20 Wiedenmann, B., Lawley, K., Grand, C. and Branton, D., *J. Cell Biol.*, 1985, **101**, 12.
21 Virshup, D M and Bennett, V., *J. Cell Biol.*, 1988, **106**, 39.
22 Goldstein, J L., Brown, M S, Anderson, R. G. W., Russell, D. W. and Schneider, W J, *Annu Rev. Cell Biol.*, 1985, **1**, 1.
23 Rothenberger, S, Iacopetta, B. J. and Kuhn, L. C., *Cell*, 1987, **49**, 423.
24. Pearse, B. M F., *EMBO J.*, 1985, **4**, 2457.
25. Mostove, K. E., de Bruyn, Kops, A. and Deitcher, C. L., *Cell*, 1986, **47**, 359.
26. Davis, C. G., Van Driel, I. R., Russell, D. W., Brown, M. S. and Goldstein, J L., *J. Biol. Chem.*, 1987, **262**, 4075.
27. Pearse, B. M. F., *EMBO J.*, 1988, **7**, 3331.
28. MacDonald, R. D., Pfeffer, S. R., Coussens, L., Tepper, M. A. and Brocklebank, C. M., *Science*, 1988, **239**, 1134.
29. Jing, S., Spencer, T., Miller, K., Hopkins, C. and Trowbridge, I. S., *J. Cell Biol.*, 1990, **110**, 283.
30. Kosaka, T. and Ikeda, K., *J. Cell Biol.*, 1983, **97**, 499.
31. Anderson, R. G. W., Brown, M. S. and Goldstein, J. L., *Cell*, 1977, **10**, 351.
32. Margh, M. and Helenius, A., *J. Mol. Biol.*, 1980, **142**, 439.
33. Patzer, E. J., Schlossman, D. M. and Rothman, J. E., *J. Cell Biol.*, 1982, **93**, 230.
34 Schlossman, D. M., Schmid, S. L., Braell, W. A. and Rothman, J. E., *J. Cell Biol.*, 1984, **99**. 723.
35. Quintart, J., Courtoy, P. J. and Bandhuin, P., *J. Cell Biol.*, 1984, **98**, 877.
36. Mellman, I., Fuchs, R. and Helenius, A., *Annu. Rev. Biochem.*, 1986, **55**, 663.
37. Helenius, A., Kartenbeck, J., Simons, K. and Fries, E., *J. Cell Biol.*, 1980, **84**, 404.
38. Tycko, B. and Maxfield, F. R., *Cell*, 1982, **26**, 643.
39. Anderson, R. G. W. and Orci, L., *J. Cell Biol.*, 1988, **106**, 539.
40. Kielian, M. C., Marsh, M. and Helenius, A., *EMBO J.*, 1986, **5**, 3103.
41. Lodish, H. *E., Trends Biochem. Sci.*, 1991, **16**, 374.
42. Dipaola, M. and Maxfield, F. R., *J. Biol. Chem.*, 1984, **259**, 9163.
43. Davis, C. G. *et al., Nature*, 1987, **326**, 760.
44. Dautry-Varsat, A., Ciechanover, A. and Lodish, H. F., *Proc. Natl. Acad. Sci. USA*, 1983, **80**, 2258.
45. Berg, T. and Tolleshang, H., *Biochem. Pharmacol.*, 1980, **29**, 917.
46. Underdown, B. J. and Shift, M. J., *Annu. Rev. Immunol.*, 1986, **4**, 389.
47. Geuze, H. J., Slot, J. W., Strous, G. J., Lodish, H. F. and Schwartz, A. L., *Cell*, 1983, **32**, 277.
48. Quintart, J., Courtoy, P. J. and Baudhuin, P., *J. Cell. Biol.*, 1984, **98**, 877.
49. Linderman, J. J. and Lauffenburger, D. A., *J. Theor. Biol.*, 1988, **132**, 203.
50. Linderman, J. J. and Lauffenburger, D. A., *Biophys. J.*, 1986, **50**, 295.
51. Abrahamson, D. R. and Rodewarld, R., *J. Cell Biol.*, 1981, **91**, 270.
52. Brown, M. G., Driscoll, J. and Monaco, J. J., *Nature*, 1990, **353**, 355.
53. Wileman, T., Boshans, R. L., Schlesinger, P. and Stahl, P., *Biochem. J.*, 1984, **220**, 665.
54 Mellman, I. and Plutner, H, *J. Cell Biol.*, 1984, **98**, 1170.
55. Ukkonen, P., Lewis, V., Marsh, M., Helenius, A. and Mellman, I., *J. Exp. Med.*, 1986, **163**, 952.
56. Anderson, R. G. W., Brown, M. S., Beisiegel, U. and Goldstein, J. L. *J. Cell. Biol.*, 1982, **93**, 523.
57. Hopkins, C. R. and Trowridge, I. S., *J. Cell Biol.*, 1983, **97**, 508.
58. Thureson-Klein, A. K. and Klein, R. L., *Int. Rev. Cytol.*, 1990, **121**, 67.
59. Wilson, D. W., Whiteheart, S. W., Orci, L. and Rothman, J. E., *Trends Biochem. Sci.*, 1991, **16**, 334.
60. Bradley, G., Juranka, P. F. and Ling, V, *Biochem. Biophys. Acta*, 1988, **948**, 87.
61. Simons, K. and van Meer, G., *Biochemistry*, 1988, **27**, 6197.

REVIEW ARTICLE

Diabetes and avian resistance

Bandana Guha and Asok Ghosh

Department of Zoology, University of Calcutta, 35, Ballygunge Circular Road, Calcutta 700 019, India

In comparison to other vertebrates, the birds are more resistant towards experimental manipulations which cause onset of diabetes mellitus. In contrast to mammals spontaneous diabetes has been reported in some parakeets only. In this paper we discuss various plausible factors behind this refractoriness. Significance of glucagon/insulin ratio, high avian somatostatin and avian polypeptide values in preventing diabetes have been emphasized.

THE advent of comparative approach to endocrine problems has sharpened the focus of many investigators on the usefulness of projecting the bird into the forefront of diabetes mellitus-related studies. Diabetes mellitus is a metabolic disorder characterized by clinical symptoms resulting from real or apparent insufficient pancreatic secretion of insulin or overabundance of some insulin-inhibiting factors.

Spontaneous diabetes mellitus

In addition to the prevalence of spontaneous diabetes in humans, it has also been observed in domestic and captive animals like horse, cattle, pig, sheep, dog, cat and monkey[1]. Among aves, spontaneous diabetes mellitus as a clinical entity to our knowledge has only been reported in some parakeets (*Melopsittacus undulatus*)[2]. The parakeets showed polydipsia, polyurea, weight loss, high-urine glucose and elevated blood

glucose level ranging from 720 mg/100 ml to 945 mg/100 ml (nonfasted normal values 210/100 ml to 520 mg/100 ml). Most cases could be regulated by single doses of NPH insulin. When insulin was withheld, hyperglycaemia and other clinical symptoms reappeared. Histopathological investigations show hepatic fibrosis and lipidosis.

Experimental diabetes mellitus

Pancreatectomy

The research activities of previous decades have established that a number of experimental manipulations can successfully cause the onset of diabetes in most vertebrates. Among these, surgical extirpations of the pancreas have been observed to bring about, hypoglycaemia, endocrine pancreatic dysfunction and disturbances in carbohydrate utilization which result in diabetes.

The intensity of the diabetic state in vertebrates after pancreas removal is, however, quite variable. The herbivorous animals appear to tolerate pancreatectomy better than carnivores. Students of carbohydrate metabolism have been intrigued for over 90 years by the apparent differences existing between birds and mammals in response to surgical ablation of discrete pancreas[3,4]. Most birds (except some carnivorous species) did not exhibit the typical diabetic symptoms after total pancreatectomies[5,6]. This premise has, however, been questioned by the more recent investigations of Mialhe[7-9] in ducks, Sitbon[10], Karman and Mialhe[11] in goose and Mikami and Kazuyuki[12] in chicken.

Sitbon *et al.*[3] reported the occurrence of permanent diabetes in granivorous as well as carnivorous birds. They were of the opinion that the so-called total pancreatectomies, as reported by earlier workers, were not complete and the existence of the smaller splenic lobe and its role was not appreciated then.

In birds, incidentally, only a few reports are available on the pancreatectomy-induced changes in the beta cells of islets of langerhans. In recorded cases of permanently depancreatized diabetic ducks, the light microscopic observations indicate the presence of vacuolated beta cells among normal alpha cells[6]. Smith[13] in his ultrastructural study observed that removal of the ventral lobe of the pancreas resulted in time-dependent alterations in the beta cell granules of the islets of Langerhans of Japanese quails. In an interesting study Cislak and Hazelwood[14] found that, in chickens, surgical removal of splenic lobe of the pancreas resulted in almost immediate enlargement of splenic remnant. This surprisingly resulted in a insulin/-glucagon molar ratio which was approximately one-half of the normal value of chicken. The altered insulin/-glucagon proportion adequately prevented permanent diabetes in chicken.

Cytotoxic agents

It is well known that injection of alloxan, an uride of mesoxalic acid, into various vertebrates produces diabetes by selectively destroying the beta cells of the islets of Langerhans[15-18].

Significantly, as in the case of pancreatectomies in birds, alloxan did not produce diabetes in owls, pigeons and chickens[19], and ducks[20]. In some species only temporary elevation of blood glucose was observed but the beta cells remained unaltered[21].

In this laboratory, Guha[22] also failed to obtain evidences of diabetes after alloxan administration in four species of Indian birds, viz. black munia, crow, kingfisher and parakeets. However in coturnix quail, a distinct hypoglycaemia was observed which was not accompanied by degenerative changes in the beta cells of the islets of Langerhans. Alloxan, at doses several times higher than that is diabetogenic in mammals, did not alter basal- or glucose-stimulated plasma insulin levels in chicken, neither was glucose tolerance impaired[23]. Danby *et al.*[24] also confirmed the ineffectuality of alloxan in inducing diabetic symptoms in most species of birds.

Streptozotocin, a highly specific diabetogen, has also been used to selectively destroy the beta cells in a variety of mammals[25-27]. In contrast to what has been reported in mammals, streptozotocin when injected into chickens is ineffective in producing the acute symptoms of diabetes mellitus[28]. In the same species Stellenwerf and Hazelwood[23] noted that even though induced insulin secretion was markedly reduced, diabetes mellitus did not occur. However, streptozotocin-treated depancreatized chickens exhibited a glucose-induced insulin secretion and impaired removal of the injected glucose load. Unlike alloxan-treated chickens, pancreatic tissue immunoreactive insulin concentration was generally reduced with streptozotocin injection.

The diabetogenic action of streptozotocin was also tested on three Indian bird species, viz. pigeon, crow and parakeet in our laboratory. Pigeon did not show any glycaemic disturbance. Marked hyperglycaemia was observed only in crow, while in parakeet the glucose upheaval was only transient. These changes were not accompanied by any discernible alterations in the beta cells[29].

Chronic treatment of large doses of ascorbic acid or its oxidation product, dehydroascorbic acid, produces hyperglycaemia and occasionally death in rats and guinea pigs[30-32]. Dehydroascorbic acid has been suggested to the original compound inducing diabetes by acting as an alloxan-like agent[33].

However, no true diabetic syndrome could be achieved by both acute and repeated treatment of ascorbic and dehydroascorbic in birds like common myna, parakeet and owl (Ghosh, unpublished data). Earlier studies[33] have indicated that in domestic fowls, ascorbic acid affects *in vitro* both insulin and avian pancreatic polypeptide (APP) secretions. Chronic treatment of ascorbic acid also resulted in release of insulin secretion after intravenous glucose injection.

The above review reveals that in birds unlike mammals and other vertebrates, true insulin-deficiency syndrome is not observed and the pancreatectomy technique is partially successful in bringing about diabetic symptoms in certain restricted birds species only. The occasionally appearing endocrine dysfunctions are not totally comparable to spontaneous diabetes mellitus of mammals. Moreover the avian endocrine pancreatic beta cells are not vulnerable to the action of cytotoxic agents. Various theories have been advanced to explain this unique refractoriness of the birds.

Refractoriness of avian β-cells

It is well known that in various species glutathione has a significant role in protecting most cells against alloxan[34]. The pancreatic glutathione level of birds is significantly higher than that of mammals[35]. However, recent endeavour in our laboratory, in ascertaining whether the high normal glutathione values of birds act as deterrent to experimental diabetogenesis, proved to be negative. It was observed that owls which have high glutathione level, compared to pigeons, are rather more prone to developing hyperglycaemia after ascorbic acid administration (Ghosh, unpublished data). Commenting on this subject, Stellenwerf and Hazelwood[23] opinied that the efficacy of alloxan in inducing diabetes in mammals is related to blood glucose concentration existent at the time of injection, since D-glucose injection into rat afforded full protection against the diabetogenic effect of subsequent alloxan injections[36,37]. According to Carter and Younathan[36] and Watkins and Cooperstein[37], the inability of alloxan to disturb carbohydrate metabolism in fowl may be due, in part, to normal 'elevated' blood glucose levels. Normal blood glucose levels in adult chickens range from 200 to 250 mg/dl, compared to 80–110 mg/dl in most mammals. Alternatively, they also suggested that the metabolic fate of alloxan in chicken may differ from that of rat. However, since the half-life of alloxan is 0.9 min *in vitro* and probably less *in vivo*, it appears unlikely that metabolic degradation of this pyrimidine-related compound account for the observed species difference in diabetogenecity[38].

Birds have undergone an adaptive radiation that in recent geological times has been revealed by no other vertebrates except the teleosts[39]. The coordination of pancreatic endocrine secretions in aves is necessary to meet the varying demands on the organism by activities as diverse as prolonged starvation, prevernal hyperphagia and migratory flight of thousands of miles. The appropriate mixture of insulin, glucagon, somatostatin and even APP is necessary for the bird to adjust to its nutrient availability disposal[40].

Glucagon/insulin ratio and somatostatin

Significantly, the quantitative and qualitative study of hormones like insulin, glucagon, somatostatin and APP reveals some remarkable avian characteristics. Sitbon *et al.*[12] indicated that plasma glucagon/insulin ratio may be one of the critical factors in maintaining a normal plasma glucose level in birds. They also commented that though the relationship of diabetes mellitus to somatostatin is not clear, the importance of somatostatin in avian glucose regulation cannot be totally ignored. Recent studies have provided evidence, indicating that somatostatin may be very important in regulating the insulin/glucagon molar ratio appropriate for metabolic condition present at any given time. Such tuning of the endocrine pancreas by somatostatin would allow the appropriate hormone mixture to be released against any metabolic even to bring about carbohydrate homoeostasis[39]. This observation merits consideration as Strosser *et al.*[41] also found that, somatostatin analogues, in addition to growth hormone release, have significant role in the pancreatic function in immature ducks (*Anas platyrhynchos*). Honey *et al.*[42] also observed that, somatostatin continuously inhibits alpha- and beta-cell output and glucose suppression of glucagon release is partially dependent upon local somatostatin secretion.

The avian delta cells

Interestingly the avian endocrine pancreas is known to contain large number of delta cells[43,44], and somatostatin is known to be contained in the pancreatic delta cells[45]. Further, the chicken pancreas has been reported to contain the highest concentration of somatostatin of all vertebrates thus far examined, being at least 13–21 times more than that in human pancreas. In pigeon, where pancreatic somatostatin was first characterized, pancreatic levels of the hormone approach 183 times that in the human pancreas[46,47].

In an earlier review Epple[1] reported that in experimentally diabetic rats and guinea pigs, there occurs a relative or even absolute increase of the delta cells[48]. Hellman and Petersson[49] and Kobayashi *et al.*[50] questioned whether the enlarged number of delta cells in human diabetes mellitus indicates reaction to

Table 1. Glycaemic effects of ascorbic acid (AA), dehydroascorbic acid (DHAA), streptozotocia and alloxan on some common birds

Bird	Beta cytotoxin used	Results	B:D cell ratio of the species (modified from Guha and Ghosh[43])
Acridotheres tristis *Common myna* Order, Passeriformes Family, Sturnidae	AA and DHAA	Slight hyperglycaemia with AA and DHAA (Ghosh, unpublished)	1:1
Psittacula krameri Parakeet	Streptozotocin, AA and DHAA	Only transitory hyperglycaemia after streptozotocin (Sinha Hikim *et al.*[29]) No significant change with other agents (Ghosh, unpublished)	1:3
Coturnix coturnix Quail Order, Galliformes Family, Phasianidae	Alloxan	Significant hypoglycaemia (Guha[22])	1:1
Corvus splendens *Crow* Order, Passeriformes Family, Corvidae	Alloxan and streptozotocin	No change after alloxan (Guha[22]) Marked hyperglycaemia after streptozotocin	1:1
Lonchura malacca Black munia Order, Passeriformes Family, Ploceidae	Alloxan	No change (Guha[22])	2:3
Halcyon smyrnensis Kingfisher Order, Coraciformes Family, Alcedinidae	Alloxan	No change (Guha[22])	2:3
Columba livia Pigeon Order, Columbiformes Family, Columbidae	Streptozotocin	No change (Sinha Hikim *et al.*[29])	1:3

diabetic disorders rather than a primary cause. They speculated that such a reaction could compensate the effect of insulin deficiency in two ways (i) by secretion of a protective hormone, e.g. substance preventing fatty liver and (ii) by transformation of delta cells into beta cells.

The finding of the potent inhibitory effect of somatostatin upon alpha and beta cells has led to the hypothesis that delta cells modulate insulin and glucagon release through paracrine secretions[51,52].

Hence, taking all the above into consideration, it may be rather exciting to speculate that, in birds, the large number of delta cells (see Table 1) in some way actively help in preventing beta cell destruction, leading to experimental diabetogenesis. Interestingly, Table 1 indicates that birds which are, at least to minor extent, susceptible to the effects of beta cytotoxic agents have rather low beta: delta ratios.

The role of APP

The dual role of APP as a gastric secretagogue and metabolic regulator in the enteric-pancreatic axis, indicate that it has a profound role in absorption, metabolism and disposition of food stuff. Since the bird is endowed with high pancreatic and plasma polypeptide concentration[53], the avian polypeptide as a factor in avian diabetogenic refractoriness cannot be ruled out. Moreover, in genetically obese mice, an intriguing study which needs further confirmation revealed that hyperglycaemia and diabetic-type glucose intolerance can be ameliorated when the animals are daily injected with avian polypeptide or bovine polypeptide for a month, or receive a graft of alloxan diabetic mice pancreatic tissue[54].

To conclude, certain critical factors like glucagon/insulin ratio, high somatostatin and avian polypeptide values may play significant roles in preventing diabetogenesis in birds. However, a possibility that also cannot be totally ignored is that, due to some special fine structural and biochemical cell membrane characters, the avian beta cells are successful in neutralizing/repulsing the physiological and chemical challenges which cause experimental diabetes mellitus. Such a feasibility thus offers immense scope for experimental work in the future.

1. Epple, A., *Endocrinol Jap.*, 1968, **15**, 107.
2. Altman, R. B. and Kirmayer, A. H., *J. Am. Anim. Hosp. Assoc.*, 1976, **12**, 531.

3 Sitbon, G., Laurent, F., Mialhe, A., Krug, E., Karman, H., Gross, R., Strosser, M. T., Cohen, L., Jean Marie, P., Foltzer, C. and Mialhe, P., *Horm. Metab. Res.*, 1980, **12**, 1.
4 Hazelwood, R. L., *Avian Physiology*, Springer Verlag, New York, 1985.
5 Mirsky, I. A., Nelson, N., Grayman, I. and Korenberg, M., *Am. J. Physiol.*, 1942, **135**, 223.
6. Nelson, N. S. and Elgart, I. A., *Endocrinology*, 1942, **31**, 119.
7. Mialhe, P., *Acta Endoc. (Kbh). Suppl.*, 1958, 36.
8 Mialhe, P., *Excerpta Medica*, 1969, **184**, 158.
9. Mialhe, P., *Excerpta Medica*, 1971, **231**, 843
10 Sitbon, G., *Diabetologia*, 1967, **3**, 427.
11. Karman, H. and Mialhe, P., *Diabetologia*, 1968, **4**, 394.
12. Mikami, F. and Kazuyuki, O., *Endocrinology*, 1962, **71**, 464.
13. Smith, P. H., *Gen. Comp. Endocrinol.*, 1975, **26**, 310.
14. Cislak, S. R. and Hazelwood, R. L., *Gen. Comp. Endocrinol.*, 1986, **61**, 469.
15. Dunn, J. S., Sheehan, H. L. and McLetchie, N. G. G., *Lancet*, 1943, **1**, 484.
16. Goldner, M. G. and Gomori, G., *Endocrinology*, 1943, **33**, 297.
17. Hughes, H., Ware, L. L. and Young, F. G., *Lancet*, 1944, **1**, 148.
18. Bailey, O. T., Bailey, C. C. and Hagan, W. H., *Am. J. Med. Sci.*, 1944, **208**, 450.
19. Scott, C. C., Harris, P. N. and Chen, K. K., *Endocrinology*, 1945, **37**, 201.
20. Mirsky, I. A., *Proc. Soc. Exp. Biol. Med.*, 1945, **54**, 35.
21. Goldner, M. G. and Gomori, G., *Proc. Soc. Exp. Biol. Med.*, 1945, **58**, 31.
22. Guha, B., *Indian Biol.*, 1976, **8**, 71.
23. Stellenwerf, Jr. W. A. and Hazelwood, R. L., *Gen. Comp. Endocrinol.*, 1979, **39**, 131.
24. Danby, R., Bluff, L., Deheny, T. P. and Gibson, W. R., *Gen. Comp. Endocrinol.*, 1982, **47**, 159.
25. Radkieten, N., Radkieten, M. and Nadkarni, V., *Cancer Chemother. Rep.*, 1963, **29**, 91.
26. Junod, A., Lambert, A. E., Orei, L., Pictet, R., Gonet, A. E. and Renold, A. E., *Proc. Soc. Exp. Biol. Med.*, 1967, **126**, 201.
27. Fischer, L. J. and Richert, D. E., *CRC Crit. Rev. Toxicol.*, 1975, 231.
28. Langlow, D. R., Butter, E. J., Hales, C. N. and Pearson, A. W., *J. Endocrinol.*, 1970, **46**, 243.
29 Sinha Hikim, A., Verma, R. and Ghosh, A., *Arch. Biol. (Bruxelles)*, 1983, **94**, 15.
30. Patterson, J. W., *Endocrinology*, 1949, **45**, 344
31. Patterson, J. W., *J. Biol. Chem.*, 1950, **183**, 81.
32. Chitterjee, I. B., Mazumdar, A. K., Nandi, B. K. and Subramaniam, N., *Ann. N.Y. Acad. Sci.*, 1975, **258**, 24.
33. Meglasson, M. D. and Hazelwood, R. L., *Gen. Comp. Endocrinol.*, 1982, **47**, 205.
34. Lazarow, A., *Proc. Soc. Exp. Biol. Med.*, 1946, **61**, 441.
35. Ghosh, B., Guha, B. and Ghosh, A., *Nat. Acad. Sci. Lett.*, 1990, **13**,
36. Carter, W. J. and Younathan, E. S., *Proc. Soc. Exp. Biol. Med.*, 1962, **109**, 611.
37. Watkins, D., Cooperstein, S. J. and Lazarow, A., *Amer. J. Physiol.*, 1973, **224**, 718.
38. McDaniel, M. L., Anderson, S., Fink, J., Roth, C. and Lacy, P. E., *Endocrinology*, 1975, **97**, 68.
39. Hinde, R. A., *Avian Biol.*, 1973, **3**, 479.
40. Hazelwood, R. L., *J. Exp. Zool.*, 1984, **232**, 647.
41. Strosser, M. T., Harvey, S., Foltzer, C. and Mialhe, P., *Gen. Comp. Endocrinol.*, 1984, **56**, 265.
42. Honey, R. N., Arimura, A. and Weir, G. C., *Metabolism*, 1981, **29**, 1242.
43. Guha, B. and Ghosh, A., *Gen. Comp. Endocrinol.*, 1978, **34**, 38.
44. Roth, A., *Acta. Anat.*, 1968, **69**, 609.
45. Polak, J. M., Bloom, S. R., Adrian, T. E., Heitz, P., Bryant, M. G. and Pearse, A. G. E., *Lancet*, 1976, **2**, 328.
46. Gerich, J., *Diabetes Mellitus*, Medical Examination Publication Co., New York, 1983.
47. Speiss, J., Rivier, J. E., Rodkey, J. A., Bennet, C. D. and Vale, W., *Proc. Natl. Acad. Sci., USA*, 1979, **76**, 2974.
48. Hellerstrom, C., *Med. Upsaliensis*, 1963, **68**, A1.
49. Hellman, B. and Petersson, B., *Endocrinology*, 1963, **72**, 238.
50. Kobayashi, K., Takahashi, Y. and Tosita, T., *Arch. Histol. Jpn.*, 1964, **25**, 165.
51. Krocker, D. J., Ruch, W., Chidcckel, E., Palmar, J., Goodner, C. J., Ensinck, J. and Gale, C. C., *Science*, 1974, **184**, 482
52. Gullman, R. and Gerisch, J. E., *Ann. Rev. Med.*, 1976, **27**, 379.
53. Hazelwood, R. L., *Pavo*, 1978, **16**, (special vol) 23.
54 Gates, R. J. and Lazarus, N. R., *Hormone Res.*, 1977, **8**, 189.

RESEARCH COMMUNICATIONS

Speed-up factors for simulation of neural networks on a parallel computer

G. Athithan

ANURAG (Advanced Numerical Research and Analysis Group), P. O. Kanchanbagh, Hyderabad 500 258, India

The Hopfield model of neural networks is one of the best-studied neural-network models, from both theoretical and experimental angles[1-3]. Simulation of the Hopfield model in its discrete version, though not strictly a supercomputer job, requires fast computers, especially when one wants to study a model of large size. High computing speeds are also necessary when one wants to study the efficacy of any newly proposed learning prescription in an exhaustive manner. Since parallel computing has proved to be a cost-effective means of achieving higher speeds, there is a case for trying it in the area of simulation of neural networks. ANURAG is in the process of building a 128-node message-passing type of parallel computer. A prototype consisting of eight nodal processors, called PACE-8, has been described earlier[4]. Here I report simulation of the discrete Hopfield model on this prototype, and compare the speed-up in computation achieved owing to parallelization with the theoretical speed-up for various sizes of neural network.

In any simulation of neural-network models there are two distinct phases to be dealt with, namely the learning phase and the recall phase. In this paper I report primarily the results of parallel simulation of the recall phase of the Hopfield model. Throughout the