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DEPARTMENT: ANECDOTE

My Time With the JFEAC

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When I finished high school in 1954, I had been admitted to several colleges around Philadelphia, since going away would add room and board to the cost. As a B student with As in math and some science courses, I received no scholarship offers, and there was no such thing as need-based support. While deciding what to do next, I looked for a summer job and came upon an ad in the *Philadelphia Inquirer*'s help-wanted section for a lab technician at the Eldridge Reeves Johnson Foundation for Research in Medical Physics. Hosted by the University of Pennsylvania, the foundation was based on a legacy from the founder of the Victor Talking Machine Company, which was later swallowed up by RCA. It seemed interesting so I called them and was interviewed on a Saturday morning.

The interviewer was probably Thomas F. Anderson, who was developing new methods of drying biological specimens for the foundation's RCA EMB electron microscope. He explained that the position was not a summer job, but they had a program: you worked full time at the Johnson Foundation and registered as a part-time student in the University of Pennsylvania's College of General Studies. By taking nine credits each term and three each summer term for a total of 24 each year, at the end of five years you would accumulate 120 credits and receive a degree. The credits came mostly from night courses, but if a course was not offered at night, you could take it during the day and make it up by working evenings. Tuition was charged by the credit, but as an employee you paid only half of the tuition. Not having any better prospect, I jumped at the chance and started immediately, working there for three years from 1954 to 1957 while a student at Penn and a fourth year part-time.

I worked in several parts of the foundation's lab, spending my first year with Anderson. Proving not to be as helpful as he needed in a wet lab full of T-phages and *E. coli*, they transferred responsibility for me to a biochemist Ronald Estabrook with whom I worked for a year on preparing catalase and peroxidase assays and detecting alkaloids in biological tissue. After that, I worked with an organic chemist Andreas Maehly on his experiments. Finally, I ended up with the care and feeding of the Johnson Foundation Electronic Analog Computer, or JFEAC, pronounced "Jiffy-ack." Someone told me that it was the largest electronic analog computer ever built. I distrust such statements on principle and, in this case, distrust it even more because it is not clear what metric is being used. At any rate, it was a large analog computer. Since it was home-brewed and focused on biomedical, not military, applications, it does not seem to have been noticed by any historian of analog computers, who are in short supply. The JFEAC had a lineage: the foundation's director, Britton Chance, had built a mechanical differential analyzer at UPenn before World War II and confirmed the Michaelis–Menten theory of the existence and interaction of enzyme and substrate compounds. Chance's construction of an electronic differential analyzer after the war improved the ease of operation and further research, and set the stage for JFEAC when he assumed leadership of the foundation.

Under Chance's predecessor Detlev Bronk, the Johnson Foundation had been involved with many different kinds of biophysics. There was Anderson and the electron microscope; Maehly and his assays; and X-ray crystallographer David Sayre, after he solved that field's phase problem and before he helped IBM create FORTRAN. Before I started, John C. Lilly, later famous for his dolphin and LSD experiments, was studying cat brainwaves with his bavatron. Gradually they all left for other institutions or departments, and the foundation became focused on Chance's ongoing work on enzyme reactions.

The first JFEAC was built in 1950 by an earlier undergraduate, Joe Higgins. At that time, the foundation, which was also Penn's graduate department of biophysics, was devoted to highly instrumented biological sciences as suggested by the interests of the faculty mentioned above. The equipment was designed by staff and built in-house in a very well-equipped machine shop. For example, they built an improved, automatic recording, ultraviolet (UV) spectrophotometer. The standard UV spectrophotometer,

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generally called the Beckman after its inventor and manufacturer, required setting a frequency on a dial and reading its output on a meter. At the foundation Chia-Chih Yang and Victor Legallais started with a Beckman, added a small motor to advance the frequency automatically, and replaced the meter with an automatic recorder. The Beckman and recorder were off the shelf, but Yang and Legalais integrated them into a working product that Chance used constantly.

The JFEAC was basically another one of those instruments. Its purpose was to solve chemical rate equations involving enzyme reactions. There is some uncertainty about how many of the computers were built. After Higgins's JFEAC, Chance and his people built another one in 1951–1953. Yang then designed and built a third JFEAC that is described at greater length below. At that time digital computing had not yet assumed the pre-eminence that we take for granted. The U.S. Navy, which funded Yang's JFEAC and had a long tradition of analog computing for gunfire direction, was not yet convinced that digital was the only game in town.

"Taking care" of the JFEAC meant mainly replacing vacuum tubes. There were two basic components to the JFEAC: a voltage amplifier and a diode switch, both made with vacuum tubes. The tubes were supplied gratis by the Navy. They had failed the Navy's acceptance test for real-world and extreme environments but worked well enough for us. The tubes arrived in big boxes and were all subminiature, which means they were maybe an inch long and had no bases, just wire leads coming through a glass envelope. These had to be soldered in place; there must have been some infallible way of detecting which wire was which, since I have no memory of how that worked.

PHYSICAL DESCRIPTION

The JFEAC occupied seven equipment racks, each about two feet wide and possibly seven feet high—somewhat taller than I am, in any case. One rack consisted exclusively of power supplies. The computer used 200 volts DC as the plate supply for the vacuum tubes; 5-, 6-, and 12-volts AC for tube heaters; and a small negative voltage supply for grid bias on the vacuum tubes. The power supply was basically a transformer, high-power rectifier tubes, and at least two stages of filtering, all standard for the time. There was also a 5-kHz signal generator that provided the timing for the computational signals, most of which were 5-kHz square waves.

There were two kinds of components in the JFEAC. The first was an operational amplifier (op amp) of a pretty much standard design, and the second was a diode switch (Figure 1).

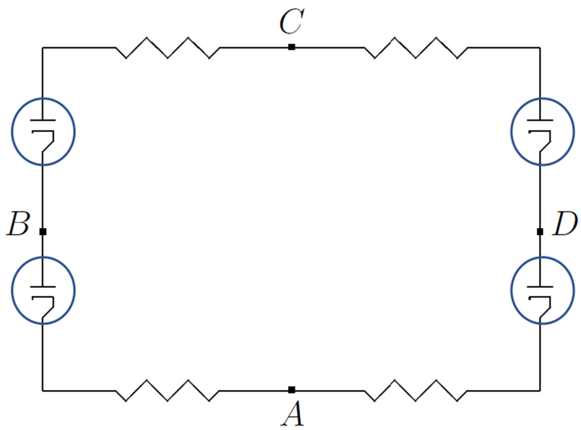

FIGURE 1. JFEAC diode switch. The resistors were the same value and point A was grounded. The result of this arrangement was that when the voltage at C was positive, B and D acted as though they were shorted together; when C was negative, B and D were insulated from each other. Of course, things were not quite that neat and in practice you always wanted the voltages on C to be quite positive or negative. In addition, B was a low-impedance output of one component while C was a high-impedance input to another one. This circuit was used, for example, to turn a DC voltage into a 5 kHz square wave by hooking a signal generator to A and C and the input to B, taking the output from D. (D was connected through a resistor to ground so the output was 0 volts when the diode switch was open.) If B was a low-impedance source and C was high impedance, the effect of the switch being closed was that the signal at B was transferred to C.

The op amp had a high-gain pentode as well as a cathode follower triode. These pentodes had average gains of around 2000, although they varied a lot. The variation was unimportant since they were all used in circuits with very high negative feedback, so individual characteristics averaged out.

CHEMICAL RATE EQUATIONS

Rather than the general-purpose computers we see today, the JFEAC was a special-purpose machine designed to solve chemical rate equations. These are systems of simultaneous initial value differential equations with the general form

$$dx_i/dt = \sum c_{ij}x_j + \sum c_{ikl}x_kx_l, \quad x_i(0) = x_{i0}.$$

Here x_i represents the concentration of a reactant and the c's are constants. A linear term represents either the spontaneous decay of x_i (whence $c_{ii} < 0$ and all the other $c_{ij} = 0$) or of one or more of the x_j into a x_i (whence $c_{ij} > 0$ for those j and 0 for the others). A quadratic term represents x_k and x_l reacting to produce x_i. Since the Johnson Foundation had, by 1956, become a high-tech biochemistry department (it was called biophysics since Penn already had two biochem departments, one in the medical school) concentrating on enzymes, these equations were supposed to represent enzyme cycles.

The simplest example of these equations is the simple enzyme reaction. An enzyme e reacts with a substrate s to produce an intermediate enzyme substrate complex q. This intermediate might decay back to its constituents e and s or into the product p liberating e. The equations were

$$\begin{aligned} ds/dt &= -c_1 es + c_{-1}q, & s(0) &= s_0 \\ de/dt &= -c_1 es + c_{-1}q + c_2 q, & e(0) &= e_0 \\ dq/dt &= c_1 e - c_2 q - c_{-1}q, & q(0) &= 0 \\ dp/dt &= c_2 q, & p(0) &= 0. \end{aligned} \qquad (*)$$

In fact, those equations were replaced by the equivalent integral equations:

$$\begin{aligned} s &= s_0 + \textstyle\int_0^t - c_1 es + c_{-1}q\,dt \\ e &= e_0 + \textstyle\int_0^t - c_1 es + c_{-1}q + c_2 q\,dt \\ q &= \textstyle\int_0^t c_1 e - c_2 q - c_{-1}q\,dt \\ p &= \textstyle\int_0^t c_2 q\,dt. \end{aligned} \qquad (**)$$

Differentiation of an electronic wave is a very chancy operation since the derivative of the noise is likely to overwhelm the derivative of the signal. Integration, on the other hand, will tend to average out noise because it is just as likely to be positive as negative.

Any computer has limitations (I am writing this on an older machine with only 1/2 GB of main memory), but the JFEAC was severely limited. Since there were only seven integrators, there could be only seven variables. Some enzyme cycles have more than seven intermediates, so it was limited even within its single-purpose design.

THE CIRCUITS

Each of the seven integrators had one chopper circuit, which adds a DC signal to the 5 kHz square wave. There were adders and constant multipliers, circuits of routine design that output waves that are the sum of two inputs or multiplied the input by a constant (with or without inversion, as required). The difficult problem on an electronic analog computer is that of multiplying two voltages. Addition (and subtraction), integration, and differentiation are linear, but multiplication is not. There are various ways of doing this. One is to use a servomechanism-driven potentiometer (variable resistance, generally called a "pot") that sets the resistance proportional to one of the input voltages. In effect, it is taking multiplication by a constant (which uses a fixed pot) and varying it. This requires a mechanical device whose reliability was uncertain. The JFEAC used the so-called quarter-square identity

$$xy = \frac{(x+y)^2 - (x-y)^2}{4}$$

to reduce the problem of squaring with a diode function generator. An explanation of Argonne National Laboratory's 1960 analog computer mentions briefly its diode function generator that could simulate any function by a series of diodes that turn on at different voltages. In effect, it produces an approximation by straight-line segments with the slope at any point determined by the number of conducting diodes. The JFEAC used a diode function generator to approximate the square function. The multiplication was arranged to create a square wave whose top was the voltage $x + y$ and whose bottom was $x - y$, using a couple of diode switches as described in Figure 1. This was then put through the squarer to create a square wave whose height (i.e., the difference between the top and bottom) was xy (up to the factor of 4, which was built into the constants). Very elegant.

When all the terms were collected, the resultant wave was clamped so that the trough was set to ground and then sent to the integrator. The output was a DC value of the variable.

PROGRAMMING

Programming the JFEAC was carried out by physically connecting components using coaxial cables with phono plugs. Let me illustrate the process with the simple enzyme equation (**). Choose four integrators and call them s, e, q, and p. Each of the four is fed first into its own chopper to produce a 5-kHz square wave.

Figure 2 is a simplified example of the circuit that would be used to solve (**). Programming involved nothing more than hooking the cables as indicated by the arrows, usually after drawing a diagram similar to this one. Note that the first row and last row are the

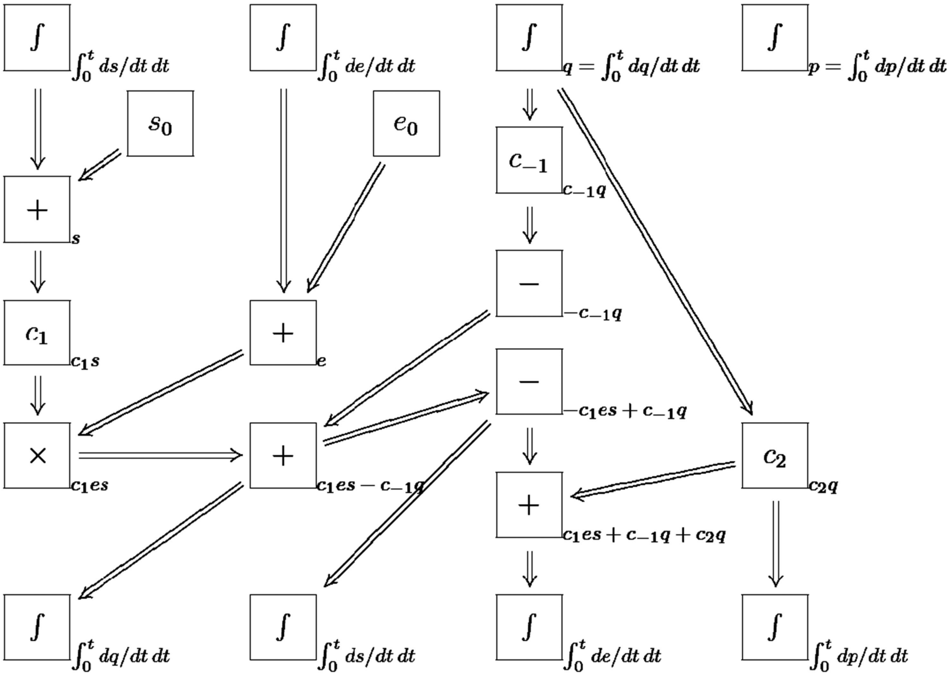

FIGURE 2. JFEAC II flowchart for programming the simple enzyme equation (**) above. The boxes represent components: integrators, adders, constant multipliers, fixed voltage sources, and multipliers. The choppers, although crucial, are omitted. The subscripts on the boxes describe their outputs. The arrows correspond to shielded cables between components. The arrow source was always a low-impedance output from one circuit while the target was always a high-impedance input to the next so that, although a wire is symmetric, the effect was to move the signal from the source to the target of the arrow.

same (although in a different order to avoid crossing arrows).

There are several comments to be made. First, what is going on here? It looks like a complicated feedback circuit, but where is the computation actually taking place? The answer can only be that the delays in the feedback are where the dynamics come from. At first, $s = s_0$, $e = e_0$, $q = p = 0$. But then the computation from the equations forces e and s to diminish and q and p to rise and so on. This raises a question that never occurred to my mathematically immature mind but jumps out immediately now. The cables were of all different lengths and I always chose the shortest ones that would fit. But the time the signals spent in the cable would obviously depend on the length of cable. Perhaps the shielded cables carried signals so much faster than the other components that it simply did not make a difference. The solution was repeated over and over, so there must have been (I have no recollection) another timing pulse that reset all the components to their initial values.

This particular set of equations is slightly faked because one generally assumed that the concentration of s was so large compared to the others that it did not vary during a reaction. But then the problem reduces to three simultaneous *linear* differential equations for which exact solutions are well known (and easy). The same simplifying assumption is made for more complicated enzyme systems that do have nontrivial quadratic terms and cannot be solved directly.

The output of a computation was the set of outputs of the integrators, since these represented the concentrations of the reactants. They were detected by running a cable from one integrator to a permanently installed oscilloscope. The results could be viewed directly or photographed for a permanent record.

LATER DEVELOPMENTS

During my tenure, there were two developments that rendered the original JFEAC obsolete. The first was the design of a transistorized version. This was much more reliable as well as smaller and less power hungry. The JFEAC II was constructed and used, although all I saw were some prototype circuits.

Second, in 1957, Penn acquired a UNIVAC I, one of the first digital computers, as a gift from Sperry-Rand

and it was decided to redo the approach to enzymatic reactions digitally. Programmers were hired and the work commenced. Chance intended to propose mechanisms of enzyme action and electron transfer, study how they responded to various changes in parameters, and compare the theoretical results to the experimental ones to see if the proposed mechanisms could be correct.

The programming was extremely complicated. The UNIVAC I contained exactly 1000 addressable memory locations, each holding 72 bits organized as 12 6-bit bytes. (As an aside, let me mention that "byte" did not originally mean 8 bits. It meant, essentially, one character, letter, number, or punctuation, and varied on early computers between 6 and 9 bits.) The eventual program consisted of about 80,000 double words, about half of which were concerned with bringing the required routine into the storage as needed. The program itself was entered on paper tape and stored on magnetic tape that was read and written by tape consoles.

THE PING-PONG BALL COMPUTER

Since I am on the subject of Johnson Foundation analog computers, it is appropriate to mention the ping-pong ball computer that I helped build. Many enzyme reactions have a string of enzymes on a solid membrane sitting in a watery environment. The reaction mechanism consists of the first enzyme in the string reacting with the substrate to produce an intermediate, which reacts with the second enzyme in the string to produce another intermediate, which reacts with . . . . The enzymes oscillate in this environment and react, with a certain probability, when they contact each other. We simulated this in the following way.

We built a machine housed in an aluminum chassis, something like 6 × 6 × 20 inches (15 × 15 × 75 cm), that had a sequence of maybe six positions in a row. Each position had a slow reciprocating motor whose speed could be set, on the order of a couple of seconds. A six-inch coiled-wire stalk was mounted on each motor and on top of each stalk protruding from the chassis we mounted a ping-pong ball that had three holes drilled in it. They were 90° apart on one great circle. Call them the south, east, and west poles. Wires came in through the south pole, which was mounted on the end of a stalk. One pair of wires powered a grain-of-wheat bulb, which pretty much describes its size. Two more pairs of wires were attached to the shafts of metal thumb tacks whose heads were glued onto the outside of the balls, covering the east and west poles. We pulled wires through the holes in the east and west poles, soldered those wires to the shafts of the tacks, pulled the wires and shafts back inside, and glued the head of the tacks to the outside of the ball. They were arranged so that as the ping-pong balls waved back and forth, the east pole of one ball might contact the west pole of the adjacent one. When they did, if one ball was "on" (that is, its light was lit) and the other was not (its light was unlit), then with a certain probability (which was settable) they would react and the light on one would go out and vice versa. The end balls in the string would go on (if off) or off (if on) also at random times, representing the reaction of the first enzyme with the substrate or the creation of the final product (that latter reaction was not assumed reversible).

Of course, it was arranged so that the probability of the forward reaction was much larger than the reverse. Thus, the whole thing functioned as an electromechanical simulation of the enzymes on a string. A series of count-up timers recorded the amount of time each ping-pong ball was on. When the whole thing was operating, the balls waved in a sinuous, almost obscene fashion, and the ping-pong balls turned on sequentially. It looked something like a string of mushrooms waving in a breeze, except that each one waved at its own preset pace.

Nowadays nothing escapes being photographed, but I doubt it ever occurred to anyone to get a picture of it. The machine shop had all kinds of tools for cutting, bending, and spot-welding aluminum sheets and we built small chassis like this all the time. Perhaps someday a researcher at the Johnson Foundation will look into some dusty cabinet, find this machine, and wonder what the hell it was. He will likely never know. I doubt that it ever did anything useful. It seemed to be intended as a demonstration for some important visitors. What I do recall is that several of us worked all night to get it running for one specific date.

I do not think we used the machine to solve an enzyme problem more than once or twice. By the time I left, they were programming the UNIVAC 1 instead.

SUMMATION

In retrospect, I think they decided I just was not very useful in the labs but, feeling some commitment, found something where I could not do much harm. But they were winding down programming on the JFEAC in favor of its successor, the JFEAC Mark II. Meantime, I found that I did not care for lab work, and discovered abstract math in an unexpected fashion. Working late one night to make up for day-time courses, I overheard an odd-sounding conversation between Joe Higgins and another grad student, Bill Holmes. Joe had spent a year at Harvard after graduation and taken a course in modern algebra there from Garrett Birkhoff. Then he returned to Penn, registered as a grad student in physics, and resumed working at the foundation. He somehow convinced Bill to sign up for an undergraduate modern algebra course. Bill was having some trouble and that was the conversation I overheard. Through it, I discovered abstract algebra, and the rest is another story.

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