



High-throughput generic single-entity sequencing using droplet microfluidics

Guoping Wang^{1#}, Liuyang Zhao^{1#}, Yu Shi^{1#}, Fuyang Qu^{2#}, Yanqiang Ding^{1#}, Weixin Liu¹, Changan Liu¹, Gang Luo³, Meiyi Li¹, Xiaowu Bai¹, Luoquan Li², Luyao Wang¹, Chi Chun Wong¹, Yi-Ping Ho^{2,4,5*}, Jun Yu^{1*}

¹Institute of Digestive Diseases and Department of Medicine and Therapeutics, State Key Laboratory of Digestive Disease, CUHK, HKSAR

²⁻⁵Department of Biomedical Engineering, Department of Electronic Engineering, Hong Kong Branch of CAS Center for Excellence in Animal Evolution and Genetics, The Ministry of Education Key Laboratory of Regeneration Medicine, CUHK, HKSAR

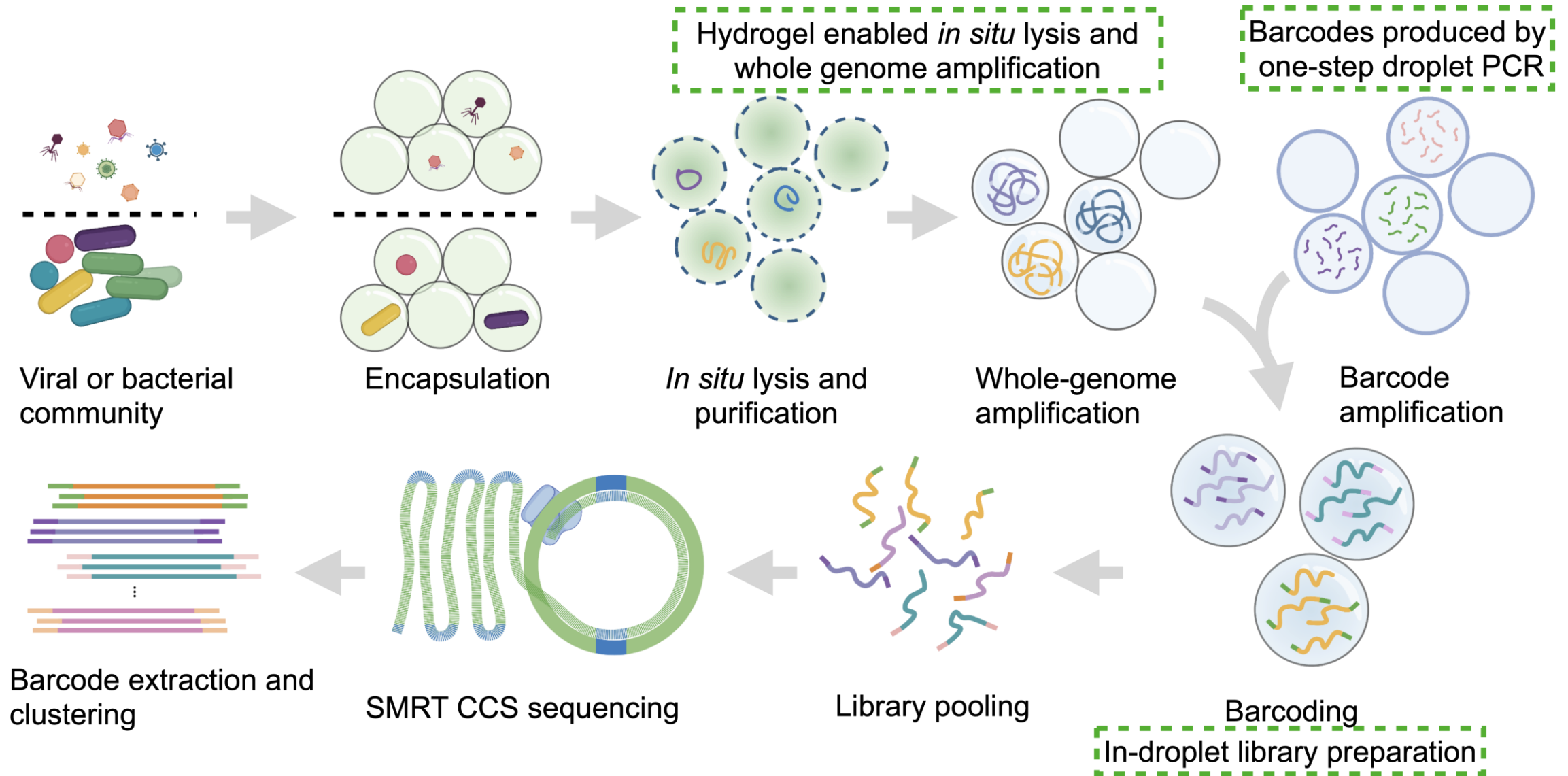
#These authors contributed equally



Guoping Wang, Liuyang Zhao, Yu Shi, Fuyang Qu, Yanqiang Ding, Weixin Liu, Changan Liu, et al. 2025. High-throughput generic single-entity sequencing using droplet microfluidics. *iMeta* 4: e70087. <https://doi.org/10.1002/imt2.70087>.



Introduction





Highlights

- **Introduces GSE-Seq, a new method for high-throughput, long-read single-entity sequencing.**
- **Utilizes degradable hydrogels for robust in situ lysis of single viruses and bacteria.**
- **Barcode-guided assembly dramatically improves the recovery and completeness of viral genomes.**
- **Reveals vast “viral dark matter” by recovering tens of thousands of genomes from complex samples.**
- **Recovers over 20,000 bacterial genomes from the human gut, including difficult-to-lyse species.**



Result 1

The overall design and barcode generation for generic single-entity sequencing

High-throughput generic single-entity sequencing using droplet microfluidics

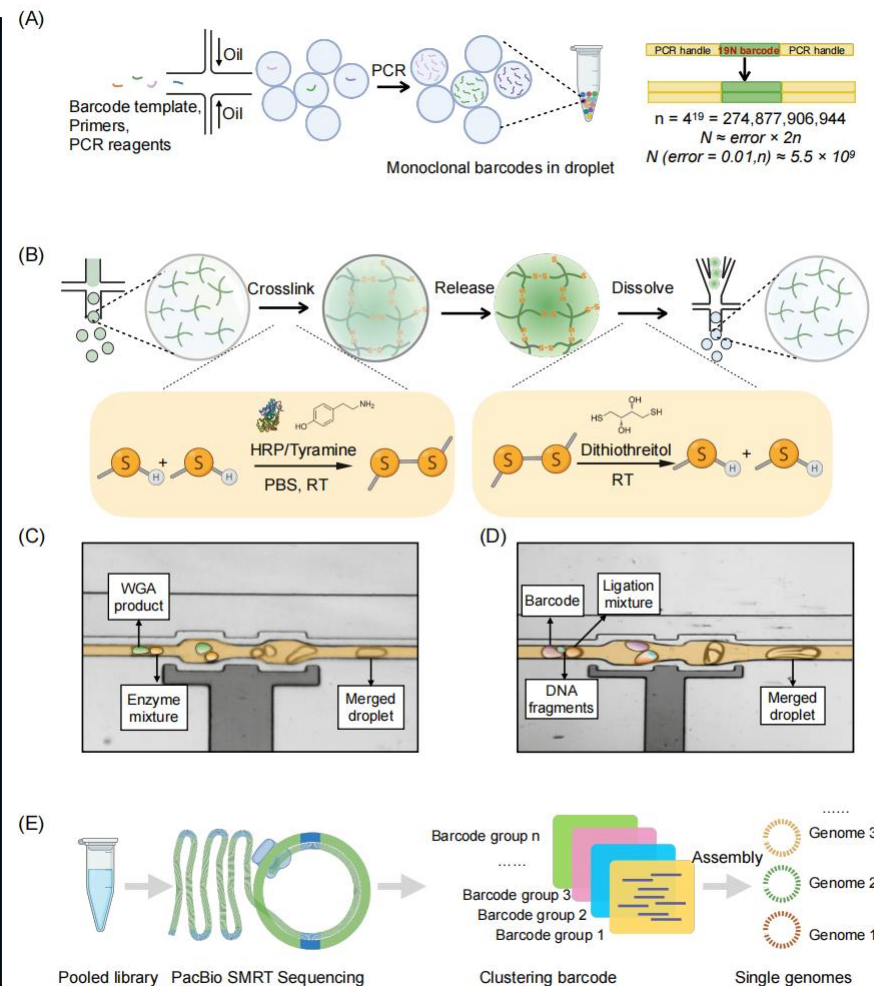
Guoping Wang, Liuyang Zhao, Yu Shi, Fuyang Qu, Yanqiang Ding, Weixin Liu, Changan Liu, Gang Luo, Meiyi Li, Xiaowu Bai, Luoquan Li, Yi-Ping Ho, Jun Yu



香港中文大學醫學院
Faculty of Medicine
The Chinese University of Hong Kong



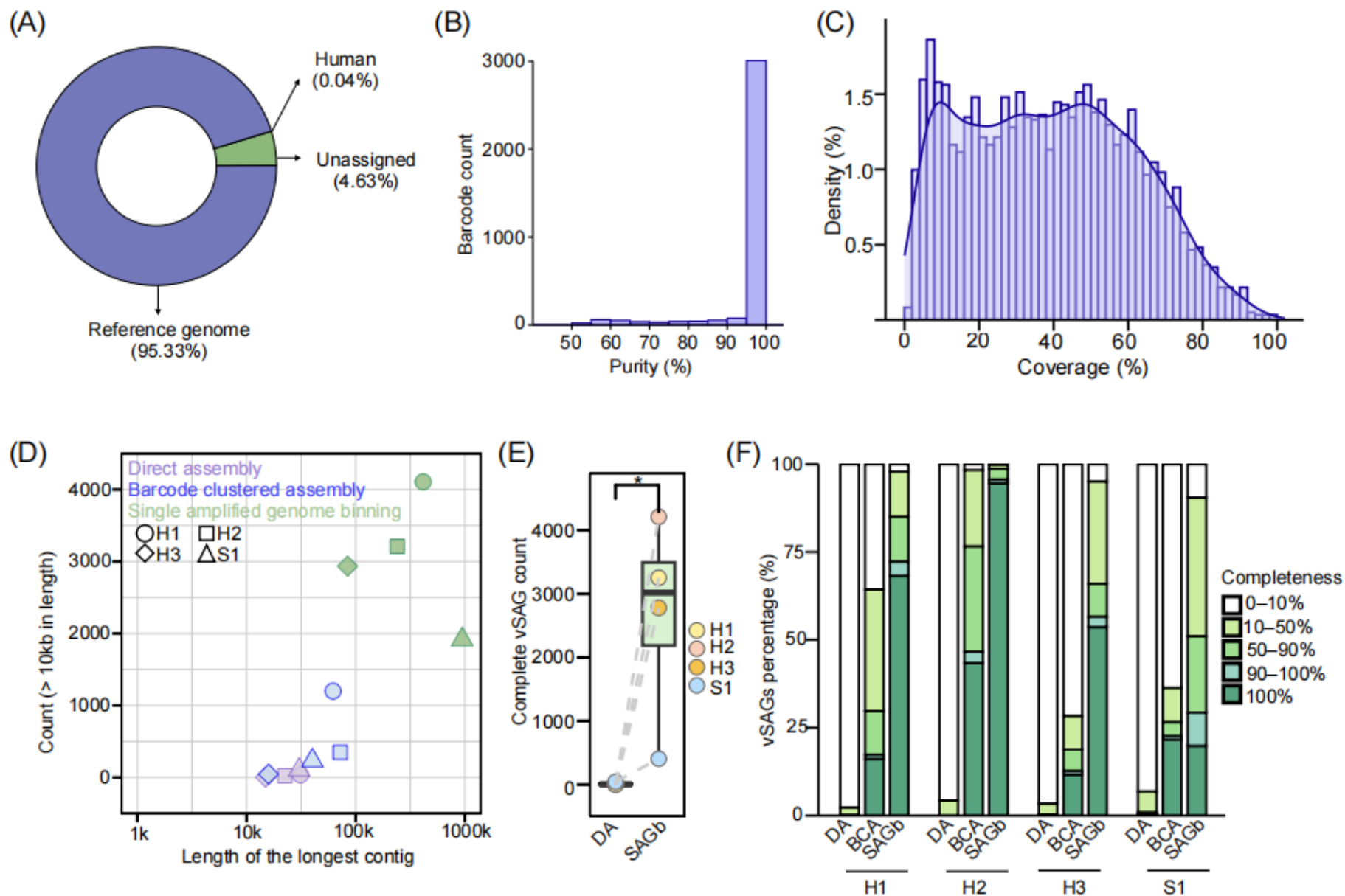
Department of
Biomedical Engineering
The Chinese University of Hong Kong





Result 2

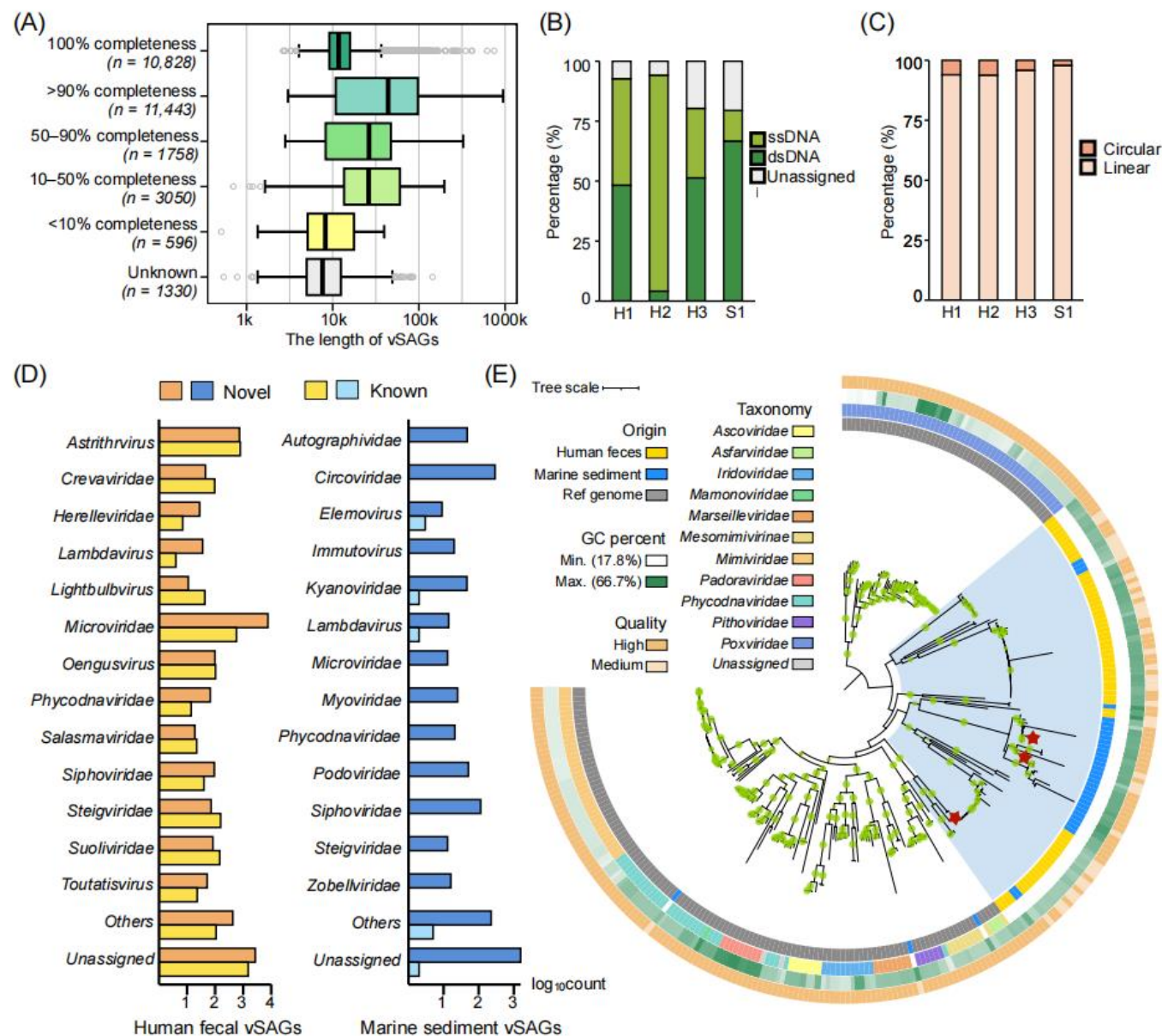
Validating the
performance
of GSE-Seq





Result 3

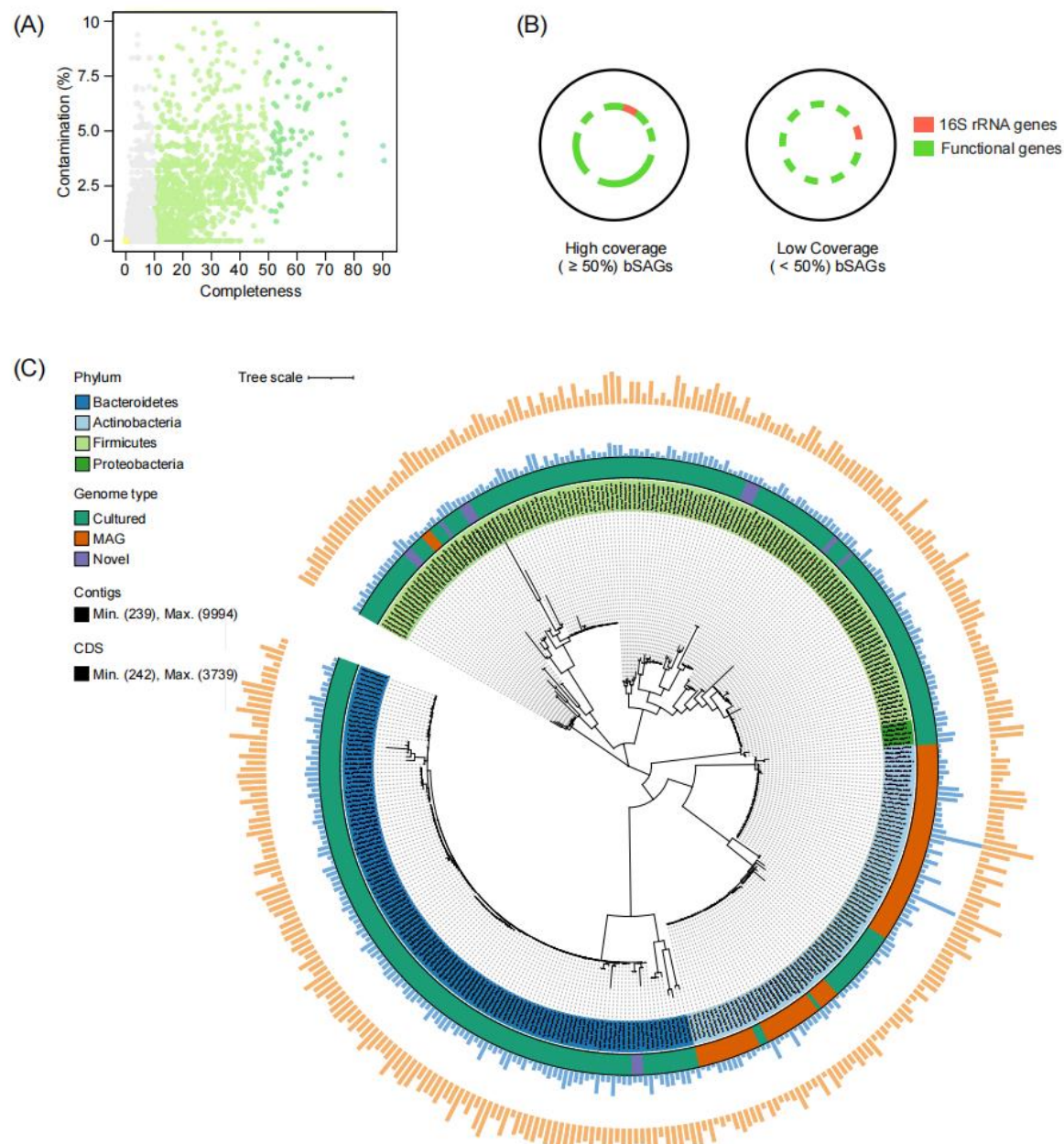
GSE-Seq uncovers vast
viral diversity in the human
gut and marine sediment





Result 4

**GSE-Seq uncovers
novel bacterial
diversity in the
human gut**





Discussion

- ❑ **Uncovering Vast Viral Dark Matter:** Over 15,000 viral single amplified genomes (vSAGs) were recovered from human feces and marine sediments, the vast majority of which likely represent newly discovered species. Only 23.1% of gut vSAGs and 0.4% of marine vSAGs showed high similarity to known species in public databases.
- ❑ **Identifying “Sly” Viruses:** Successfully identified giant viruses (NCLDV) and highly variable crAssphage, which are often overlooked by conventional methods.
- ❑ **Expanding Knowledge of Bacteria:** Obtained over 23,000 bacterial single amplified genomes (bSAGs), covering numerous putative new species and difficult-to-lyse Gram-positive bacteria.
- ❑ **Precise Phage-Host Linkage:** Identified 1494 phage-host pairs at the single-cell level, breaking through a major technical bottleneck in metagenomics.



CONCLUSION

❑ Key Breakthrough

The GSE-Seq technology represents a significant breakthrough by innovatively integrating three core modules: ultra-high-throughput droplet generation, universal hydrogel-based sample processing, and long-read sequencing. This integration successfully overcomes the technical bottlenecks in capturing broad biodiversity from complex samples.

❑ Core Achievement

Achieving Single-Cell Microbial Profiling: This method was successfully applied to complex environmental samples, enabling the genomic profiling of microbial communities at single-cell resolution. It led to the discovery of a vast number of potential new viral and bacterial species from human feces and marine samples.

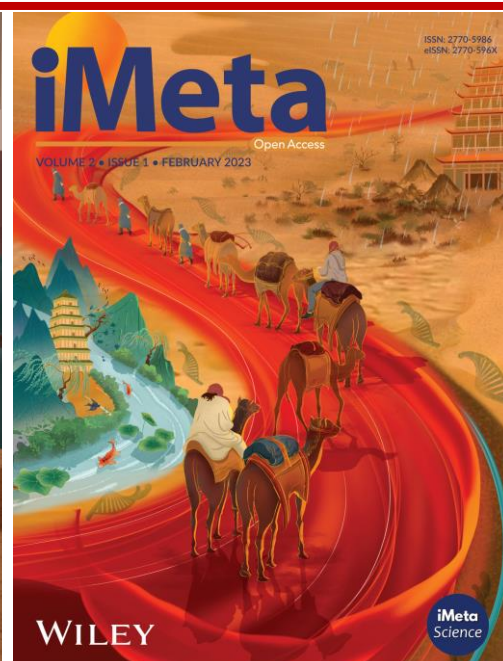
❑ Significance & Outlook

The versatility and accessibility of GSE-Seq provide an unprecedented and powerful platform for single-entity genomics research across diverse biological systems.

Guoping Wang, Liuyang Zhao, Yu Shi, Fuyang Qu, Yanqiang Ding, Weixin Liu, Changan Liu, et al. 2025. High-throughput generic single-entity sequencing using droplet microfluidics. *iMeta* 4: e70087. <https://doi.org/10.1002/imt2.70087>.

iMeta: To be top journals in biology and medicine

WILEY



“***iMeta***” launched in 2022 by iMeta Science Society, **impact factor (IF) 33.2**, ranking **top 65/22249 in world and 2/161 in the microbiology**. It aims to publish innovative and high-quality papers with broad and diverse audiences. **Its scope is similar to *Cell*, *Nature Biotechnology*/*Methods*/*Microbiology*/*Medicine*/*Food***. Its unique features include video abstract, bilingual publication, and social media with 600,000 followers. Indexed by **SCIE/ESI**, **PubMed**, **Google Scholar** etc.

“***iMetaOmics***” launched in 2024, with a **target IF>10**, and its scope is similar to ***Nature Communications*, *Cell Reports*, *Microbiome*, *ISME J*, *Nucleic Acids Research*, *Briefings in Bioinformatics***, etc.

“***iMetaMed***” launched in 2025, with a **target IF>15**, similar to ***Med*, *Cell Reports Medicine*, *eBioMedicine*, *eClinicalMedicine*** etc.



Society: <http://www.imeta.science>

Publisher: <https://wileyonlinelibrary.com/journal/imeta>

iMeta: <https://wiley.atyponrex.com/journal/IMT2>

Submission: iMetaOmics: <https://wiley.atyponrex.com/journal/IMO2>

iMetaMed: <https://wiley.atyponrex.com/journal/IMM3>



[iMetaScience](#)



[iMetaScience](#)



office@imeta.science

imetaomics@imeta.science



[Promotion Video](#)

Update
2025/7/6