

matter appear to be symmetric, and any asymmetry is more centrally located. Despite the symmetric shape, there are brightness variations around the shell that persist with time (1). One possible reason for this behavior is that the efficiency of particle acceleration at the outer shock front depends on the magnetic-field orientation. The magnetic field in a stellar wind should have a spiral pattern aligned about the stellar rotation axis. The magnetic field is too weak to affect the shock-wave dynamics, but it

could imprint a pattern on the radio synchrotron emission.

The observations thus confirm the basic wind-interaction model but raise issues that will require more detailed modeling and computer simulation. The combination of high densities and high velocities creates extreme conditions that are comparable with those in quasars, but here we have a clear picture of the physical situation. When the radio observations are combined with observations at optical, ultraviolet,

and x-ray wavelengths, we have a chance to follow and understand the initial expansion phases of the most extreme explosive events in nearby galaxies—supernovae.

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6. My research on supernovae is supported in part by NSF grant AST-9314724.

# Molecular Mimicry in Protein Synthesis?

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This week's issue of *Science* includes the first report by the Aarhus group of the crystal structure of elongation factor Tu (EF-Tu) complexed with aminoacylated phenylalanyl transfer RNA (tRNA) and guanosine triphosphate (GTP)—the EF-Tu ternary complex (1). EF-Tu and its eukaryotic homolog EF-1 $\alpha$  deliver aminoacyl tRNAs to the ribosome during the elongation phase of protein synthesis (see figure). In addition to providing insights into the way aminoacyl tRNAs get to the ribosome, this structure addresses a long-standing, mechanistic question: Why does EF-Tu deliver only aminoacylated elongator tRNAs to the ribosome, never uncharged tRNAs or initiator tRNAs? Both because of the biological importance of protein synthesis and because of the long scientific history of this complex, the publication of its structure is a landmark.

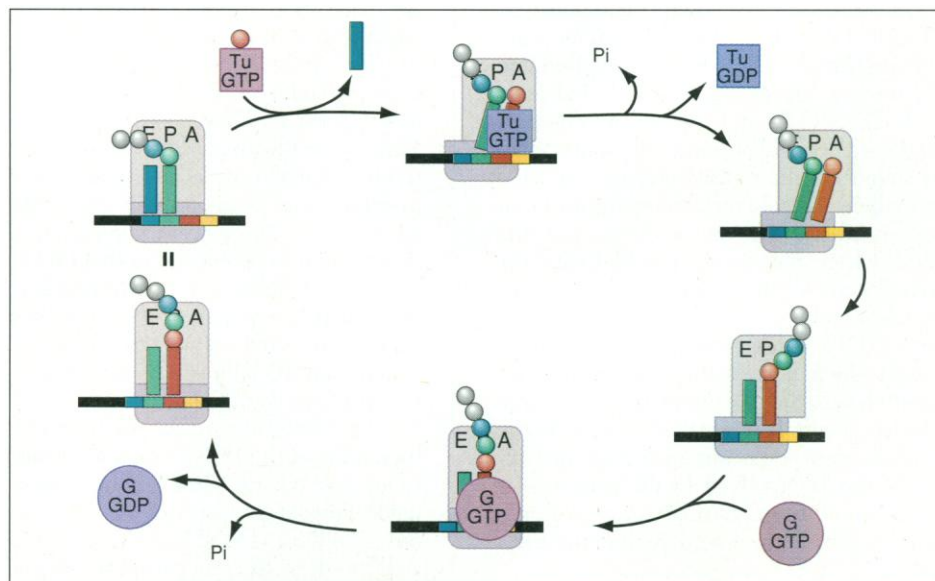
The article by the Aarhus group does more than present an important structure, however. Nissen and co-workers have discovered that the overall shape of the ternary complex resembles that of the guanosine diphosphate (GDP) form of elongation factor G (EF-G; EF-2 in eukaryotes), the protein that catalyzes the translocation step of elongation (see figure). During translocation, the ribosome moves down its messenger RNA (mRNA) by three bases, and the tRNAs bound to it are rearranged so that the ternary complex called for by the next codon can be accepted.

That EF-G and EF-Tu are structurally related was already known. Their amino-terminal domains bind guanine nucleotides and

are conformationally similar, as are their second domains (2–5). The new observation is that three domains at the carboxyl-terminal end of EF-G, which have no homologs in EF-Tu, together resemble tRNA and, relative to EF-G's nucleotide binding site, are positioned the same way as tRNA in the ternary complex. It seems that we have just been given a huge—albeit Delphic—hint about the mechanism of protein synthesis.

It was also known that EF-G and EF-Tu are functionally related (6, 7). EF-G and EF-Tu compete for a single factor binding site on the ribosome. Both bind to the ribosome when complexed with GTP and have guanosine triphosphatase (GTPase) activities that are activated by binding. Furthermore, both adopt conformations that have a low affinity for ribosomes after GTP hydrolysis. Nevertheless, the discovery that EF-G resembles the ternary complex suggests that the mechanism of EF-G-catalyzed translocation resembles the mechanism of EF-Tu-catalyzed tRNA binding at a far deeper level.

EF-G's function is easier to understand than EF-Tu's (6, 7). Translocation results when an elongating ribosome switches from its pretranslocational state to its posttranslocational state. EF-G-GTP binding



**Elongation cycle of protein synthesis.** The cycle starts with the binding of ternary complex to the ribosome (upper left), which results in the discharge of deacylated tRNA from the E site, placement of a new aminoacyl tRNA in the A site, and conversion of the ribosome from the post- to the pretranslocational state. Peptide transfer follows (right, middle). The binding of EF-G-GTP to the ribosome (lower right) restores the ribosome to the posttranslocational state, the mRNA advances by one codon, and its tRNAs are rearranged so that another cycle of elongation can ensue (8). Ribosomes are shown as rectangles; the upper third is the large subunit and the lower third is the small subunit. When the subunits are aligned, the ribosome is in its posttranslocational state. When they are misaligned, ribosomes are in the pretranslocational state. Transfer RNAs appear as colored bars, and their amino acids as small circles of the same color. Square, EF-Tu; large circle, EF-G. Messenger RNA is shown as a horizontal line that crosses the small subunit. Its colored segments represent specific codons, whose colors match those of the corresponding amino acids.

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reduces the activation energy required for this change. EF-G leaves the ribosome after translocation because its GTPase is activated in the posttranslocational complex. The return of the ribosome to the pretranslocational state occurs at some point between the stage when the ternary complex binds to the ribosome and the formation of the next peptide bond. If the ternary complex is like EF-G, shouldn't its binding to the ribosome trigger that conformational change? Otherwise, what is the common function that calls for a common structure?

GTP cleavage has a huge effect on the arrangement of domains in EF-Tu (2, 3, 8). Furthermore, in the placement of its first two domains, EF-G-GDP resembles the ternary complex, not EF-Tu-GDP (4, 5). Nissen *et al.* argue that the reason EF-G-GDP resembles the ternary complex is because it is associated with the ribosomal state to which ternary complexes bind. This is not convincing. Because neither EF-G-GDP nor EF-Tu-GDP bind to the ribosome, their conformations do not necessarily tell us anything about the ribosome. Only the structures of EF-G-GTP—which is unknown—and of the ternary complex are relevant; they both bind. Furthermore, Nissen *et al.* suggest that EF-G-GTP ought to resemble EF-Tu-GDP, and if EF-G-GTP is as different from EF-G-GDP as EF-Tu-GTP is from EF-Tu-GDP, the case for molecular mimicry could disappear entirely.

It seems at least equally plausible that EF-G-GTP will be found to differ only slightly from EF-G-GDP; it also will mimic the ternary complex. If this is so, binding of both EF-G-GTP and the ternary complex could facilitate changes in ribosomal state by stabilizing the transition state that separates them. Because the conformation of that state is independent of the direction of the state change, the similarity of EF-G and the ternary complex makes sense in this context.

Clearly, the structure of EF-G complexed with GTP is needed more than ever, and it is critically important that the step in elongation where the post- to pretranslocational change occurs be identified. Since, as the Aarhus group points out, molecular mimicry could also be involved in the activities of initiation and termination factors, research in these areas may also prove illuminating.

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# The United Nations Climate Convention: Unattainable or Irrelevant

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*"The ultimate objective of this Convention and any related legal instruments that the Conference of the Parties may adopt is to achieve, in accordance with the relevant provisions of the Convention, stabilization of greenhouse gas concentrations in the atmosphere at a level that would prevent dangerous anthropogenic interference with the climate system (1)."*

According to general circulation models (GCMs), a doubling of atmospheric CO<sub>2</sub> concentration would increase the global mean temperature by 1.5° to 4.5°C (2–4). This change would be dangerous in drought-prone regions and low coastal areas. Although other regions might benefit and the net global effect could be positive, some would suffer.

The United Nations Convention as quoted above tries to maintain the status quo by protecting the losers and minimizing the immense risks of global climate change. Although laudable, the specific wording of the "ultimate objective" does not express these aims correctly and realistically.

The atmospheric concentration of CO<sub>2</sub> was stable at 280 ± 5 parts per million (ppm) for 1000 years before the year 1800, according to ice-core records. As a result of human-made emissions, it has now increased by about 30% above this baseline (5). The current population of about 6 billion people emits about 6 billion tons of carbon into the atmosphere per year (6). A population of 10 billion people, projected for the year 2030 (7), would emit 10 billion tons if consumption patterns do not change.

The concentration of CO<sub>2</sub> started increasing in the 19th century according to ice-core records, although the human-made emissions were on the order of only 1 billion tons (5). If the aim is to stabilize the CO<sub>2</sub> concentration, annual emissions of less than 1 billion tons are therefore probably required; emissions must certainly be less than 2 billion tons per year.

With the current pattern of fossil fuel use, the population trend, and the trends in per capita emissions of CO<sub>2</sub> (6), a level

of emissions as low as 1 to 2 billion tons annually will not be reached in the next 50 years. A mere stabilization of emissions at the current level of 6 billion tons would be an achievement (8).

To avoid danger, greenhouse gas concentrations would need to be stabilized at a level less than double the pre-industrial value. However, reasonable emission scenarios indicate that a doubling of the greenhouse gas concentrations is inevitable in the 21st century. If the GCM projections are right, the climate will change, there will be dangerous effects, and the Convention objective will be unattainable.

Although the latest analyses suggest otherwise (4), let us assume that the GCM projections are wrong. If the climate dynamics are such that strong negative feedback prevents the doubling of greenhouse gas concentrations from inducing significant changes in climate, there will be no dangerous impacts. In that case, there is no need to control the greenhouse gas emissions, and the Climate Convention is irrelevant.

As phrased, the "ultimate objective" is either unattainable or irrelevant. We can all wish that it were irrelevant. More likely, however, it is relevant but unattainable.

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