SATURALIST TO HIS ROYAL HIGHNESS THE GRAND DUKE OF TUSCANT, AND DIRECTOR OF HIS CARINET OF NATURAL HISTORY,

BY JOSEPH SKINNER,

NAVY SURGEON, AND MEMBER OF THE CORPORATION OF SURCEONS OF LONDON.

THE SECOND EDITION.

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M. DCC. XCV.

"Principal methods of good experimentation"

- The first is, to multiply the experiments exceedingly. ..
- "The second is, to vary them in a thousand ways, changing the circumstances as the nature and species of them may require, and giving them all the precision and simplicity they are capable of...
- The third method is [...] to attain to a discovery of the source of the errours that others have fallen into" (Fontana, 1787).

Fontana

• "I have made more than 6000 experiments; I have had more than 4000 animals bit; I have employed upwards of 3000 vipers and may have been deceived; some essential circumstance may have escaped me: I may have neglected some other, not thinking it necessary; my consequences may have been too general, my experiments too few in number. In a word, I may very easily have been mistaken..." (Treatise on the Venom of the Viper, 1781)



"Whether the Volatile Alkali is a certain Remedy against the Bite of the Viper"

I deemed it necessary to examine this first question in the most circumstantial way, and therefore multiplied the experiments extremely, and diversified them very much. This is the only method that could lead to demonstration, and I flatter myself that my readers will be freed from all doubt" (Fontana 1787)

Experiments on the effects of volatile alkali

- I had a pigeon bit in the leg by a viper, and instantly treated the part. At the end of a minute it fell forward, and could no longer support itself. In twenty seconds more it died. I had another pigeon like the first bit in the same way, but did not treat it. At the end of two minutes it fell forward, and in two minutes more it died.
- I had two other pigeons bit in the leg; one was treated, and the other not. The first fell at the end of three minutes, and died at the end of the twentieth. The other fell at the end of a single minute, and died likewise after the twentieth.
- Of two other pigeons bit in the leg, I treated only one. The one treated died at the end of forty hours, the other at the end of an hour...."

American herpetologist Laurence Klauber, 1962:

Fontana is "the first of the great experimentalists to use adequate controls"

gettyimages" Alah Grant

> Getty images http://www.gettyimages.com

Experimentalism, repetitions, variations, and circumstances

- The investigation of the circumstances attending the experiment was part of an extended effort to give the experimental design the precision and simplicity that the principal methods for successful experimentation required.
- Experimenters must multiply their experiments extremely and diversify them very much. Through these variations, the circumstances attending the experiment could be identified and managed.

"Discovering the sources of error that others have fallen into"

- Richard Mead had observed sharp crystals in viper venom. Fontana could find no such thing, even though he tried carefully.
 - Mead was "not well acquainted from habit with the shape of the different salts that are found in liquors" (in other words, he did not have the observational skills)
 - Fontana varied the instrument, using an English lens as well as a solar microscope.
 - Fontana made <u>additional</u> experiments to make himself "still more certain" and "to remove all doubt and suspicion on a matter so important and so generally adopted" – observing how a drop of venom dried and cracked.

Redi, Charas, & Fontana

- Described comparative trials (comparisons with "controls").
- Assumed that reliable conclusions can be drawn from successful comparative trials
- Emphasized repetitions.
- Main concern: the practical challenges of dealing with accidents and contingencies.
- Accidents cannot be treated in a systematic way.

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- Described comparative trials (comparisons with "controls").
- Assumed that reliable conclusions can be drawn from successful comparative trials
 - Emphasized variations and circumstances.
- Optimistic that through multiple variations of experimental settings, the circumstances impinging on experiments could be identified.



Charas

Fontana

"Imitation" in the 17th & 18th c.

- Not much explicit discussion
- Not many instances
- If it was done, there were different approaches
 - Re-doing the same procedure. If unsuccessful, the original experiment is deemed flawed or it was the wrong experiment for the purpose
 - Doing "more" to amplify the process
 - Using more venom
 - Cutting deeper wounds
- Providing other kinds of evidence ("replicating an effect")

- For scientists, it becomes increasingly important to be able to give and receive criticism and to articulate standards of good practice. To be effective peer critics and collaborators in interdisciplinary contexts, scientists need to be evaluate other people's works according to these standards. To do so, they need to have the necessary conceptual tools to express, explain, critique, and justify their methodological standards and their values to different audiences.
- Moreover, the number of critical articles about scientific methods in the popular media is growing (including the social media), which means that scientists are increasingly challenged to articulate and defend standards of good practice vis-à-vis broader publics.
- Historical and philosophical study can contribute to this task by analyzing scientists' methods discoursehow working scientists themselves understand, conceptualize, apply, and communicate norms and standards for good research practice.

http://www.slideshare.net/ geraldcarter1/academia-51559796

http://ohmyevidence.blogspot.com/2012/12/burden-and-standard-of-proof_16.html



The puzzle of control

- Comparative experimental trials performed by Fontana, Redi, and others - instances of control experiments avant la lettre?
- Solution Start Mill's method of difference from the System of Logic as the first philosophical conceptualization of controlled experiments?
- The very term "control" came to be used only in late 19th-century experimental science.

