When the exception becomes the rule

Life is full of surprises. For a long time scientists thought that genes, which carry the information needed to make proteins, were the only useful things to be found in DNA. Finding out that much more than the 2% of DNA that encodes proteins is transcribed into RNA created a big puzzle. How is all of this RNA made and what does it do?

Intrigued by these questions, Lars Steinmetz at EMBL Heidelberg and Wolfgang Huber at the EMBL-EBI took a closer look at transcription in yeast. The fairly simple model organism with a small genome allowed Zhenyu Xu and Wu Wei, two computational biologists in Lars' group, to simultaneously monitor all transcription events happening at different places in the genome. This global view of the process revealed that most promoters give rise not to one but to several transcripts. "But instead of firing in the same direction, we found that many promoters support transcription in two directions," notes Lars. "This was really surprising because transcription is conventionally considered a one-way process – comparable to reading a text."

In order to translate a sentence from a book, a translator needs to know not only where to start reading, but also in which direction the language is supposed to be read. Similarly, the cellular machinery involved in transcribing a particular sequence of DNA into RNA starts at defined promoter regions, and was thought to move only in one direction. But, as it turns out, the transcription machinery is one step ahead of the translator. It can read DNA code and produce RNA in two directions: upstream and downstream of a promoter. Scientists had occasionally encountered transcripts that appeared to have been generated in this way, but such 'antisense' transcripts were regarded as exceptions, and dismissed as noise. The EMBL scientists have now proved that such transcripts are very common and that bidirectional promoters are the rule, not the exception.

Having solved the mystery of how all the RNA found in cells is made, Lars and Wolfgang are now dealing with the second, more difficult question of what all these transcripts do. So far, all they have for answers are speculations. The transcripts could help regulate gene expression, or provide 'raw material' for evolution and acquire new roles in the future. "Or maybe we should ask not whether the transcripts have function but whether the act of transcription itself does," Lars says. Transcribing one stretch of DNA might help or hinder the transcription of a nearby gene, for example. "Most likely, the real answer is a combination of all of the above. Or it may come as yet another surprise," Lars concludes, as his team sets out to study the effects of each of the individual RNA molecules.

Xu Z, Wei W, Gagneur J, Perocchi F, Clauder-Münster S, Camblong J, Guffanti E, Stutz F, Huber W, Steinmetz LM (2009) Bidirectional promoters generate pervasive transcription in yeast. *Nature* **457**: 974-5