until 0.31 g in 125 ml absorbed 3.74 Mrad. 2-Hydroxyestrone (13 percent) was isolated, as well as recovered estrone (50 percent). No other products could be identified by gas chromatography. Estradiol similarly gave 2-hydroxyestradiol (9 percent), and recovered starting material (54 percent), with an absorbed dose of 3.38 Mrad. The $G_{(-\mathrm{M})}$ values (molecules reacted per 100 ev absorbed) were 1.14 and 1.54, for estrone and estradiol, respectively. No estrolactone was detected, although a trace (1 percent) of estrolactone acetate had been found in the radiolysis products of estrone in acetic acid (*2*).

The bromination (*3*) and nitration (*4*) of estrone lead to substitution at both carbon-2 and carbon-4. However, biological oxidation appears to occur at the carbon-2 rather than at the carbon-4, in that 2-methoxyestrone was isolated from the urinary metabolites of estradiol (*5*). Radiolytic hydroxylation often parallels biological hydroxylation (*6*).

The radiolysis of estrone and estradiol offers a simple method of preparing their 2-hydroxy derivatives, and it is a convenient alternative to chemical synthesis (*7*).

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Earth Tremors Generated by Old Faithful Geyser

Abstract. *Several types of earth tremors that could be associated with the eruption cycle of Old Faithful Geyser were registered by a seismograph placed a few meters from the geyser's orifice. Each tremor type was indicative of a specific geyser action. A totally unexpected result was an observed bimodal distribution in frequency of the interval between eruptions.*

During January 1965, I took advantage of a winter stay (*1*) in Yellowstone National Park to investigate the earth tremors generated by Old Faithful Geyser. Because of its predictability and repeatability, the geyser is especially convenient for study. Absence of tourists during the winter months insured that background noise would be low. Although geyser action would be expected to generate very small earth tremors, only one study seems to have been made of them, that of the Onikôbe Geyser in Japan (*2*) which showed the development of pulsative tremors of roughly 10 cy/sec in the neighborhood of the geyser, the tremors becoming particularly prevalent as eruption time approached.

In my study, a Hall-Sears model HS-10-1 geophone, placed on the geyserite cone of Old Faithful about 20 m from the geyser vent, was used to detect the tremors. This geophone senses particle velocity, and in this case was set up to measure the vertical particle velocity of the ground surface. The frequency response of the instrument is fairly flat from 30 to 1 cy/sec. Sensitivity of the instrument falls off rapidly at frequencies less than 1 cy/sec. Signals generated by the geophone were amplified and fed to a Sanborn strip recorder, located about 70 m from the geyser, which had recording speeds of 5 and 50 mm/sec.

In general, two somewhat different types of sequences were observed, one corresponding to a long interval between eruptions, and the other to a short interval. (The bimodal distribution of intervals is discussed later). The sequence shown in Fig. 1 is typical of that occurring during the long interval. Immediately after the eruption and for 20 to 30 minutes thereafter (trace A), there is a complete absence of any regular tremors. This quiescent period is followed first by a short series of substantial long-period movements (approximately 0.1 cy/sec; trace B) lasting for a minute or so. In some cases, these are repeated a few minutes later, but then cease entirely. The geophone is quite insensitive to this frequency, so that the record indicates very substantial earth movement, most likely extensive tilting. Occasionally this motion is accompanied by audible booming.

The large low-frequency movement seems to initiate, or be an indicator of, a subterranean change; for shortly after, the long-period motion ceases and a regular series of sharp signals, shown in trace C, begins. Since the geophone responds well to this frequency, each signal corresponds to only a relatively weak tremor which occurs at the rate of about one per second. In making this recording, heat input to the recording pen was kept low in order to obtain a fine-line trace. Under this condition, the pen does not record high-frequency components. Thus each signal in trace C which appears as a sawtooth pulse is in reality the short packet of wavelets evident in the more rapid recording, with higher heat input to the recording pen, shown in trace D. Each of these packets consists of two to four wavelets having a frequency of from 15 to 30 cy/sec.

At about the same time that the weak tremors begin, a series of much stronger but less frequently occurring pulses starts. The pulses are not exhibited in trace C since they would be way off scale. A rapid recording at much reduced (24 db) amplification of a series of three of these short-period strong pulses is reproduced in trace E. Each strong pulse lasts for about 0.1 second, a length of time similar to the duration of the weak signals; but the strong pulse does not have the same oscillatory character of the weak bursts. Generally, a strong pulse or a group of these heralded a violent ejection of steam which occurred 15 to 20 seconds after the pulse. The weak and strong signals continue in this fashion until eruption occurs, after which the sequence begins anew.

When the interval between eruptions is short, the above sequence is somewhat different: both weak tremors and strong pulses start immediately after cessation of the previous eruption. The introductory, long duration movements (trace B) may or may not occur.

The frequency and temporal distribution of strong pulse activity typical of short and long intervals between eruptions is shown in Fig. 2. This figure represents the total (up to particular times), for one typical short interval and one typical long interval, number of strong pulses occurring after the cessation of an eruption. In this example, there were about 120 strong pulses up to the time of the next eruption in the case of the short interval, and about 140 in the case of the long interval. When the interval was short, strong signals began at once and continued at about a constant rate (2.5 per minute) until eruption occurred. When the interval was long, the start of strong signals was delayed about 20 minutes, after which a moderate, roughly constant, frequency of occurrence of one per minute was followed by a much more rapid rate of eight per minute, with the strong signals decreasing almost entirely 3 or 4 minutes before eruption. Frequently two or three strong pulses were spaced close together (trace E is an example). Unluckily no easily identifiable precursor to the main eruption was found.

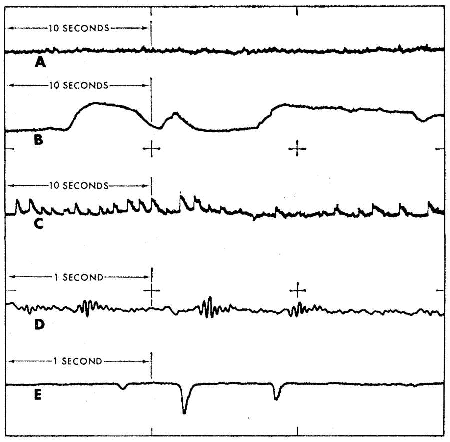
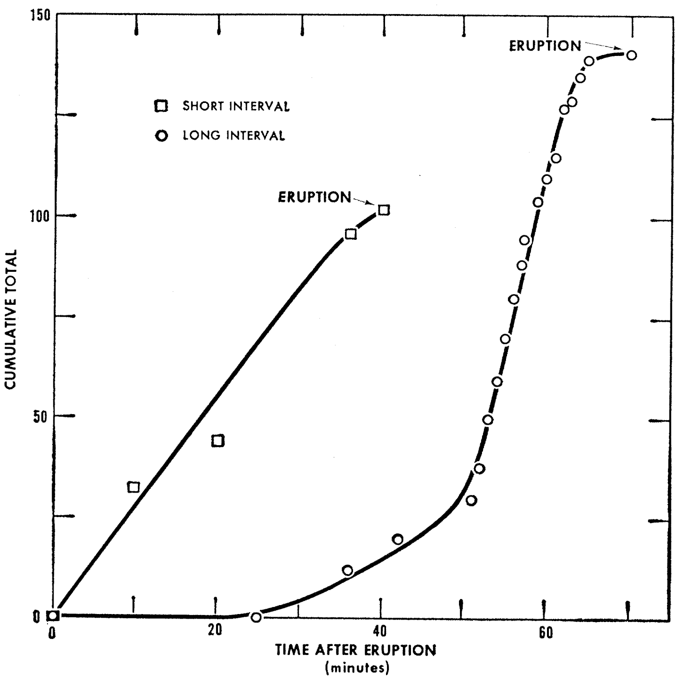


Fig. 1. Traces, recorded on a Sanborn strip recorder, of signals generated by earth tremors associated with a long interval between two eruptions of Old Faithful. *A*, shortly after last eruption; *B*, long duration signal, about 20 minutes after eruption; *C*, weak signals, shortly after trace B; *D*, weak oscillatory signals at high paper speed, approximately same time as trace C; *E*, strong pulses at high paper speed and low amplification, 24 db below traces A, B, C, and D. Trace taken about 40 minutes after eruption.

A most unexpected result has been the observation for the first time that the frequency of occurrence of intervals of time between eruptions is bimodally distributed. The histogram of Fig. 3, measured by the National Park Service (*3*), shows the most probable intervals as 50 minutes and 72 minutes, with the longer period occurring more often, in the ratio of about two to one. This histogram was constructed when it was found that the overall pattern of earth tremors and pulses was different for short intervals than for long ones. No regularity, except for the two-to-one ratio in frequency of occurrence, has yet been found with respect to the distribution of long and short intervals in the eruption cycle, short intervals being more or less randomly mixed with long ones.

Another indication of the double character of Old Faithful's action is the duration of play of water during eruption as a function of interval between eruptions (*4*). In general, duration of play, which ranges from 1.5 to 4.5 minutes, increases with increasing interval, but there is a discontinuity in the slope of the curve at about 60 minutes. Unfortunately, no detailed measurements have been made of total water flow.

These several facts suggest that Old Faithful's geological structure is fairly complex with perhaps two mechanisms operative in producing an eruption. Possibly two cavities exist below the surface, their respective actions being somehow coupled. Of special interest in this connection is the inactive, warm cone of geyserite that lies about 60 or 70 m from the vent of Old Faithful Geyser. The reservoir or vent serving this now extinct geyser could have broken through to Old Faithful's own reservoir or vent. Emptying of the first reservoir at some times, and of the second at other times, would account qualitatively for the observed complications in the eruption cycle.



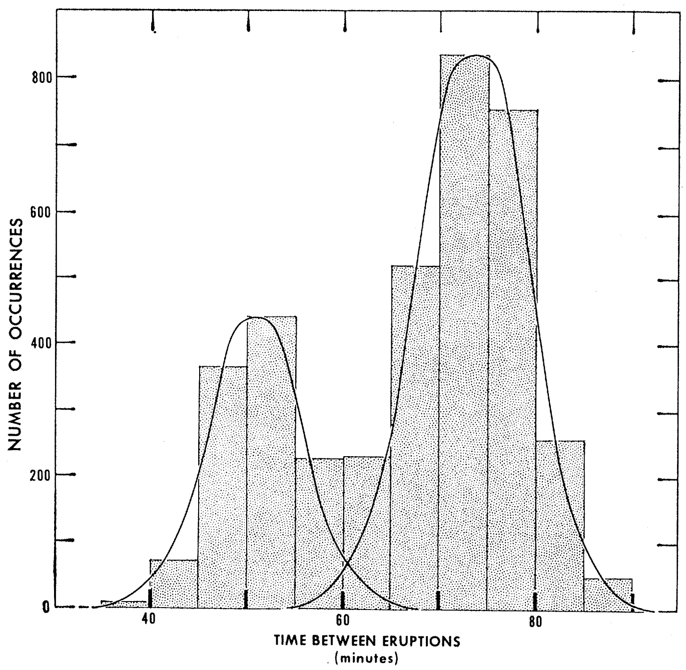


Fig. 2 (left). Frequency and temporal distribution of strong pulse activity for a typical short interval between eruptions and a typical long interval. Termination of each curve indicates time of occurrence of next eruption. Fig. 3 (right). Frequency distribution histogram for intervals of time between eruptions. National Park Service data on 4000 intervals over a several year period.

In an attempt (*5*) to test the reasonableness of this hypothesis, computer calculations were made to predict the performance of two coupled sinusoidal oscillators having different amplitudes and frequencies. The assumption made was that the amplitudes of the two motions were to be superposed and that, whenever the amplitude reached a threshold value, eruption would be initiated. Such a model is yielding encouraging but not yet definitive results.

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4. From a graph on the wall of the Old Faithful Ranger Station, Yellowstone National Park.
5. Dr. L. Alldredge, U.S. Coast and Geodetic Survey, suggested the model and helped carry through the calculations.

20 July 1965

Delta-Aminolevulinate Dehydratase Activity in Mice with Hereditary Anemia

Abstract. *Homozygous* (f/f) *but not heterozygous* (f/+) *mice of the highly congenic strain, FL/Re, manifest a severe transitory siderocytic fetal anemia. Adults of both* f/f *and* f/+ *genotype manifest decreased hepatic, splenic, and renal levels of Δ-aminolevulinate dehydratase (ALD) activity compared to homozygous* (+/+) *mice of the same strain. The degree of augmentation in splenic ALD activity following phenylhydrazine administration is high in* +/+, *intermediate in* f/+, *and low in* f/f *mice. These findings suggest that perhaps a deficiency in the fetal level of ALD may be responsible for the transitory fetal anemia.*

Detailed study of the effects of genic substitutions at the "flexed" (*f*) locus upon hematopoiesis has become possible through the development at the Jackson Laboratory of an inbred mouse strain, FL/Re, which is homozygous f/f, along with congenic FL/Re–$+/+$ and FL/Re–$f/+$ stocks (*1*). Homozygous f/f mice suffer from a transitory siderocytic anemia which is severe at fetal stages but disappears shortly after birth, whereas hematopoiesis appears normal in $f/+$ and $+/+$ mice at all ages (*2*). The anemia of f/f mice, first apparent on the 12th day of fetal development, is especially marked from the 13th to the 16th day, and seems to be especially associated with the first generation of nonnucleated red cells formed in the fetal liver (*1*). In 13- to 15-day f/f anemic fetuses, the new red cells are very deficient in hemoglobin (*1*) and contain large quantities of nonheme iron in the form of siderotic granules (*2*).

The activity of a key enzyme in the pathway of heme biosynthesis, Δ-aminolevulinate dehydratase (ALD), was investigated in adult mice of the FL/Re strain to determine whether the fetal accumulation of nonheme iron, resulting from the action of the gene *f*, might be associated with an enzymic lesion which impairs heme biosynthesis. A preliminary account of this work has been presented (*3*). Variations in hepatic level of ALD activity, apparently controlled by alleles at a single locus (Lv^a versus Lb^b), have been reported in normal adult mice (*4*). Also, the ALD activity in spleen, but not in liver, of adult rabbits is known to be susceptible to alteration by phenylhydrazine (*5*).

The ALD activity was determined according to a modification of the method of Russell and Coleman (*4*) at *p*H 6.2 in the presence of β-mercaptoethanol rather than glutathione during the preliminary incubation period. Hepatic, renal, and splenic levels of ALD activity were determined in 2- or 3-month-old $+/+$, $f/+$, and f/f mice. It may be seen in Table 1, rows 1–3 (for the mice not given phenylhydrazine treatment), that the ALD activity per gram in each of the three organs is about the same in $f/+$ and f/f mice, and that this level is substantially lower than that observed in the $+/+$ mice ($P < 0.01$). All probabilities quoted in this paper were calculated by the Wilcoxon rank sum test (*6*). The ALD activity in livers of Lv^a/Lv^b mice is intermediate between the high level in Lv^a/Lv^a mice and the low level in Lv^b/Lv^b mice (*4*). For these reasons, and because the gene *f* has previously been considered recessive in all its effects, it was surprising to find the same low level of ALD activity in the organs of heterozygous $f/+$ and homozygous f/f mice.

To test for possible effects of heterozygosity on the activity of this enzyme, anemia was induced in FL/Re mice by phenylhydrazine treatment. Adult $+/+$, $f/+$, and f/f mice were rendered anemic by five 1-mg intraperitoneal injections of neutralized phenylhydrazine at 12-hour intervals and were killed approximately 12 hours after the last injection. Microhematocrit determinations were performed on blood obtained from the retro-orbital sinus just prior to sacrifice. The hematocrit percentages of injected mice fell to little more than half of their pretreatment values (Table 1, column 5), and similar levels of reticulocytosis were observed in all mice (14 to 23 percent in f/f; 18 to 26 percent in $+/+$). Significant splenic enlargement was observed in mice of all three genotypes (Table 1, column 6), although the extent of enlargement was less in f/f than in $f/+$ and $+/+$ mice ($P < 0.01$). The ALD activity per gram of spleen increased above pretreatment levels in $+/+$ ($P < 0.01$) and $f/+$ ($P = 0.05$) mice, but

Table 1. Δ-Aminolevulinate dehydratase activity in various organs of mice of the FL/Re strain, without and with phenylhydrazine treatment, and hematocrit values and spleen weights.

Genotype	Δ-Aminolevulinate dehydratase*						Hematocrit (%)		Spleen weight (mg)	
	Liver		Kidney		Spleen					
				No phenylhydrazine treatment						
$+/+$	3.32	0.42†	1.43	0.27†	2.25	0.36†	49	1.6†	72	17†
$f/+$	1.20	.25	0.68	.09	0.80	.27	48	1.8	83	15
f/f	1.22	.16	.63	.10	.61	.20	50	2.5	70	14
				With phenylhydrazine treatment						
$+/+$	2.38	.15	1.02	.07	5.30	1.77	29	1.3	252	72
$f/+$	0.90	.20	0.43	.07	1.23	0.15	28	1.5	249	73
f/f	.86	.14	.44	.06	0.55	.32	24	2.4	155	34

* Activity of ALD is expressed in micromoles of porphobilinogen synthesized per hour per gram of liver (wet weight) ± standard deviation. † Values in these columns are standard deviations. The standard deviations of the hematocrits are expressed in percentage points, not percentages.