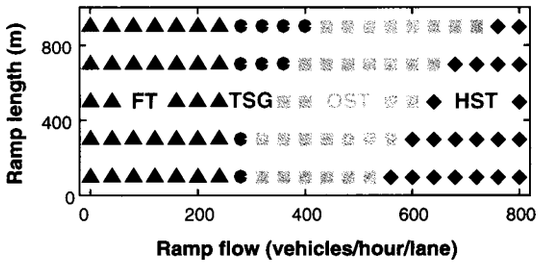

On the highway. Phase diagram of the various traffic states that can occur close to an on-ramp in the presence of small perturbations in the ramp flow. We show the dependence of the traffic states on the ramp flow and the ramp length for a flow of 1800 vehicles per hour and lane on the freeway. For small ramp flows, free traffic (FT) survives. At higher inflows, two different kinds of RH states can build up, either triggered stop-and-go waves (TSG) or oscillatory synchronized traffic (OST). High ramp flows are associated with a homogeneous form of synchronized congested traffic (HST).

localized clusters (small moving jams) and stop-and-go waves. In addition, Kerner and Rehborn (*2*) have recently discovered a hysteretic phase transition from free traffic to a new form of congested traffic (mostly appearing close to on-ramps) that had not been identified in more than 40 years of traffic research, they say. Kerner and Rehborn call it "synchronized" traffic because of the synchronization of velocities among lanes. However, the more characteristic feature is its high flow in spite of the breakdown of velocity, which is in contrast to typical traffic jams. Downstream of the ramp, the breakdown of velocity eventually relaxes to free traffic in the course of the freeway. Another interesting property is the wide scattering of synchronized traffic states, when plotted in the flow-density plane, which differs from the quasi-linear density dependence of free traffic flow.

Lee *et al.* (*1*) have now suggested an explanation for this hysteretic phase transition. They simulated freeways, including on- and off-ramps, with a fluid-dynamic traffic model that is closely related to the Navier-Stokes equations for viscous, compressible fluids. However, it contains an additional relaxation term describing adaptation of average vehicle velocity to an equilibrium velocity, which monotonically decreases with growing density. In comparison with previous simulation studies, Lee *et al.* used another velocity-density relation and a considerably different set of parameters. With a temporary peak in the on-ramp flow, they managed to trigger a form of oscillating congested traffic that is propagating upstream, but pinned at the location of the ramp (see figure on previous page). They call it the "recurring hump" state (RH) and compare it with autocatalytic oscillators in chemistry. Free traffic would correspond to a point attractor and the oscillating traffic state to a stable limit cycle. In terms of nonlinear dynamics, the transition corresponds to a Hopf bifurcation, but a subcritical one, because the critical ramp flow depends on the size of the perturbation.

Lee *et al.* point out that free traffic survives the assumed pulse-type perturbation of finite amplitude, if the ramp flow is below a certain critical value. However, once a RH state has formed, it is self-maintained until the ramp flow falls below another critical value that is smaller than the one for the transition from free traffic to the RH state. This proves the hysteretic nature of the transition. Moreover, Lee *et al.* could show the gradual spatial transition from the RH state to free flow downstream of the ramp. They also managed to reproduce the synchronization among neighboring freeway lanes as a result of lane changes. Therefore, they suggest that their model can describe the empirically observed first-order phase transition to synchronized traffic. The two-dimensional scattering of synchronized traffic states is understood as a result of the fact that the amplitude of the oscillating traffic state depends on the ramp flow.

Although the interpretation of synchronized traffic by Lee *et al.* does not quantitatively agree with the observations, in various respects it comes pretty close to reality. Meanwhile, our recent work has offered a more complete explanation (*4*). Above all, the findings are also of great practical importance. A detailed analysis shows that there is a whole spectrum of different states that can form at ramps. Their occurrence decisively depends on the inflow as well as the ramp length (see figure on this page). This is relevant not only for an appropriate dimensioning of ramps, but also for an optimal on-ramp control.

Traffic theory is now more interesting than ever before. Recent advances have yielded a better understanding of traffic flow phenomena as well as realistic and fast simulation models. Scientists are now prepared to design on-line controls for efficient traffic optimization, calculate the environmental impact of congestion, and develop methods for traffic forecasts.

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PERSPECTIVES: MOLECULAR BIOLOGY

Nuclear Functions Charge Ahead

Anita K. Hopper

In eukaryotic cells, chromosomal genes are first transcribed into RNA as large precursors and processed into mature RNAs in the cell's nucleus. These mature RNAs are then exported out of the nuclear interior to the cytosol, where they direct protein synthesis. What prevents the transcripts from traversing the boundary between the nucleus and the cytosol before they are completely processed? The report by Lund and Dahlberg on page 2082 of this week's issue provides surprising answers to this question. By injecting test RNAs into *Xenopus* oocytes, Lund and Dahlberg show that a proofreading system located within the nucleus and an ordered pathway of pre-tRNA processing are responsible for exclusion of pre-tRNAs from the cytosol. The proofreading system monitors both the appropriate three-dimensional structure of tRNAs and the fidelity of the processing at the 5′ and 3′ ends of the RNAs. Only properly folded tRNAs with mature termini leave the nucleus.

How is this proofreading accomplished? Even though there was no previous evidence that the enzymes that load amino acids onto tRNAs (aminoacyl synthetases) function in the nuclear interior, the fact that they process only tRNAs with mature 3′ termini (*1*) and that there are nuclear pools of these enzymes (*2*) led Lund and Dahlberg to propose that aminoacylation might be the proofreading step. Now they provide compelling evidence that, contrary to dogma, tRNAs are charged in the nucleus and that inhibition of aminoacylation retards tRNA export from the nucleus. Thus, nuclear tRNA aminoacylation is a proofreading mechanism which ensures that only properly folded tRNAs with mature ends are exported to the cytosol (see the figure).

Previous studies of tRNA processing in *Xenopus* oocytes indicated that removal of intervening sequences (introns) from pre-

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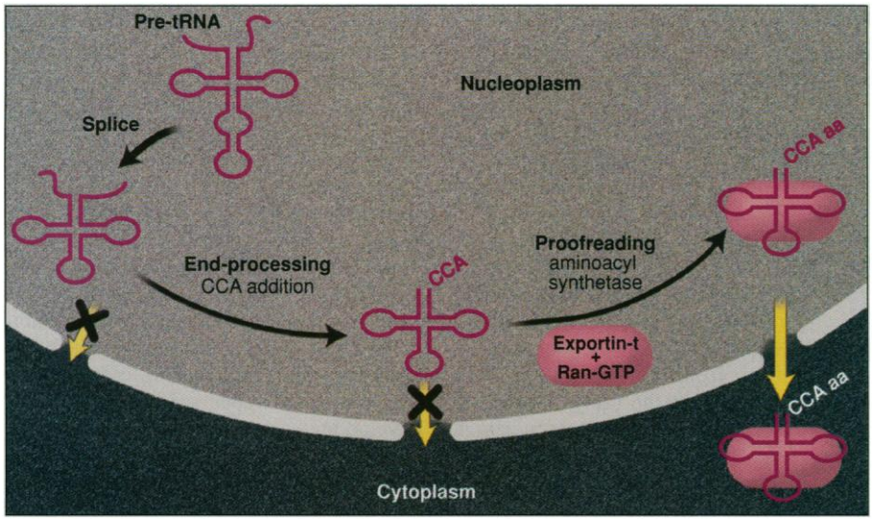
tRNAs occurred after 5′- and 3′-end maturation (*3*). Because intron-containing pre-tRNAs possessing mature 5′ and 3′ termini can be exported from the nucleus to the cytosol (*3*), one might expect to find intron-containing pre-tRNAs in the cytosol. Lund and Dahlberg report that the ordered pathway of pre-tRNA processing explains why this does not occur. They show that the accepted order of events—end processing preceding splicing—is incorrect. Rather, when exogenous tRNAs are expressed in low, close to normal amounts, splicing precedes 5′- and 3′-termini processing. Therefore, there are usually few intron-containing tRNAs with mature termini in the nucleus. Moreover, Lund and Dahlberg show that intron-containing pre-tRNAs are poor substrates for aminoacyl synthetases. The combination of the kinetic path of pre-tRNA processing and the role of tRNA aminoacylation in nuclear export accounts for the presence of only appropriately folded, mature tRNAs in the cytosol.



Transfer RNA travels from the nucleus. Proofreading and the ordered path of pre-tRNA processing prevent accumulation of misfolded or unprocessed tRNA in the cytosol. Light blue color, low nuclear concentrations of aminoacyl synthetase and Cca1p; dark blue, high cytosolic concentrations of these enzymes.

The data provide an explanation for the nuclear pools of aminoacyl synthetases as well as of proteins that interact with aminoacyl synthetases (*4*). They also explain the subcellular distribution of other enzymes that interact with tRNAs. For example, tRNA nucleotidyl transferase (Cca1p), the enzyme that catalyzes addition of CCA to the 3′ end of tRNAs, is found in both the nucleoplasm and the cytoplasm, and the cytosolic Cca1p pool is important for tRNA 3′-end repair (*3*, *5*). Before the studies of Lund and Dahlberg it was unclear why there should be a nuclear pool of Cca1p if CCA can be added to tRNAs in the cytosol. Because tRNA aminoacylation requires the CCA 3′ end, the proofreading system is dependent on a nuclear Cca1p pool, thereby providing an explanation for the subcellular distribution of this tRNA-processing enzyme.

Does the aminoacylation proofreading system for nuclear export of *Xenopus* tRNAs also function in tRNA export in other eukaryotes? There are interesting differences in the processing and export pathways between the budding yeast *Saccharomyces cerevisiae* and *Xenopus*. In contrast to *Xenopus*, pre-tRNA splicing and 5′- and 3′-end processing are apparently unordered in yeast (*6*). In addition, Lund and Dahlberg show that inhibition of the RanGTPase cycle in *Xenopus* has no apparent effect on pre-tRNA splicing even though inhibition prevents nuclear export of tRNAs. In contrast, in budding yeast pre-tRNA splicing and nuclear export are tightly coupled; mutations of components of the RanGTPase cycle (*7*), nucleoporins (*8*), and the tRNA exportin Los1p (*9*, *10*) all cause the accumulation of intron-containing pre-tRNAs in the nuclear interior (*10*). How pre-tRNA processing and nuclear export are coupled in budding yeast is unknown, and the coupling will make it difficult to determine whether there is a *Xenopus*-like proofreading system for nuclear export of tRNAs encoded by intron-containing genes in budding yeast. It should be possible however, to determine whether nuclear export of tRNAs encoded by genes lacking introns requires appropriate mature 5′ and 3′ termini.

Are there proofreading systems that monitor the structure of other RNAs before their export? In all eukaryotes that have been so far examined, there is a system that destroys mRNAs with codons that would cause premature translation termination. This nonsense codon–mediated mRNA decay process can act upon mRNAs while they are in the nucleus, and decay depends on mRNA translation (*11*). How nucleus-associated RNA turnover is coupled to translation is unknown. One possible explanation is that concomitant translation and export occur so that mRNAs are proofread as they exit the nuclear interior (*11*). Theoretically, an intranuclear translation process that scans mRNAs for inappropriate stop codons and targets them for degradation would also suffice. Even though ribosomes and at least some translation factors are located inside the nucleus (*12*), the latter notion is heretical because there is little support for the existence of active translation in the nuclear interior. Before the new work by Lund and Dahlberg, however, there was no support for the notion that tRNA charging with amino acids occurs within the nucleus.

In addition to providing novel mechanisms to ensure that unprocessed or misfolded tRNAs are retained in the nuclear interior, the report by Lund and Dahlberg leads to re-evaluation of the biological roles of the various eukaryotic subcellular compartments. Clearly, aminoacylation is no longer the sole domain of the cytosol, as Lund and Dahlberg show that tRNA charging also occurs in the nucleus. Future work will determine whether nonsense codon–mediated mRNA decay occurs in the nuclear interior and whether nuclear functions also include translation.

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