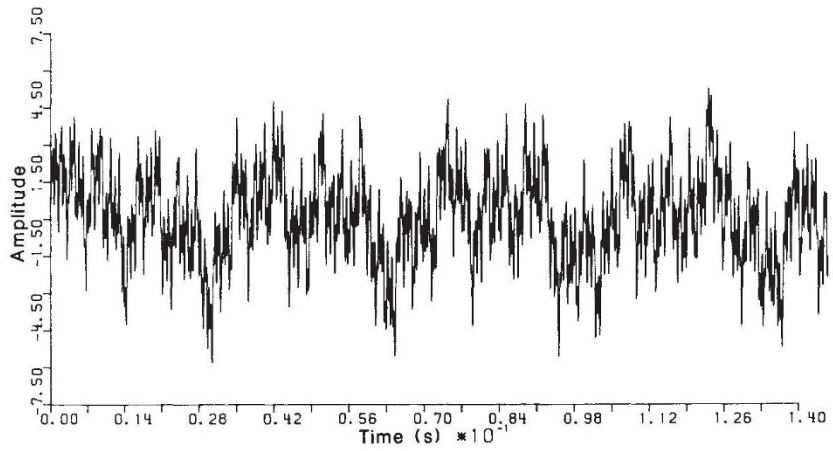

Fig. 1 Fractal waveform leading to paradoxical pitch perception.

the tape speed, it will sound a semitone lower in pitch rather than an octave higher (the usual percept engendered by tape speed doubling).

The explanation for this curious percept is based on the importance of adjacency in pitch perception[6,7]. Thus, the tone component with a frequency of 428 Hz turns into one at 856 Hz upon doubling. But in comparing the two chords, the human auditory system will identify the frequency-doubled component at 856 Hz with the nearest component in the original complex, namely 907 Hz. And 856 Hz is a semitone lower than 907 Hz. The same is true for all other components and thus a lowered pitch will be perceived.

Self-similar fractal structures are applicable not only in the frequency ('pitch') domain but can also be introduced into the time ('rhythm') domain with interesting consequences. In fact, certain self-similar number-theoretic sequences, such as the binary Morse–Thue and 'rabbit' sequences[2], give rise to very appealing rhythms.

MANFRED R. SCHROEDER
Drittes Physikalisches Institut,
Universität Göttingen,
Bürgerstrasse 42–44,
D-3400 Göttingen, FRG

1. Campbell, P. *Nature* **324,** 523-528 (1986).
2. Schroeder, M.R. *Number Theory in Science and Communication. With Applications in Cryptography, Physics, Digital Information, Computing and Self-Similarity* 2nd edn Ch. 30 (Springer, New York 1986).
3. Risset, J.C. *Proc. 7th Int. Conf. Acoust., Budapest,* Vol. 3, 613-616 (Akadémiai-Kiadó, Budapest, 1971).
4. Charbonneau, G. & Risset, J.-C. *C. r. hebd. Séane. Acad. Sci., Paris* **B281,** 289-292 (1975).
5. Schroeder, M.R. *J. acoust. Soc. Am.* **79,** 186-189 (1986).
6. Shepard, R.N. *J. acoust. Soc. Am.* **36,** 2346-2353 (1964).
7. Terhardt, E. Hear. Res. **1,** 155-182 (1978).

PHILIP CAMPBELL REPLIES — Musical quantities such as pitch and loudness have been found to exhibit 1/(frequency) type power spectra (ignoring spectral peaks due to the basic rhythms of the pieces concerned), while noise synthesized with $1/f$ characteristics sounds more 'pleasant' or 'interesting' than Brownian ($1/f^2$) or completely random noise[1]. In view of Dr Schroeder's comments it is interesting that $1/f$ noise has fractal properties. Since writing my article I have learnt that at least one composer is investigating musical design using fractals[2].

1. Voss, R.F. & Clarke, J. *Nature* **258,** 317-318 (1975); *J. acoust. Soc. Am.* **63,** 258-263 (1978).
2. McNabb, M. in *The Language of Electroacoustic Music* (ed. Emmerson, S.) 150-153 (Macmillan, London, 1986).

The mechanism of chromogranin A processing

SIR—Two groups have recently conjectured that chromogranin A or a related protein may serve as a precursor for biologically active peptides in a number of cells of the diffuse neuroendocrine system[1,2], based upon the realization that pancreastatin, a peptide from porcine pancreas that inhibits insulin secretion, is closely related in sequence to residues 2 51–294 of bovine adrenal medullary chromogranin A[3]. What other evidence is there for this relationship?

Chromogranin A immunoreactivity in the pancreas is localized to a variety of endocrine cells of the islets of Langerhans[4-6]. The fact that pancreastatin as isolated has undergone C-terminal amidation suggests that it is produced in an intracellular, indeed intragranular, environment rather than being an artefact of tissue disruption. Enzymes which might excise pancreastatin from the chromogranin. A sequence through cleavage at single basic residues and which could catalyse its C-terminal amidation are certainly present in islets as such reactions occur in the processing of propancreatic polypeptide and proglucagon[7,8]. Chromogranin A might also be processed at any of the eight sites of dibasic amino-acid sequence as endopeptidases with this specificity also exist in islet tissue.

In the adrenal medulla, where chromogranin A was first described as a protein of relative molecular mass (M_r) 72,000, there is little indication of major proteolysis of chromogranin A apart from N-terminal signal peptide removal. The half life of the protein in these cells is comparable to that of the enkephalin precursor, being of the order of 6–8 days[9]. But a very different situation prevails in the pancreatic B-cell, where we first encountered chromogranin A as protein of M_r 21,000 (ref. 10). This protein, which we called betagranin, was cosecreted with insulin and, was shown to have an amino-acid composition and N-terminal sequence similar to bovine chromogranin A[11].

Pulse-chase labelling experiments in insulinoma cells show that betagranin is synthesized as a precursor indistinguishable in size and immunoreactivity from rat chromogranin A (M_r 80–100,000). This precursor undergoes rapid proteolysis soon after reaching the *trans* Golgi cisternae and entering the secretory granule compartment[12]. The M_r 21,000 peptide appears to be a stable end product generated by initial cleavage of the chromogranin A-like precursor at a site equivalent to Lys114 Arg115 in the bovine sequence by the action of a Ca^{2+}-dependent acidic endopeptidase[13]. The C-terminal amino acids so exposed are removed by carboxypeptidase H. As the antiserum used in these experiments is directed towards the M_r 21,000 N-terminal fragment we can say little about the fate of the rest of the precursor apart from the fact that it too is processed but at a lower rate.

On a molar basis, the estimated amount of chromogranin-related peptides in insulin granules would at most represent one per cent of the insulin content[14]. As the circulating insulin level generally lies in the nanomolar range it would take a molecule with an exceptionally long half life to achieve a blood concentration approaching the 10 nM or so at which pancreastatin was shown to exert its effect *in vitro*. This might indicate that the chromogranin A-related peptides act locally on endocrine cells or adjacent vasculature. The concept that the pancreatic B cell responds to a product of its own secretion or to other islet hormones as part of an autoregulatory cycle has frequently been invoked. It would now appear that chromogranin A-derived peptides should also be seriously considered in this context.

J.C. HUTTON
H.W. DAVIDSON
M. PESHAVARIA
Department of Clinical Biochemistry,
University of Cambridge,
Cambridge CB2 2QR, UK

1. Eiden, L.E. *Nature* **325,** 301 (1987).
2. Huttner, W.B. & Benedum, U.M. *Nature* **325,** 305 (1987).
3. Tatemoto, K. *et al. Nature* **324,** 476 (1986).
4. O'Connor, D. *et al. Life Sci.* **33,** 1657 (1983).
5. Wilson, B.S. & Lloyd, R.V. *Am. J. Path.* **115,** 458 (1984).
6. Cohn, D.V. *et al. Endocrinol.* **114,** 1963 (1984)..
7. Schwartz, T.W. *FEBS Lett.* **200,** 1 (1986).
8. Andrews, P.C. *et al. J. biol. Chem.* **261,** 8128 (1986).
9. Falkensammer, G. *et al. Neuroscience* **14,** 735 (1985).
10. Sopwith, A. *et al. Biochim. biophys. Acta.* **803,** 342 (1984).
11. Hutton, J.C. *et al. FEBS Lett.* **188,** 336 (1985).
12. Hutton, J.C. *et al. Biochem. J.* (in the press).
13. Hutton, J.C. *et al. Biochem. J.* (in the press).
14. Hutton, J.C. *et al. Endocrinology* (in the press).