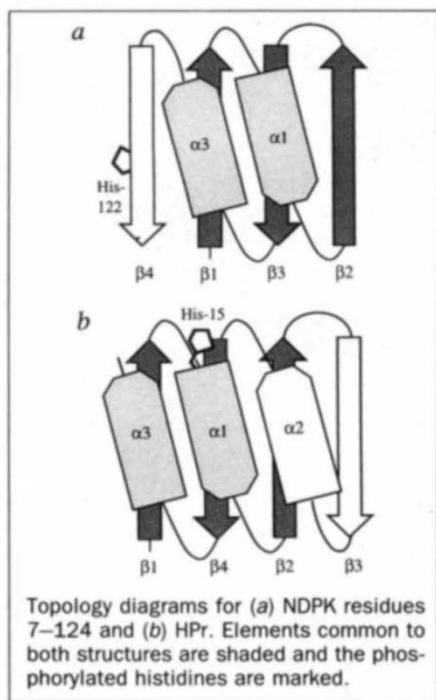


Shared structural motif in proteins

SIR — Swindells *et al.* in Scientific Correspondence¹ observe that the phosphocarrier protein HPr shares with acylphosphatase (APt) a structural motif made of three antiparallel β -strands and two connecting α -helices. They ask whether this is a recurrent phosphate-binding motif. The answer is no.

Alpha/beta motifs are usually built around a parallel β -sheet, but antiparallel β -sheets are not uncommon. Ferredoxin² is an early example of the antiparallel α/β fold. Its four-stranded β -sheet has the same topology as in APt³, the activation domain of procarboxypeptidase⁴ and the RNA-binding domain of the U1 ribonucleoprotein⁵, but HPr (ref. 6) is different. When we determined the X-ray



structure of nucleoside diphosphate kinase (NDPK)⁷, we found that the NDPK subunit is like all these proteins, and also like the allosteric domain of *Escherichia coli* aspartate transcarbamylase⁸, which binds nucleotides.

We suggested⁷ that the four-stranded antiparallel α/β structure of NDPK is a nucleotide-binding motif, different from the one based on a parallel β -sheet found in most kinases⁹. I think that this proposal has a stronger basis than that of Swindells *et al.*¹. First, the fourth strand makes the motif less likely to occur by chance. With three strands, the β -sheet can have only three different topologies, two of which accept α -helix connections. All antiparallel α/β structures contain one of these two topologies. With four β -strands,

there are twelve topologies; eight can accommodate helix connections. Second, our comparison is based on known positions of the binding sites, whereas that of APt is unknown. The NDPK active site is a histidine which becomes phosphorylated as part of the catalytic cycle. It is on the face of the β -sheet that is not covered with α -helices. So are the nucleotide-binding site of the allosteric domain⁸ and the RNA-binding site of the U1 domain as defined by mutation studies⁵.

I predict that APt will have its active site on this face of the β -sheet rather than near helix $\alpha 1$ as in HPr. Part of the HPr β -sheet can be superimposed on NDPK just as for APt (see figure). The fit is excellent for the three common β -strands, but very poor for α -helices, and the remainder cannot be superimposed at all. Both NDPK and HPr carry phosphorylated histidines. They are 28 Å apart, about as far as possible in proteins of this size. In my view, this precludes the common three-stranded structural motif from having a functional significance.

Joël Janin

Laboratoire de Biologie Structurale
UMR 9920,
CNRS-Université Paris-Sud,
Bât. 433, 91405-Orsay, France

SWINDELLS *ET AL.* REPLY — The chief aim of our Scientific Correspondence¹ was to point out the structural similarity between HPr and APt. With the coordinates of NDPK kindly provided by Professor Janin but not yet available in the protein databank, we can confirm that this protein belongs to the same structural family.

But a structural similarity on its own does not constitute a functional motif, which requires some evidence of conserved functional residues in the sequence. There are many examples of proteins with the same structural motif but different functions, such as the Rossmann fold. The phosphate-binding histidine of HPr is replaced in APt by the sole conserved arginine. This was the basis of our hypothesis, and is also in agreement with the tentative experimental data presented on the phosphate binding site in APt (ref. 3). The fold of NDPK is actually much more complex than APt and HPr, with two additional helices inserted (not shown in Janin's

figure). This is important because in NDPK these helices form a cleft on one side of the sheet into which the nucleotide binds. Unfortunately, current structure and sequence data are inconclusive and only experimental work will accurately pinpoint the active site of APt.

Mark B. Swindells

Protein Engineering Research Institute,
6-2-3 Furuedai, Suita,
Osaka 565, Japan

Christine A. Orengo

David T. Jones

Laurence H. Pearl

Janet M. Thornton

Department of Biochemistry and Molecular
Biology,
University College London,
London WC1E 6BT, UK

Bird or dinosaur?

SIR — Perle *et al.*¹, in reporting their find of the fossil *Mononychus*, call it a 'bird' in the title of their paper and a 'dinosaur' in its third and fourth lines. They endorse the view² that *Archaeopteryx*, although a bird, is not a member of Aves. Instead, *Archaeopteryx* is a member of Aviales^{1,2}, a more inclusive taxon than Aves that now also includes the taxa Ornithurae², Metornithes¹ and Ornithothoraces³. Each of these new taxa differs from Aves only by including one or more fossil species; when new fossils are discovered or the relationships of known fossils are analysed with greater care, many more such taxa will surely be necessary. Hennig^{4,5} foresaw the problem: "This kind of procedure would lead to unimaginable nomenclatorial complications — and in some cases has already done so"⁵.

Hennig^{4,5} showed that there are three ways of circumscribing a monophyletic group with living and fossil members. The first (method 1) is to limit it to the species that "appear to have descended from the latest common stem-species"⁵; this, the 'crown-group'⁶ concept, is adopted by Perle *et al.*¹ in circumscribing Aves. The second (method 2), the 'total-group'⁶ concept, is to include all fossil species that are more closely related to the crown-group than to its extant sister-group. The third (method 3), which Hennig called "the method usually followed in palaeontology", is to select one or more of the characters of a group as "essential", and to include in the group only those fossils possessing the key character(s); this method is used by Perle *et al.* in circumscribing 'birds', with feathers as the key character. Hennig settled on method 2 as "the most suitable one for phylogenetic research". Perle *et al.* have chosen a combination of methods 1 (in circumscribing Aves) and 3 (in circumscribing 'birds') which, apart from the nomenclatorial complications that method 1 demands,

- Swindells, M. B., Orengo, C. A., Jones, J. T., Pearl, L. H. & Thornton, J. M. *Nature* **362**, 299 (1993).
- Adman, E. T., Sieker, L. C. & Jensen, L. H. *J. Biol. Chem.* **248**, 3987–3996 (1973).
- Pastore, A., Saudek, V., Ramponi, G. & Williams, R. J. P. *J. molec. Biol.* **224**, 427–440 (1992).
- Coll, M., Guasch, A., Avilés, F. X. & Huber, R. *EMBO J.* **10**, 1–9 (1991).
- Nagai, K., Oubridge, C., Jessen, T. H. & Evans, P. R. E. *Nature* **348**, 515–520 (1990).
- Herzberg, O. *et al. Proc. natn. Acad. Sci. U.S.A.* **89**, 2499–2503 (1992).
- Dumas, C. *et al. EMBO J.* **11**, 3203–3208 (1992).
- Gouaux, J. E., Stevens, R. C. & Lipscomb, W. N. *Biochemistry* **29**, 7702–7715 (1990).
- Schultz, G. E. *Curr. Opin. Struct. Biol.* **2**, 61–67 (1992).