# Writing exercise 06: Using Transitional Words

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Using transitional words/phrases can help make your train of thought logical and clear. They can be used to establish comparisons or contrasts, place events in order, qualify statements, and so on. Examples of transition words/phrases include:

* However
* Moreover
* In spite of
* Although
* For example
* Therefore

### Example from a published paper1 (transitional words/phrases highlighted):

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c-di-GMP is monomeric in solution at physiological concentrations ([Gentner et al., 2012](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4151990/)). However, intercalated c-di-GMP dimers have been observed in crystal structures of the nucleotide alone and in complexes with effector proteins. Higher order c-di-GMP structures such as tetramers and octamers have thus far only been inferred from NMR and spectroscopic studies and require very high c-di-GMP concentrations (up to 30 mM) and monovalent cations ([Zhang et al., 2006](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4151990/)). These higher order structures are characterized by G-quartet interactions with a centrally bound potassium ion coordinated by four guanines. There are minimal base contacts and no base stacking interactions in these structures ([Figure S4](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4151990/figure/figs4/)A) ([Zhang et al., 2006; Gentner et al., 2012](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4151990/)). By sharp contrast, the BldD-bound tetrameric c-di-GMP is a tightly packed structure that is not secured by ions. Rather, the c-di-GMP molecules are closely spaced and optimally positioned for interbase pairing, leading to the formation of a multistranded, base-stacked structure with top, middle, and bottom layers ([Figures 5](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4151990/figure/fig5/)D and [​andS4A).S4](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4151990/figure/figs4/)A). There are 12 hydrogen bonds between the two intercalated dimers within the c-di-GMP tetramer, including contacts between the N3 atoms and exocyclic NH2 amides of an adjacent base ([Figures 5](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4151990/figure/fig5/)C and [​andS4B).S4](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4151990/figure/figs4/)B). Such contacts could not be formed with c-di-AMP due to its lack of an exocyclic NH2 atom. Therefore, in addition to contacts from motifs 1 and 2, guanine-guanine base hydrogen bonds serve to specify c-di-GMP tetramer binding to BldD. Notably, formation of the c-di-GMP tetramer buries 24% of the total surface area (buried surface area [BSA]) of the c-di-GMP molecules ([Figure S4](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4151990/figure/figs4/)B). By comparison, in most protein oligomers the BSA between protomers is ∼15% ([Wang et al., 2009](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4151990/)). Finally, the interface between the intercalated c-di-GMP dimers that forms the tetramer is remarkably complementary in shape ([Figure S4](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4151990/figure/figs4/)B). Thus, the combination of multiple contacts between the c-di-GMP moieties along with its extensive BSA and molecular shape complementarity lead to the creation of a compact and highly specific c-di-GMP tetramer. However, BldD is necessary to stabilize this tetramer and template its formation.

### Exercise 6A.

Read each example and identify the transition words, evaluating whether they are necessary/unnecessary, and identify any places where the writing could be improved by the addition of transition words/phrases.

**Sample 6.1** 2

Given the benefits conferred to microbial cells that form encapsulated communities, it is no surprise that the biofilm lifestyle arose early and has persisted for billions of years. However, commitment to the biofilm lifestyle also presents challenges. Chief among them is that prolonged maturation of a biofilm community can lead to crowding and starvation[2](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10914755/). As a consequence, many bacteria have evolved the ability to transition between the biofilm and free-swimming lifestyles and encode elaborate signaling mechanisms to regulate their collective states[15](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10914755/). Yet, whether and how bacteria gauge the presence of lethal threats in their environments to drive biofilm formation remains unclear.

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| Transition words?  | Why are they necessary (or unnecessary)? |
| Are there any places where the writing can be improved by adding transition words? |

**Sample 6.2.** 3

In the present study, small RNA (sRNA) data from *Ascosphaera apis* were filtered from sRNA-seq datasets from the gut tissues of *A. apis*-infected *Apis mellifera ligustica* worker larvae, which were combined with the previously gained sRNA-seq data from *A. apis* spores to screen differentially expressed milRNAs (DEmilRNAs), followed by trend analysis and investigation of the DEmilRNAs in relation to significant trends. Additionally, the interactions between the DEmilRNAs and their target mRNAs were verified using a dual-luciferase reporter assay. In total, 974 *A. apis* milRNAs were identified. The first base of these milRNAs was biased toward U. The expression of six milRNAs was confirmed by stem–loop RT-PCR, and the sequences of milR-3245-y and milR-10285-y were validated using Sanger sequencing. These miRNAs grouped into four significant trends, with the target mRNAs of DEmilRNAs involving 42 GO terms and 120 KEGG pathways, such as the fungal-type cell wall and biosynthesis of secondary metabolites. Further investigation demonstrated that 299 DEmilRNAs (novel-m0011-3p, milR-10048-y, bantam-y, etc.) potentially targeted nine genes encoding secondary metabolite-associated enzymes, while 258 (milR-25-y, milR-14-y, milR-932-x, etc.) and 419 (milR-4561-y, milR-10125-y, let-7-x, etc.) DEmilRNAs putatively targeted virulence factor-encoded genes and nine genes involved in the MAPK signaling pathway, respectively. Additionally, the interaction between *ADM-B* and milR-6882-x, as well as between *PKIA* and milR-7009-x were verified. Together, these results not only offer a basis for clarifying the mechanisms underlying DEmilRNA-regulated pathogenesis of *A. apis* and a novel insight into the interaction between *A. apis* and honey bee larvae, but also provide candidate DEmilRNA–gene axis for further investigation.

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**Sample 6.3.** 4

*F. tularensis* is an intracellular bacterium and has a unique intracellular life cycle. *Francisella* can infect macrophages, neutrophils, dendritic cells, and several other cell types ([9](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8570275/),[–12](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8570275/)); however, macrophages are targeted primarily to initiate the infection. Upon phagocytosis, *Francisella* remains in phagosomes for a short duration, prevents the maturation of phagosomes, disintegrates the phagosomal wall, and escapes into the cytosol, where the replication occurs ([12](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8570275/)). The genes required to escape from the phagosome are encoded on a *Francisella* pathogenicity island (FPI) ([13](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8570275/)). The regulation of virulence mechanisms of *Francisella* is not entirely understood. *Francisella* possesses very few transcription regulators. The three well-characterized transcriptional regulators, the macrophage growth locus protein A (MglA), the stringent starvation protein A (SspA), and the pathogenicity island gene regulator (PigR), regulate the expression of genes encoded on the FPI ([14](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8570275/),[–16](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8570275/)). The other transcriptional regulators, PmrA and QseC, function as response regulators of the two-component system and regulate the expression of virulence-associated genes in *F. tularensis* ([17](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8570275/), [18](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8570275/)). Additionally, *F. tularensis* encodes specialized transcriptional regulators such as Fur, which regulate the expression of genes involved in iron uptake ([19](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8570275/)), and OxyR, which plays a central role in regulating the essential genes required for oxidative stress resistance and virulence ([20](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8570275/)).

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| Transition words?  | Why are they necessary (or unnecessary)? |
| Are there any places where the writing can be improved by adding transition words? |

### Exercise 6B.

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Look at your introduction thus far (or any other piece of writing). Go through it, and examine your use (or lack of use) of transition words. Consider how your writing can be improved and make the appropriate edits.

### References

1. Tschowri N, Schumacher MA, Schlimpert S, et al. Tetrameric c-di-GMP mediates effective transcription factor dimerization to control *Streptomyces* development. Cell. 2014;158(5):1136-1147.
2. Prentice JA, van de Weerd R, Bridges AA. Cell-lysis sensing drives biofilm formation in *Vibrio cholerae*. Nat Commun. 2024;15(1):2018. Published 2024 Mar 6. doi:10.1038/s41467-024-46399-1
3. Transcriptional dynamics and regulatory function of milRNAs in *Ascosphaera apis* invading *Apis mellifera* larvae. Fan et al (2024) Front. Microbiol, https://doi.org/10.3389/fmicb.2024.1355035
4. Marghani D, Ma Z, Centone AJ, Huang W, Malik M, Bakshi CS. An AraC/XylS Family Transcriptional Regulator Modulates the Oxidative Stress Response of *Francisella tularensis*. J Bacteriol. 2021;203(23):e0018521. doi:10.1128/JB.00185-21