

Fig. 3. (a) An arrangement of helices in the unit cell of tRNA^{Met} which will account for the Patterson synthesis (b) of the experimental ($h k 0$) reflections.

from the two short helices to the main helix; and (iv) the rotational orientation of the model in the unit cell. The search through each of the variables was done separately. Each of the optimizations revealed a fairly sharp minimum in R and no great interaction of one optimization with another. The optimized main helix axis location was within 0.5 Å of the position determined in the first search of the net. The residual obtained with the 21 nucleotide pair model was $R = 0.32$, and the agreement of the calculated and observed Pattersons was also improved.

This model included slightly more than half of the nucleotides of the entire molecule. The $R = 0.32$ seemed good enough to justify the calculation of phases. These were assigned to the experimental structure amplitudes, and the projected electron density was computed (Fig. 2d). The dominant features are the rings of charge surrounding the positions of the long helix axes of the model. The rest of the molecule was then added with the least possible alteration of the charge density distribution of Fig. 2d. This can be achieved reasonably well with the model previously described (3) in which the helices of the CCA arm (a) and T ψ CG arm (e) form a continuous 12 base pair double helix. Below this at the T ψ CG end, and coaxial with it, the anticodon arm (c) is placed in the Fuller-Hodgson configuration (6). The crystallography demands a somewhat more asymmetric cross section than was used in (3). We place the dihydrouracil arm (b) about 8 Å from the main helix axis rather than 4 or 5 Å. The complete molecule gives the same phases as those calculated from the 21 nucleotide pair partial model. The Patterson calculated from the complete model is shown in

Fig. 2b, and the electron density at a resolution of 12 Å is in Fig. 2c. The residual is $R = 0.24$.

The most interesting result of the analysis is the evidence for a long double helix parallel to the c -axis. We emphasize that this evidence is quite convincing. The experimental Patterson projection shows peaks which are sharp, circular, and centered at vectors which represent the distances between neighboring molecules. There are two classes of neighboring molecules which, because of the lattice symmetry, are related by rotations of 90° and 180° in the plane of projection. The fact that the Patterson peaks arising from both classes of vectors are similar, sharp, and circular, suggests that at this resolution the molecule's projected electron density is likely to be nearly circular. To check the model dependence of our results, the base plane of the unit cell was searched by use of one turn of a DNA B helix instead of the RNA helix. The residual showed no significant minimums and no sharp Patterson peaks were observed corresponding to translational vectors between molecules. The principal difference in the axial projections of the two helices is the existence of a much higher charge density near the helix axis in the DNA. One expects the translation of a ring of charge to give a Patterson more strongly peaked about the translation vector than does the translation of a disc of charge.

Finally, we point out that if the molecule is in fact 80 or 85 Å long then the pairs whose projections are about 12 Å apart have some end-to-end overlap along the c -axis. The crystal structure is essentially a side-by-side array of chains of overlapping molecules.

Figure 3a shows an arrangement of

helices in the unit cell of tRNA^{Met} which will account for the peaks in the Patterson synthesis (Fig. 3b) of the experimental $h k 0$ reflections. A model similar to that used for tRNA^{Leu} gives a Patterson in excellent agreement with experiment. The residual is 0.27. The pairs of helices are separated by 12 Å just as in the case of tRNA^{Leu} . An end-to-end chaining is possible, but, because in tRNA^{Met} there are dyad axes perpendicular to c , alternate molecules along the chain must be inverted. In tRNA^{Leu} they all point in the same direction.

The model we have used meets the demands of the x-ray data in a natural and straightforward way, but other arrangements of the arms are no doubt possible which give a continuous double helix and compact packing of the rest of the molecule.

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Physalia Nematocysts: Utilized by Mollusks for Defense

Abstract. *Nudibranchs* *Glaucus* and *Glaucilla store* and utilize for their own defense the nematocysts of the venomous siphonophore *Physalia*.

During early 1968, bathers in the sea at Port Stephens, New South Wales, Australia, were being unpleasantly

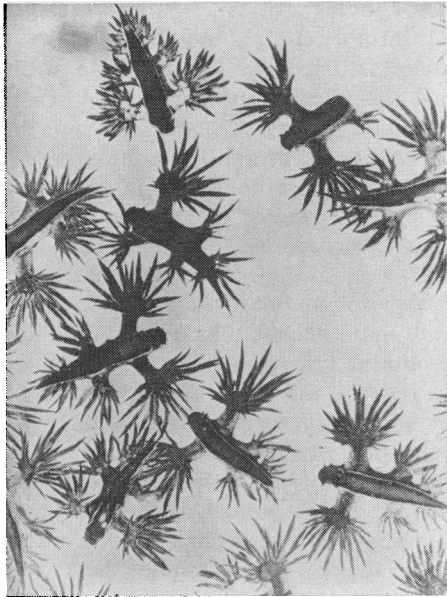


Fig. 1. *Glaucilla* floating in the usual attitude, upside down near the seawater surface, buoyed up by bubbles of air gulped into the stomachs. [Photograph by J. Myers.]

stung by numerous small blue invertebrates brought in with the surf. Although the stings were not severe (mild pain for 1 or 2 hours), specimens were sent to the Australian Museum from where they were passed to us for examination. They proved to be nudibranch mollusks (sea slugs) of the planktonic family Glaucidae (Fig. 1), of which two species occur sporadically in eastern Australian waters—*Glaucus atlanticus* Forster, 1777, and *Glaucilla marginata* Bergh, 1868. Hitherto nudibranchs were not thought to be harmful to man. It has been known, however, that

many eolidiform species utilize for defense (against fish and perhaps other predators) the nematocysts (stinging cells) of the coelenterates upon which they prey (1).

Microscopic preparations of the dorsal papillae or cerata of the Port Stephens specimens of *Glaucus atlanticus* revealed (Fig. 2) that the cnidosacs contained nematocysts which corresponded exactly with nematocysts of the venomous siphonophore *Physalia utriusculus*, the Portuguese man-of-war. It became clear that *Glaucus* and *Glaucilla*, which feed upon the chondrophores *Velella* and *Porpita* and the siphonophore *Physalia*, store the nematocysts of *Physalia* preferentially and employ them for their own defense. Other nematocysts are customarily digested and were found in the lumina of the digestive gland diverticula and in food vacuoles in the digestive cells. With respect to size, the nematocysts of *Physalia* fall into two classes which do not usually overlap (2). Australian *Glaucus* and *Glaucilla* utilize in their cnidosacs principally the largest nematocysts (which possess the longest penetrants when discharged). This is the explanation for the painful stings experienced by bathers at Port Stephens. Specimens from the Gulf of Aden, St. Helena, and Japan in the natural history collections of the British Museum were also examined, and the same type of *Physalia* nematocysts was identified.

Both *Glaucus* (3) and *Glaucilla* (4) are therefore potentially harmful to man over their whole geographical range. Both are warm-water species; the latter is restricted to the Pacific Ocean, but the former (despite the specific name *atlanticus*) occurs in the three major oceans.

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Purine Metabolism in Heterozygous Carriers of Hypoxanthine-Guanine Phosphoribosyltransferase Deficiency

Abstract. *The urate pool and daily turnover of urate, together with the rate of incorporation of glycine into urate, were measured in three asymptomatic mothers who had sons with various degrees of deficiency of hypoxanthine-guanine phosphoribosyltransferase activity. Two of these mothers had abnormally increased values for the urate pool, urate turnover, and 24-hour urinary excretion of uric acid. These two mothers also had reduced hypoxanthine-guanine phosphoribosyltransferase activity and increased adenine phosphoribosyltransferase activity in erythrocyte lysates. All three mothers showed an abnormal increase in urate production, as judged by the rate of incorporation of glycine into urate.*

The Lesch-Nyhan syndrome, characterized by mental deficiency, choreo-athetosis, and self-mutilation, is associated with gross overproduction of urate and excessive glycine incorporation into urate (1). Patients with the disorder have abnormal activities of the phosphoribosyltransferase enzymes involved in the reutilization of the purine bases; in erythrocyte hemolysates the activity of the enzyme for hypoxanthine and guanine is virtually absent, whereas that for adenine is increased (2). The disorder occurs only in males and is inherited in an X-linked fashion. In the mothers of patients with the Lesch-Nyhan syndrome (obligate heterozygotes), cultures of skin fibroblasts have two cell populations (3); one population has normal, and the other shows no hypoxanthine-guanine phosphoribosyltransferase (E.C. 2.4.2.8) activity. However, enzyme activities in hemolysates of erythrocytes have not been distinguishable from normal (4, 5). Studies of urate turnover in such heterozygotes have also been normal, although preliminary studies suggested that *de novo* purine synthesis might be increased (5, 6). A few patients with overproduction gout have also been described as having erythrocyte hypoxanthine phosphoribosyltransferase activities of less than 10 percent of normal (5), and other patients have manifestations intermediate between such gouty subjects and those with the full Lesch-Nyhan syndrome (7).

The three families studied illustrate

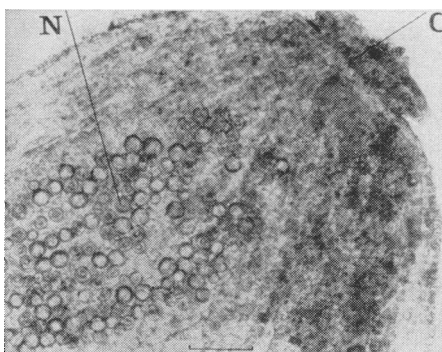


Fig. 2. Photomicrograph of an unstained squash preparation of the tip of a cerata (dorsal papilla) of *Glaucus*, showing the nematocysts causing injuries to bathers at Port Stephens in February 1968; N, nematocysts in cnidosac; C, cnidopore (scale 100 μ m).

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