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Review Article

Sustainable rare earth biomanufacturing powered by synthetic biology engineering

Yangyi Liu[1,2], Juanjuan Su[1], Fan Wang[3] ✉, Huijing Cui[2] ✉, Kai Liu[2] ✉, and Hongjie Zhang[2,3]

[1] *Center of Materials Science and Optoelectronics Engineering, College of Materials Science and Optoelectronic Technology, University of Chinese Academy of Sciences, Beijing 100049, China*
[2] *Engineering Research Center of Advanced Rare Earth Materials (Ministry of Education), Department of Chemistry, Tsinghua University, Beijing 100084, China*
[3] *Changchun Institute of Applied Chemistry, Chinese Academy of Sciences, Changchun 130022, China*

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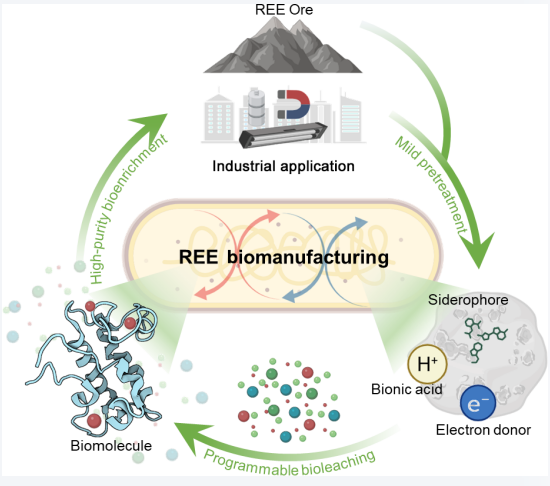
ABSTRACT: Rare-earth elements (REEs) are critical components of low-carbon technologies and advanced defense systems. However, their conventional extraction and separation processes, which rely on energy-intensive hydrometallurgy with harsh chemical reagents, pose significant environmental challenges. Synthetic biology offers a transformative alternative by enabling the programmable dissolution, precise molecular recognition, and selective capture of REEs under mild conditions. Specifically, engineered microbes can be designed to secrete tailored organic acids, siderophores, and redox-active metabolites for bioleaching REEs from ores, tailings, and industrial wastes. Concurrently, high-affinity biological binders—such as lanmodulin, lanthanide-binding peptides, and de novo-designed proteins—provide picomolar-level affinity and tunable selectivity ideal for biosorption. The integration of these functional motifs into advanced platforms, including immobilized sorbents, magnetic composites, and elastin-like polypeptides, enables continuous and regenerable REE recovery with minimal chemical input. Collectively, these biological strategies support an environmentally considerable approach to REE extraction and separation from diverse sources. Future efforts should focus on machine-learning-guided protein design, enhancing biomolecule stability, developing integrated leaching-adsorption bioreactors, improving tolerance to complex leachates, and incorporating biological modules into industrial flowsheets. These advances collectively establish synthetic biology as the foundation for a new paradigm in sustainable rare-earth production.



KEYWORDS: synthetic biology, rare-earth, bioleaching, biosorption, lanthanide-binding peptides

1 Introduction

Rare earth elements (REEs) have become critical materials underpinning modern low-carbon energy and advanced defense systems, with extensive applications in high-performance permanent magnets, wind turbine generators, and laser systems. In 2024, China accounted for approximately 34% of global rare earth reserves, contributed 69.2% of the world's rare-earth production, and dominated nearly 90% of global refining and separation capacity, underscoring its central role in the sector [1]. According to a McKinsey 2025 research report, the demand for key magnetic REEs such as Neodymium (Nd), Praseodymium (Pr), and Dysprosium (Dy) is projected to triple by 2035, intensifying concerns over supply security [2]. However, current mainstream REE extraction and separation processes still heavily rely on the "high-temperature roasting–strong acid leaching–multi-stage solvent extraction" route. This approach is not only highly energy-intensive, but also generates large volumes of acidic wastewater and radioactive tailings. It requires 5 to 10 times more energy per unit mass of rare earth metal produced compared to the recycling of

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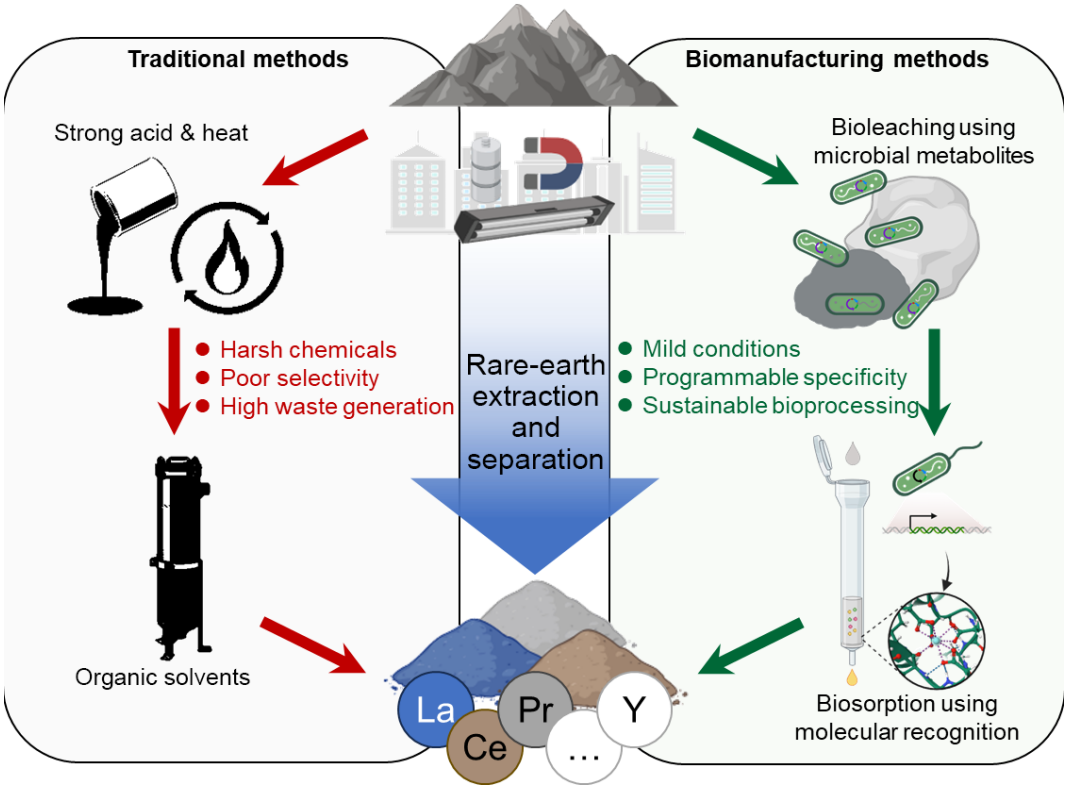
✉Address correspondence to Fan Wang, wangfan@ciac.ac.cn; Huijing Cui, tsuihj@mail.tsinghua.edu.cn; Kai Liu, kailiu@tsinghua.edu.cn

base metals such as copper, aluminum, and steel [3]. These challenges motivate the development of sustainable, low-energy strategies that can diversify the upstream and accelerate the circular use of strategic metals.

In response to these challenges, synthetic biology-driven biohydrometallurgy for rare earths has emerged as a promising alternative. This technological framework leverages rational design of microbial metabolic networks, engineering of highly selective REE-binding proteins, and development of living or hybrid biological devices to achieve efficient leaching and separation under mild conditions (Scheme 1). Microbial metabolism can generate organic acids and siderophores capable of mobilizing REEs from ores and tailings, achieving leaching efficiencies of 50%–90% for bastnäsite or monazite under mild conditions [4, 5]. *Bacillus* and *Shewanella* species naturally participate in redox-driven metal mobilization. Synthetic biology increasingly enables these microbes to assemble functional inorganic–organic hybrid materials or overproduce metal-binding metabolites. Beyond dissolution, bio-derived sorbents based on such engineered systems can reach adsorption capacities of 150–300 mg/g and maintain high performance across more than 20 reuse cycles [6, 7]. In separation and purification, the natural REE-binding protein Lanmodulin (LanM) and its engineered dimers, such as *Hans*-LanM, provide picomolar-level affinity. These natural binders deliver > 10,000-fold selectivity over calcium, enabling unprecedented molecular discrimination [8]. Advances in protein design and machine learning have produced artificial peptide/metal-organic framework (MOF) hybrids and computationally optimized REE-binding domains with selectivity rivaling industrial extractants, which operate at room temperature and neutral pH [9, 10]. These synthetic biology strategies have demonstrated broad applicability across both primary and secondary resources. In mining residues such as ion-adsorption clays, bio-mobilization can extract 5–15 kg REE per ton of tailings, typically without aggressive chemical reagents [11, 12]. In secondary streams, including NdFeB magnets, red phosphor powders (Y_2O_3:Eu^{3+}), spent light-emitting diodes and other electronic wastes (e-waste), the REE content is typically 10×–30× higher than natural ore, enabling biological processes to recover 20–80 kg REE per ton of waste, depending on material type and pre-treatment [13, 14]. Collectively, these advances highlight the significant potential of synthetic biology in enabling efficient extraction, high-precision separation, and circular utilization of rare earth resources.

This review systematically summarizes recent advances in synthetic biology for REE extraction and separation. The metabolic engineering for enhanced metal dissolution, biomacromolecular tools for selective REE binding and separation, and engineered living or bio-hybrid devices capable of continuous metal purification were highlighted. The applications across two major material classes, primary ores/tailings and high-value waste streams were examined. The article further discussed critical challenges in scaling these technologies from the laboratory to industrial implementation, including metabolic instability during bioreactor amplification, interference from competing ions in complex leachates, limited cycling stability of biomaterials under harsh process conditions. Future directions in scaling, system integration, and computational design are outlined, underscoring the potential of synthetic biology to reshape the technological foundation of rare-earth recovery and enable genuinely sustainable resource extraction.



Scheme 1 Contrasting pathways for REE manufacturing. Conventional methods (left) rely on harsh chemicals and high energy inputs, leading to significant environmental footprint. In contrast, emerging biological strategies (right) leverage microbial metabolites for bioleaching and biomolecular recognition for biosorption, offering a sustainable and selective alternative under mild conditions.

2 Synthetic biohydrometallurgy: Novel pathways from dissolution to separation

The understanding of REEs in biological systems underwent a fundamental paradigm shift during the 2010s. Previously regarded primarily as geochemical curiosities, lanthanide-dependent enzymes like methanol dehydrogenase in methylotrophic bacteria were discovered [15, 16], which revealed their crucial role as biological cofactors [17]. This breakthrough not only established the role of REEs in microbial biochemistry but also demonstrated that microorganisms naturally interact with them through the secretion of organic acids, specific ligands, and redox processes [18]. Building upon these innate capabilities, synthetic biology has further expanded microbial potential by rationally designing recognition domains, optimizing secretion systems, and constructing hybrid biomaterials. These efforts have yielded a diverse toolkit for the identification, enrichment, and controlled release of REEs in aqueous systems. Such engineered biological components provide the technical foundation for achieving highly efficient dissolution, specific recognition, and precise separation of REEs at the molecular level.

2.1 Microbial metabolism-driven REE dissolution

Metabolite-driven bioleaching offers an environmentally compatible alternative for solubilizing REEs and facilitating their downstream capture. This process leverages microbial metabolites, such as organic acids, siderophores or electron donors, to mobilize target ions from solid phases, eliminating the need for harsh organic solvents and strong extractants. From a taxonomic and physiological perspective, microorganisms employed in REE bioleaching primarily fall into three strategic groups: filamentous fungi, acidophilic chemolithoautotrophic bacteria, and heterotrophic bacteria (including siderophore producers). Each group offers distinct advantages and faces specific challenges, making them suitable for different resource types and process conditions (Table 1 and Fig. 1).

Table 1 Microbial bioleaching of REEs

Microbe	Main mechanism	Resource(s) tested	Typical conditions	Representative leaching performance	Ref.
Aspergillus niger	Organic acids (e.g., citric)	Ion-adsorption type rare earth ore	28 °C; pH 1.58; 7 days	A total REE leaching rate of 93%	[18]
Aspergillus fumigatus	Organic acids (e.g., citric) and siderophores	Ion-adsorption type rare earth ore	28 °C; pH 1.64; 7 days	A total REE leaching rate of 86%	
Penicillium pinophilum	Organic acids (e.g., citric)	Ion-adsorption type rare earth ore	28 °C; pH 1.76; 7 days	A total REE leaching rate of 71%	
Penicillium tricolor	Organic acids (e.g., citric, oxalic)	Red mud	30 °C; pH 2–4; 10 days	A total REE leaching rate of 55%	[19]
Paecilomyces spp.	Organic acids (e.g., citric, oxalic)	Monazite sand	25–28 °C; pH 2–4; 2 days	A total REE leaching rate of 3%–5%	[20, 21]
Aspergillus spp.	Organic acids (e.g., citric, oxalic, gluconic)	Monazite sand and coal fly ash	25–28 °C; pH 2–4; 2 days	For monazite, a total REE leaching rate of 3%–5%; for coal fly ash, a total REE leaching rate of ~ 30.91%	
Gluconobacter oxydans	Organic acids (e.g., gluconic)	Waste phosphors and cracking catalysts	30 °C; pH 2–4; 1 day	For waste phosphors, a total REE leaching rate of 2%; for cracking catalysts, a total REE leaching rate of 49%	[22]
Candida bombicola	Inorganic acid generation (sulfur/iron oxidation)	Coal fly ash	28 °C; pH 1–3; 6 h	A total REE leaching rate of 59.7%	[23]
Acidithiobacillus thiooxidans	Inorganic acid generation via sulfur oxidation	Gold mine tailings	30 °C; pH 0.7; 7 days	The leaching rates were Pr 76%, Ce 46%, and Eu 14%.	[24]
		Phosphogypsum	30 °C; pH < 0.6; 25 days	The leaching rates were Y 62%, La 58%, Ce 60%, and Nd 98%.	[25]
Acidithiobacillus ferrooxidans	Sulfur/iron oxidation coupled with ion-exchange	Phosphate rock	30 °C; pH 2; 7–14 days	The leaching rates were Y 35.7%, La 37.03%, Ce 27.92%, and Nd 32.53%.	[26]
		Ion-adsorption type REE ore and tailings	30 °C; pH 1.5–2.0; 10–20 days	The leaching rates were Y 93.5%, La 99.5%, Ce 78.1%, and Nd 95.8%.	[27]
Pseudomonas spp.	Pyoverdine-type metallophores	Nickel-metal hydride batteries	28 °C; near-neutral pH; 27 days	The leaching rate of La was 14.8%.	[28]
	Siderophore-type metallophores	Acid mine drainage-derived solids/aqueous systems	Ambient temperature; acidic to circumneutral pH	Selective binding and mobilization of multiple REEs	[29]
Shewanella putrefaciens	Reductive dissolution	Ferromanganese (Fe-Mn) nodules	25–30 °C; neutral pH; anaerobic; 20 days	Simultaneous release and fractionation of REEs	[30]
Sphingomonas desiccabilis	Not fully detailed	Basalt (analogous to lunar and Martian material)	20–22 °C; pH 4.16–6.12; 21 days. Tested under microgravity, Mars gravity, and Earth gravity.	A total REE leaching rate of 0.02%–0.12%	[31]

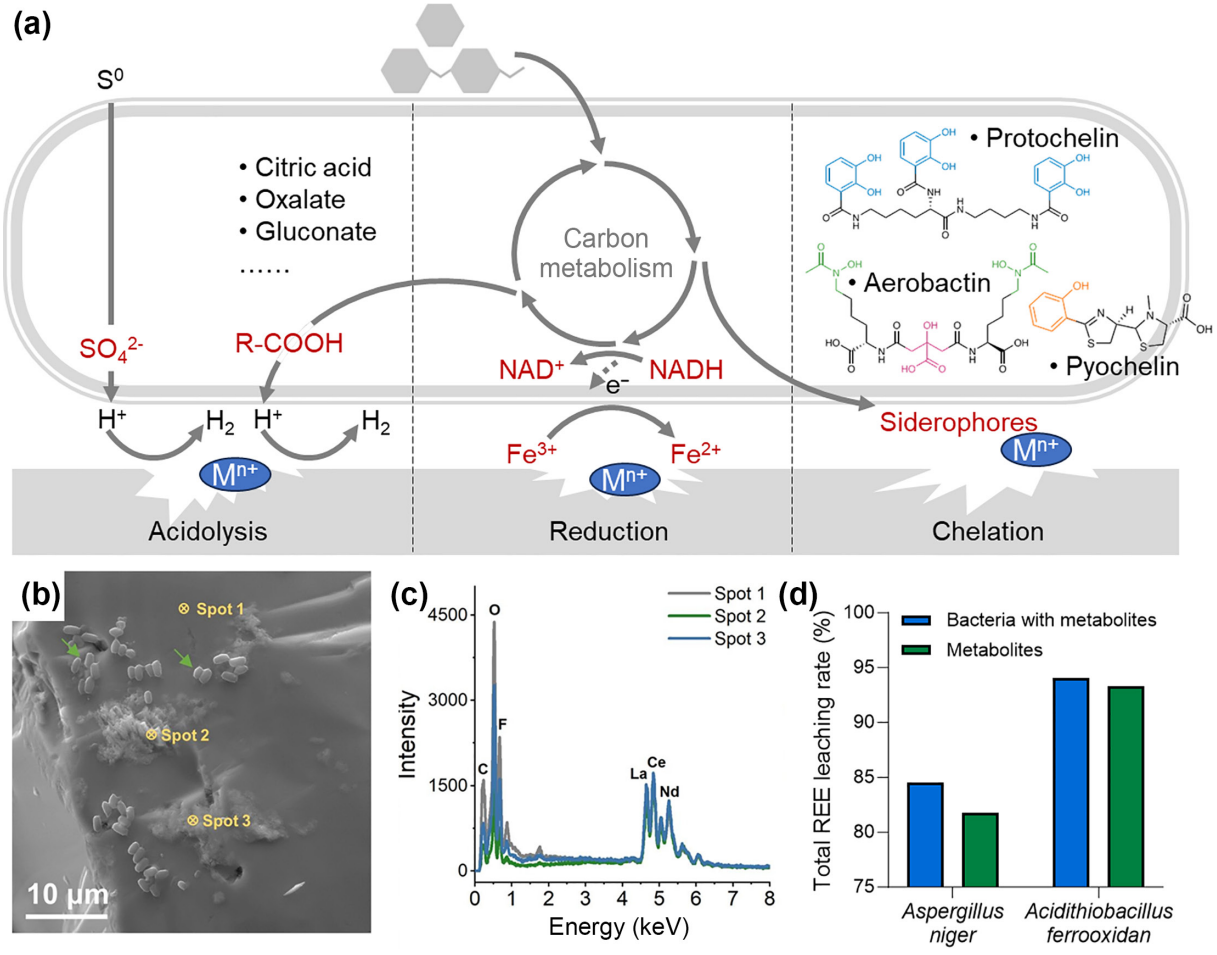


Figure 1 Engineered metabolite-driven REE solubilization. (a) Schematic illustration of three biological dissolution mechanisms: chelation, acidolysis, and reductive dissolution. Highlighted in blue are the catechol chelating groups; in green the hydroxamates; in pink the carboxylates and in orange the phenolates. The stereochemistry of the chemical structures of the siderophores presented is not specified. (b) SEM images of bastnaesite surfaces at the end of the leaching experiments [5]. Secondary-electron micrographs show etch pits and secondary precipitates in the vicinity of microbial cells (green arrows). (c) Corresponding EDS spectra are shown for the points marked with yellow circles. Reproduced with permission from Ref. [5], © Elsevier Ltd. All rights are reserved, including those for text and data mining, AI training, and similar technologies 2025. (d) Leaching efficiencies of Fe-REE ores by different microbial systems, including *Aspergillus niger* and *Acidithiobacillus ferrooxidans*, representing organic-acid secretion and sulfur-oxidation pathways, respectively. Reproduced with permission from Ref. [32], © Wang, M. et al. Licensee MDPI, Basel, Switzerland 2025.

In heterotrophic microbial systems, fungi (e.g., *Aspergillus* [20, 33], Penicillium [19]) and bacteria (e.g., *Bacillus* [34]), excrete low-molecular-weight organic acids such as citric, oxalic, and gluconic acid. These acids act as potent chelators that reduce the activation energy for dissolution and preferentially complex REE^{3+} ions, thereby enhancing their solubility from minerals such as monazite and bastnäsite [20]. In conventional hydrometallurgical leaching, strongly acidic chloride solutions with pH 1.8–3.7 are often required to mobilize REEs. For example, a solution at pH 1.8 can reach 19.2 mg/L of dissolved REEs. In comparison, microbial metabolite broths are effective at much milder acidity, typically between pH 2 and 6. Synthetic biology builds upon this foundation by regulating acidogenic metabolic fluxes, enhancing the stability of acid production at scale, and integrating acid secretion with pretreatment strategies for selective REE leaching, thereby systematically improving bioleaching performance [35].

Another microbial mechanism involves redox transformations of iron or sulfur, which indirectly promote REE release by altering the local geochemical environment [36]. Chemolithoautotrophic iron- or sulfur-oxidizing bacteria, for instance, acidify their microenvironment, while dissimilatory iron-reducing bacteria (e.g., *Shewanella*) facilitate the reductive dissolution of iron oxides, releasing associated REEs [37]. Synthetic biology interventions, such as overexpressing key oxidases, reductases, or electron transfer proteins, can amplify these natural pathways to achieve controlled and enhanced leaching [38, 39].

In addition, many bacteria produce siderophores, high-affinity iron-chelating compounds that also effectively bind trivalent lanthanide ions due to their similar coordination radii [40]. Recent studies confirm that these native metallophores can effectively mobilize REEs from solid matrices. The promise of synthetic biology lies in reprogramming siderophore biosynthesis pathways or even de novo designing custom "lanthanophores". The goal is to secrete molecules engineered for superior lanthanide affinity and selectivity, paving the way for highly effective bioleaching systems [29].

2.2 Molecular recognition and selective binding

Molecular recognition provides the foundation for achieving high selectivity in REE recovery. This approach utilizes proteins and

peptides capable of specifically identifying and binding REE ions in aqueous solutions, leveraging complementary binding sites that discriminate target ions based on subtle differences in ionic radius and charge characteristics.

The natural REE-binding protein LanM serves as a representative recognition element, exhibiting picomolar affinity for lanthanide ions and remarkable selectivity against common divalent cations, substantially advancing our understanding of biological REE recognition mechanisms (Fig. 2(a)) [41]. Through synergistic coordination via its EF-hand-like domains and second-sphere interactions, the protein discriminates metal ions based on differences in ionic radius and hydration energy [42]. Protein engineering is pivotal for transforming these natural blueprints into tailored separation tools. Efforts focus on tuning affinity, specificity, and stability for process conditions. A notable example is the development of *Hans*-LanM dimerization, where engineered variants create metal-dependent interfaces enabling single-stage separation of adjacent lanthanides, a task extremely challenging for conventional chemistry (Fig. 2(b)) [43]. For practical deployment, immobilized LanM on chromatographic supports enables the capture and mild elution of REEs, facilitating the fractionation of light from heavy REEs with minimal solvent consumption [44].

Beyond LanM, other natural protein scaffolds, such as the periplasmic protein LanD from *Methylorubrum extorquens*, further enrich the diversity of recognition elements, demonstrating that even initially weak chelating units can be engineered for high selectivity (Fig. 2(c)) [45]. Meanwhile, short lanthanide-binding peptides (LBTs), derived from LanM loops or discovered via phage display, offer advantages of low production cost, facile immobilization, and rapid binding kinetics (Fig. 2(d)) [46]. The binding affinity of these metal-binding proteins is the key determinant for both the efficiency and selectivity of rare-earth separation (Fig. 2(e)). Therefore, they can be grafted onto polymers, hydrogels, or membranes. Furthermore, fusing LBTs or LanM fragments to surface anchors on microbial cells creates living, high-surface-area adsorbents through cell display, compatible with packed-bed systems and offering inherent regenerability [47]. Beyond known proteins, bioinformatic analyses continue to identify novel candidate domains, such as the PepSY-containing protein lanpepsy, expanding the repertoire of scaffolds for the sustainable purification of REEs [48]. To fully exploit these scaffolds in practical applications, biosynthetic engineering aims to enhance acid/thermal stability, proteolysis resistance, and expression yields in scalable hosts.

In recent years, the scope of molecular recognition research has expanded from purified proteins to microbial surface structures [49]. Cyanobacterial matrices (e.g., *Nostoc sp.*) achieve adsorption capacities of 84–92 mg/g for Ce, Nd, Tb, and La under mildly acidic conditions [50]. Engineered microorganisms displaying customized binding motifs enable high-fidelity separation, yielding product streams with purities of 99.9% (Eu), 97.1% (La), and 92.7% (Dy) [51]. Microbial composite interfaces based on ferrous sulfide templates achieve approximately 68% REE recovery and exhibit strong affinity for heavy REEs such as Y [52]. Biopolymer-derived sorbents such as chitosan-ethylenediaminetetraacetic acid (EDTA)-gelatin materials reach ~ 189 mg/g and retain over 85%

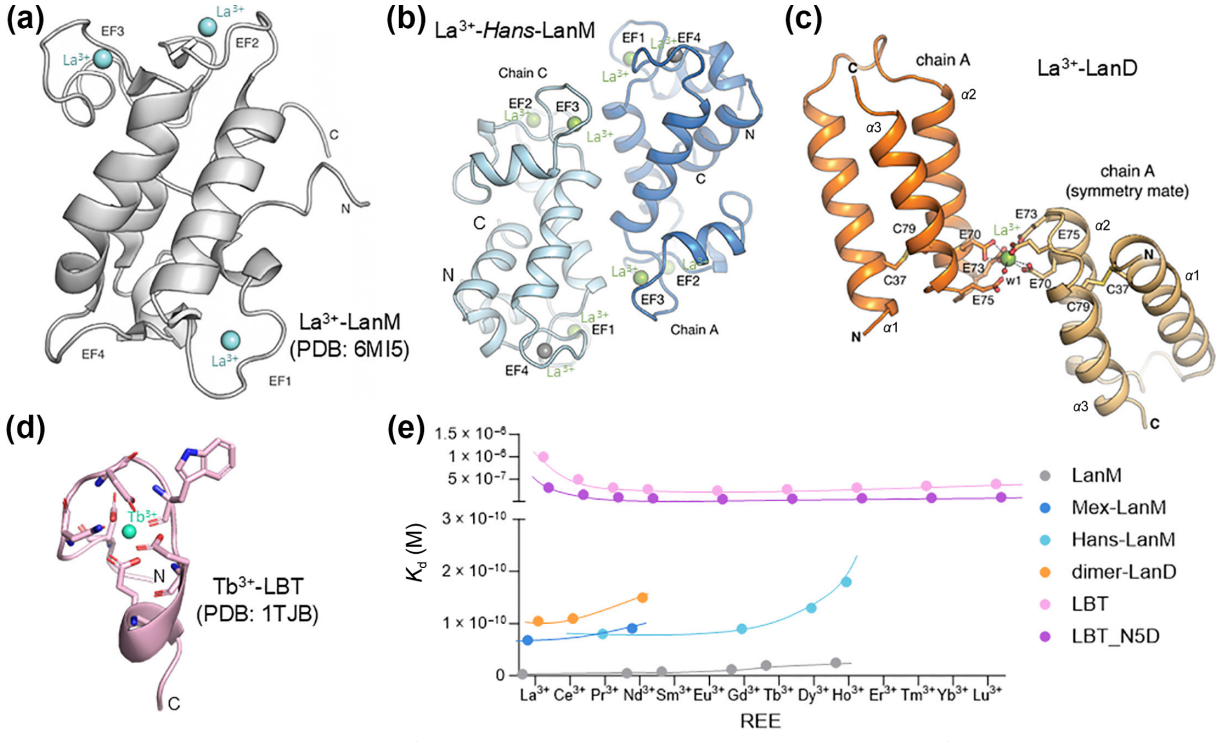


Figure 2 Molecular architectures and binding behaviors of representative lanthanide-binding proteins. (a) Crystal structure of La^{3+}-bound LanM (PDB: 6MI5), showing its four EF-hand-like motifs (EF1–EF4) arranged around three REE^{3+}-binding sites [41, 55]. Reproduced with permission from Ref. [55], © Elsevier Ltd. All rights are reserved, including those for text and data mining, AI training, and similar technologies 2025. (b) Dimeric structure of La^{3+}-bound *Hans*-LanM, in which inter-chain EF-hand cooperativity reshapes the overall binding topology and stabilizes multivalent metal engagement [43]. Reproduced with permission from Ref. [43], © Mattocks, J. A. et al. 2023. (c) Crystal structure of La^{3+}-LanD highlighting the helix–turn–helix architecture and the unique coordination environment formed by residues E70, E73, E75, and C79 [45]. Reproduced with permission from Ref. [45], © Larrinaga, W. B. et al. Published by PNAS 2024. (d) Structural model of a designed lanthanide-binding peptide LBT (PDB: 1TJB) showing its compact coordination geometry around Tb^{3+} [56]. (e) Representative binding curves illustrating the distinct affinity ranges of natural proteins (LanM, LanD), engineered variants (*Hans*-LanM), and designed peptides toward different lanthanides.

performance after 20 reuse cycles [53]. Phosphorylated yeast strains enable 10–19-fold enrichment of REEs from geothermal water, confirming the effectiveness of rational microbial surface design for specific capture of dilute REE species [54]. Collectively, these advances highlight the considerable potential of microbial interfaces as modular, high-performance adsorption platforms for REE recovery from complex resources.

2.3 Biomacromolecular devices and functional materials

Synthetic biology is advancing REE bioprocessing beyond simple soluble binders toward integrated, functional biomacromolecular devices [64]. These systems embed biologically derived recognition elements, such as proteins, peptides, or entire cell surfaces, into solid-state matrices or functional units. They can then perform device-level operations, including solid-phase adsorption, flow-through capture, membrane separation, and stimulus-responsive release. This integration translates exquisite molecular specificity into engineered processes, effectively bridging the gap between laboratory discovery and industrial biorefining (Table 2).

The programmability of peptides enables the creation of customized binding interfaces on solid supports. For instance, machine learning-assisted optimization of peptides inspired by native binding loops of LanM has yielded polymer-composite adsorbents that enhance Dy purity from 5% to 83% in Nd/Dy separation systems while accelerating binding kinetics [43]. To translate molecular recognition into practical process modules, various innovative immobilization strategies have been developed, including LanM immobilized on agarose microbeads (Fig. 3(a)) [44] or magnetic nanoparticles (Fig. 3(b)) [47], peptide-functionalized polymer scaffolds [65], and recombined protein materials [62]. For instance, LanM functionalized magnetic nanoparticles exhibit rapid kinetics, > 90% desorption efficiency, and multi-cycle stability, proving that immobilization preserves bio-selectivity while enabling engineering-level operation [47, 66].

Engineered microbial cells represent a class of macroscale biomacromolecular devices, where the entire cell surface or envelope functions as a high-density and multifunctional sorbent. Surface display of LBTs or LanM fragments on *Escherichia coli* (Fig. 3(c)) [61, 67], *Bacillus subtilis* [68] or *yeast* [60] creates robust and regenerative biosorbents with capacities (10–100 mg REE per gram dry cell weight) comparable to purified proteins. Owing to the protective cell wall, these whole-cell devices exhibit high tolerance to harsh pH conditions and complex matrices, making them suitable for packed-bed or membrane bioreactor systems. Certain bacterial systems, such as *Shewanella oneidensis*, offer an integrated bioleaching-biosorption function [38]. They naturally secrete organic acids and siderophores that solubilize REEs from minerals, while their extracellular polymeric substances rich surfaces concurrently bind the liberated ions, enhancing overall recovery by 30%–60% compared to abiotic controls.

To enhance stability and introduce environmental responsiveness, researchers have developed recombinant

Table 2 Biomacromolecular based devices for REEs separation

System	Matrix	Resource	Adsorption capacity	Desorption efficiency	Cycles tested	pH	Strategic application	Ref.
Immobilized LanM column	Amine-functionalized agarose beads	Synthetic leachates; mixed REE solutions	5.77 ± 0.67 μmol REE per mL resin	88.2 mol% REE purity	10 cycles	pH > 3.0 absorption/ pH < 2.5 desorption	High-purity separation	[44]
Immobilized LanM column	Amine-functionalized agarose beads	Mixed lanthanide solutions; Sc/Y containing leachates	~ 90% of the column capacity	88 mol% purity	10 cycles	pH 3.0 absorption/ pH 1.5 desorption	High-purity separation	[57]
Immobilized SpyCatcher-LanM nanoparticle	Magnetic nanoparticle	Buffer; model REE solutions; simulated waste leachates	6.01 ± 0.11 μmol Tb^{3+} per gram sorbent	> 95% desorption	8 cycles	pH ~ 5 absorption/ pH < 2.0 desorption	Rapid capture and separation	[47]
Immobilized LanM EF-hand loop 1 nanoparticle	Gold nanoparticle	Model REE solutions	~ 3.5 μmol REE per gram gold nanoparticle surface	—	—	pH > 5.5 absorption/ pH < 2.5 desorption	High-density capture	[58]
Caulobacter crescentus-surface display LBT	Cell surface	Acid leachates/model solutions	12.9 ± 4.6 μM Tb^{3+} adsorbed amount	—	3 cycles	pH 6.0 absorption/ 1–5 mM citrate desorption	High-capacity biosorption	[59]
Yarrowia lipolytica-surface display LanM	Cell surface	Single REE solutions	48.7–50.4 mg REE per gram dry cell weight	—	—	pH 4.0 absorption/ pH 2.0 desorption	High-capacity biosorption	[60]
Escherichia coli surface display LBT	Cell surface	Model solutions/ simple leachates	12 mg REE per gram dry cell weight	~ 80 mol% purity	10 cycles	pH 5 absorption/ pH 1.7 desorption	High-capacity biosorption	[61]
Thermo-responsive genetically encoded polypeptide	Elastin-like polypeptide	Model REE solutions; coal fly ash leachates	366.2 μg REE per mL sorbent	—	8 cycles	pH 5.8 absorption/ pH 2.2 desorption	Green elution via thermal stimulus	[62]
Supramolecular Assembly of LBT variant peptide	LBT peptide	REE pairs solution	—	—	5 cycles	pH 5.8 absorption/ pH 2.0 desorption	Exploratory platform for interfacial REE separation	[63]

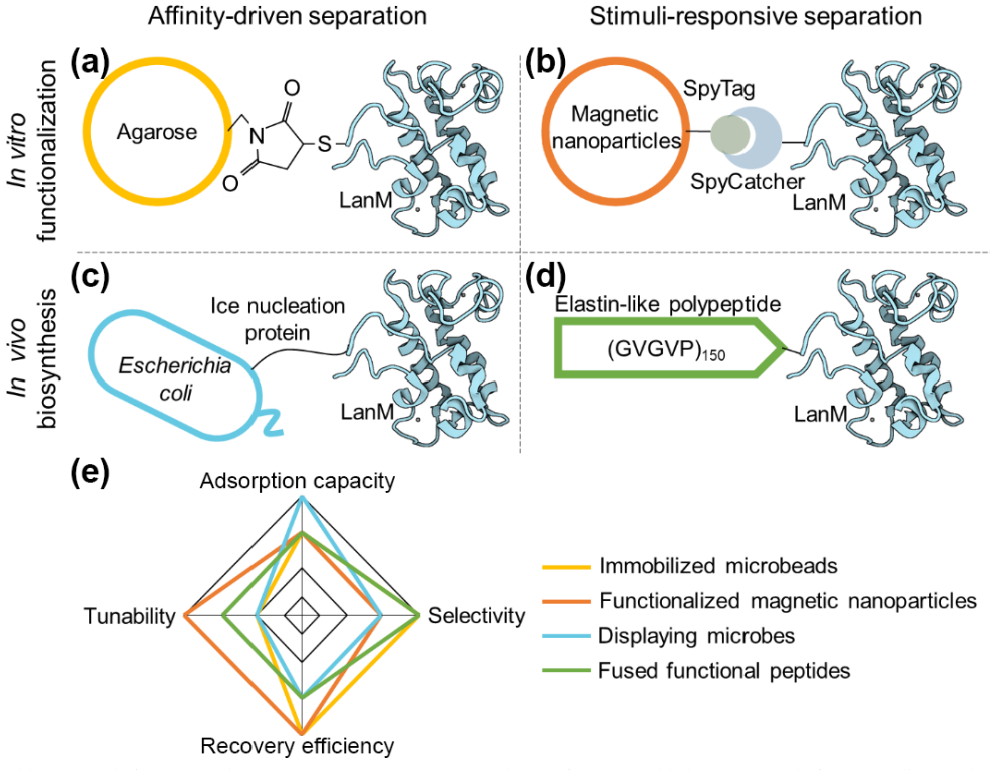


Figure 3 Protein-based biomaterials for rare-earth separation. Four representative classes of LanM-enabled separation platforms are illustrated: (a) LanM-immobilized agarose microbeads, where purified LanM is covalently coupled to agarose for affinity-based REE capture [44]. (b) LanM-modified magnetic nanoparticles, which combine LanM binding with magnetic responsiveness for rapid and controllable separation [47]. (c) LanM-displayed microbial systems, in which engineered cells express LanM on the surface to enable whole-cell biosorption [61]; and (d) LanM-fused functional peptides, where LanM is genetically fused to phase-transition or assembly-responsive peptides (e.g., elastin-like sequences) to enable stimulus-controlled recovery [62]. (e) Semi-quantitative radar plot comparing the relative performance of the four platforms across four metrics: binding affinity, selectivity, regeneration feasibility, and process scalability.

protein–polymer hybrid materials. A prominent example is the fusion of LanM with elastin-like polypeptides, which enables thermally reversible aggregation (Fig. 3(d)) [62]. This allows for pure temperature-driven adsorption-desorption cycles, eliminating the need for corrosive acid eluents and drastically reducing chemical waste. Engineered LanM variants have also found uses beyond separation. For instance, the LanM mutant (LanND-Gd) shows markedly improved relaxation efficiency, which highlight the broader adaptability of LanM-derived scaffolds while remaining complementary to their separation-focused applications [69].

The integration of biomolecules with advanced materials has led to hybrid devices that combine biological precision with engineering robustness and stimulus responsiveness (Fig. 3(e)). Immobilizing LanM [66] or LBTs [70] on iron-oxide nanoparticles creates magnetic sorbents that achieve rapid adsorption equilibrium (< 30 min) and enable easy, low-energy separation and recycling. Similarly, LanM1 peptide-conjugated gold nanoparticles selectively adsorb various REE ions (Ce, Nd, Eu, Y) with a capacity of approximately 3.5 μmol/g [58]. Expanding this device concept, microbial encapsulation represents a shift from molecular to living functional units. For instance, the confinement of engineered bacteria within porous matrices creates a living sorbent that not only exhibits high selectivity but also maintains metabolic activity for continuous regeneration, offering a robust and sustainable route for REE recovery from complex real-world streams [71]. These nanomaterials, characterized by a high surface-area-to-volume ratio, minimal diffusion barriers, and interfacial properties that promote local ion enrichment, significantly enhance the performance of immobilized biorecognition elements (e.g., LanM, LBTs). This improvement is reflected not only in a higher density of functional sites and faster reaction kinetics but also enhanced efficiency in capturing REEs from low-concentration leachates.

A frontier in the field is the development of digital biomacromolecular devices for single-ion discrimination. Pioneering work has engineered the *Mycobacterium smegmatis* porin A nanopore to resolve individual REE ions based on their distinct current-blockade signatures [72]. Assisted by machine learning pattern recognition, this system can distinguish all 14 lanthanides with accuracies up to 99.6% [73]. Although primarily a sensing platform at present, this technology lays the foundation for future devices capable of electrophoretic sorting at the single-ion level.

3 Applications for different rare earth resources

Synthetic biology-enhanced bioprocessing technologies have demonstrated significant potential across multiple resource types, offering a new approach for sustainable and highly selective recovery of REEs [74]. This section focuses on applications at both ends of the resource spectrum — low-grade geological residues and anthropogenic waste streams. Although these resources differ in mineralogy and matrix complexity, they share a common biological processing framework: biolixiviant-driven dissolution followed by biomolecular purification under mild conditions.

3.1 Ores and tailings

Primary ores and mining tailings constitute the largest long-term

reservoir of REEs, yet their conventional processing remains environmentally costly and chemically intensive. Declining ore grades and highly heterogeneous mineral matrices, typically 0.1–5 wt% REEs in ores [75] and < 1% in tailings [76], developing low-energy, high-selectivity extraction processes has become increasingly urgent (Fig. 4(a)). Although tailings pose substantial environmental challenges, they remain a valuable secondary reservoir. Recent analyses suggest that circular-economy strategies could increase secondary REE supply by 701 kt and reduce primary demand by 2306 kt over the next three decades [77].

The chemical speciation of REEs in ores dictates the barriers to their liberation. Ion-adsorption clays host hydrated REE^{3+} on weakly bound edge sites, historically extracted by ammonium sulfate leaching, yet requiring substantial reagent consumption and generating ammonium-rich effluents [78]. Bastnaesite [$RECO_3F$] requires proton attack and ligand complexation, whereas monazite and xenotime incorporate REEs in phosphate lattices that resist dissolution except under high acidity or elevated temperature [79]. Scandium in red mud (80–120 ppm) is dispersed in Fe-oxides and aluminosilicates, becoming mobile only when the Fe phase is dissolved or reduced [80]. These mineralogical constraints limit the feasibility of green leaching unless new catalytic or biological routes are introduced.

Synthetic biology enables the design of biolixiviants tailored to the mineralogical characteristics of specific REE ores. For example, engineered *Acidithiobacillus ferrooxidans* with regulated sulfur oxidation can generate controlled sulfuric acid titers, enhancing bastnaesite dissolution while avoiding over-acidification [32]. Heterotrophic chassis such as *Bacillus megaterium*, *Gluconobacter oxydans*, *Aspergillus niger* and *Shewanella oneidensis* have been optimized to secrete organic acids, such as citrate, lactate, oxalic acid and gluconate, that both acidify microenvironments and form strong REE-organic complexes, significantly enhancing dissolution of fluorocarbonates and clays [18]. Beyond acidogenic pathways, siderophore-producing microbes such as *Pseudomonas fluorescens* mobilize REEs from phosphate-hosted minerals through ligand-assisted dissolution [29, 40]. Complementing this strategy, iron-reducing microbes like *Shewanella oneidensis* enhance scandium liberation by reductively solubilizing Fe-hydroxide matrices [38]. Surface-display systems further extend biological control by concentrating lanthanides at cell surfaces, accelerating desorption from dilute solutions such as geothermal fluids and seawater [54, 81].

Following biolixiviant-driven release, the resulting leachates from ores and tailings remain chemically complex, typically containing high concentrations of Ca^{2+}, Mg^{2+}, Al^{3+}, Fe^{3+}, and Mn^{2+}. Biomolecular separation technologies provide a uniquely selective purification step under mild conditions. Immobilized LanM has emerged as a benchmark biosorbent: its picomolar affinity, fast kinetics, and exceptional REE selectivity (> 10^8 over Ca/Mg) are retained upon anchoring to solid supports [55]. Synthetic-biology-guided tuning of metal-binding residues has enabled intra-lanthanide fractionation, producing separated light rare earth elements (LREE), heavy rare earth elements (HREE), and Y/Sc fractions through gentle elution with citrate or malonate [44]. Beyond LanM, engineered lanthanide-binding peptides, peptide amphiphile films, and biomimetic polymer-biomolecule hybrids provide interfacial concentration steps that reduce downstream solvent volumes [46, 82, 83].

These biological and biomolecular tools can be integrated into modular ore-processing flowsheets. In integrated process designs, pre-columns can remove humic substances, while sacrificial

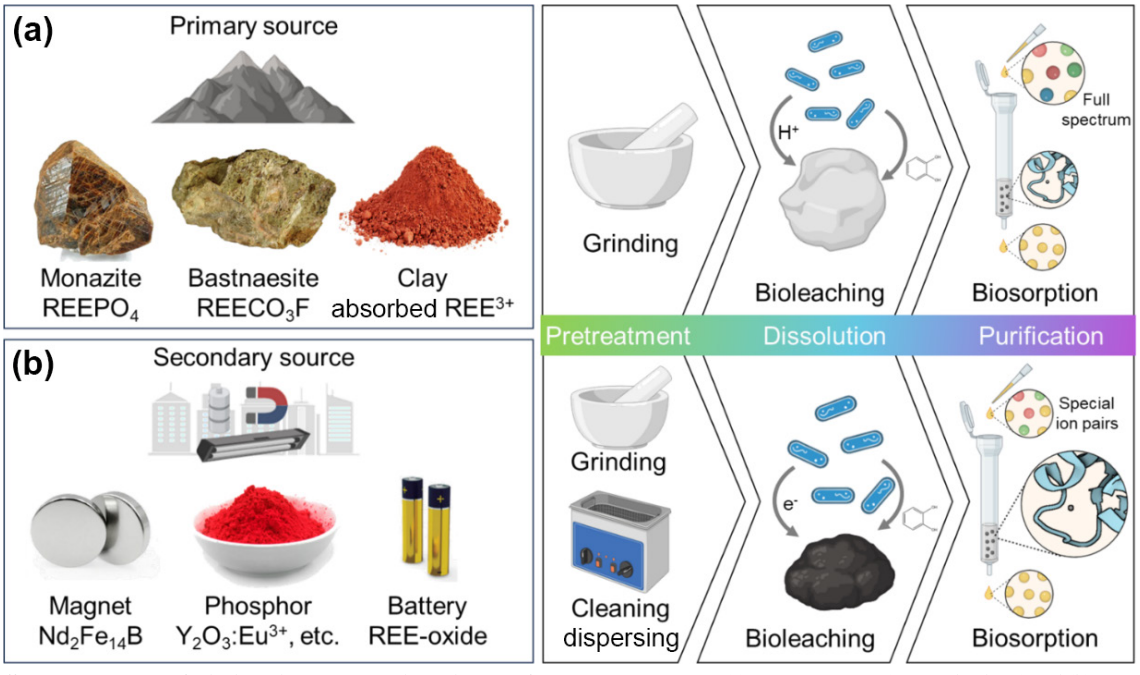


Figure 4 Different REE resources for biological processing and REE biomanufacturing. Representative (a) primary sources (ores and tailings) and (b) secondary sources (NdFeB magnets, phosphors, and battery scraps) illustrating the differences in grade, mineralogical form, and matrix complexity. Despite distinct origins, both resource classes follow the same downstream bioprocess after pretreatment. Pretreatment (grinding or mechanical liberation) exposes REE-bearing phases; biological dissolution uses microbial metabolism (organic acids, sulfur/iron cycling, or siderophores) to solubilize REEs; and purification employs biomolecular capture modules such as LanM-based binders or engineered affinity media. The unified workflow highlights the broad applicability of synthetic-biology-enabled REE recovery across diverse resource types. Image credits: monazite photo © The Arkenstone/iRocks.com (photo by Rob Lavinsky), reproduced with permission; bastnaesite photo by Kouame, licensed under CC BY-SA 3.0 via Wikimedia Commons.

cartridges capture colloidal Fe and Al species before biomolecular capture. In-line sensing further enables real-time monitoring of breakthrough and binding-state transitions, thereby extending the operational lifetime of affinity media [84, 85]. Collectively, synthetic biology is establishing a comprehensive "ore-to-metal" technological framework encompassing mineral-specific bioleaching, high-selectivity biomolecular capture, and scalable aqueous purification. This marks a fundamental shift from brute-force acid leaching toward precision, low-carbon bio-refining of ore and tailing resources.

3.2 End-of-life and industrial wastes

Secondary resources (e-waste, magnets, phosphors, coal ash) are increasingly attractive because they contain REE concentrations several times higher than natural ores [86]. However, these materials exhibit complex matrices requiring multi-step chemical pre-treatment [87] (Fig. 4(b)). In black mass from batteries, lithium, cobalt, and nickel occur in layered oxides, such as those found in nickel manganese cobalt batteries. The powder also contains graphite, binder, salt, and aluminum foil. In NdFeB magnets, neodymium and dysprosium occur in an iron-boron alloy. In lamp phosphors and polishing powders, rare earths, gallium, and indium occur as stable oxides or phosphors.

Current REE recycling from secondary sources predominantly relies on combined pyrometallurgical [88] and hydrometallurgical [89, 90] approaches. Conventional recycling routes involve either high-temperature treatment at approximately 1000 °C or multi-step purification via ambient-temperature leaching, precipitation, and solvent extraction/ion exchange. These limitations have motivated growing interest in biological recovery strategies that can reduce chemical consumption and energy input while improving selectivity [91]. Microbial hydrometallurgy provides a promising alternative for recovering REEs from low-grade materials. *Thiobacillus ferrooxidans*, for example, achieves leaching efficiencies of 83% for La and 23% for Ce from spent fluid catalytic cracking catalysts [92]. In coal fly ash, *Candida bombicola* [23] yields leaching efficiencies of 37%–76% for Y, La, and Ce, while optimized pH conditions for *Aspergillus niger* [21] lead to total REE leaching of approximately 31%.

Permanent magnets from end-of-life electronics represent a major REE reservoir, and their Nd and Dy concentrations often exceed several tens of weight percent. Synthetic biology strategies applied here include chemical pretreatment and bioseparation. Dissolution of NdFeB in mild acid followed by LanM-based column capture allows selective recovery of Nd and Dy without harsh organic solvents [93]. Engineered LanM dimers (*Hans*-LanM) enable single-column separation of Nd vs Dy with > 98% purity [43]. This method offers strong environmental and economic advantages, including lower chemical consumption, milder operating conditions, and fewer purification steps.

E-waste streams such as printed circuit boards and magnets contain multiple REEs including Nd, Pr, Ce, Y, and Eu. These can be targeted using LanM or peptide-based binding modules immobilized on microbeads or membranes, enabling selective biosorption from polymetallic leachates [94]. Engineered microbial accumulation, where cells uptake REEs, concentrate them, and are harvested for downstream processing [95]. According to a recent review, lanmodulin-derived peptides (e.g., LanM1) have been immobilized on biosorbents to selectively extract REEs from e-waste streams with promising selectivity and regeneration potential [91].

Fluorescent lamp phosphors, rich in Y, Eu, Tb, and other REEs, are processed via fungal or bacterial leaching to dissolve the phosphor matrix [22, 33, 96]. The deployment of LanM or peptide-based biosorbents enables the highly specific capture of target ions (Y, Eu, Tb) from the leachate. Furthermore, these sorbents undergo iterative regeneration without loss of binding affinity, thereby enabling highly efficient cyclic processing [97]. Iterative regeneration of these adsorbents allows cyclic operation, further enhancing process economics and environmental compatibility.

4 Challenges and future outlook

Although substantial laboratory-scale progress has been made, industrial deployment of synthetic-biology-enabled REE recovery requires overcoming challenges in scalability, integration, and selectivity.

4.1 Scaling biomolecular performance into robust processes

A major challenge is translating the high performance of engineered biomolecules into robust industrial operations. Cost-effective manufacturing requires microbial hosts optimized for high-yield protein or peptide expression and streamlined purification workflows. Simultaneously, these biological components must be integrated in a whole microbial metabolism or transformed into durable materials [98]. Immobilization on robust supports is essential, but these composites must resist denaturation, proteolytic degradation, and fouling over hundreds of adsorption-desorption cycles in complex leachates [99]. To achieve this, it is critical to address the root causes of capacity loss over cycles, which primarily include the denaturation of proteins under harsh elution conditions, the gradual leaching of ligands from the solid matrix, and the fouling of active sites by contaminants. Furthermore, the ultimate test of scalability is continuous operation. Moving from batch to continuous processes, using fixed-bed or membrane reactors, is vital for industrial throughput and necessitates biomaterials engineered for consistent performance under constant flow [100].

4.2 Achieving system-level integration and selectivity

The value of a biosorptive process depends not only on binding affinity but also on its ability to deliver high-purity products within an integrated flowsheet. Although tools such as the *Hans*-LanM dimer represent major progress, further engineering is required to achieve the purities needed for commercial intra-lanthanide separation [43]. Beyond this, biosystems must maintain selectivity against competing ions (e.g., Ca^{2+}, Fe^{3+}, Al^{3+}) prevalent in real resources like tailings and e-waste [101]. Success in this arena enables practical process integration, where biological capture steps must be seamlessly interfaced with upstream leaching and downstream finishing operations (e.g., precipitation) [102]. Demonstrating compatibility with upstream leaching and downstream precipitation will require rigorous techno-economic and environmental assessments.

4.3 Forging the next generation of bio-recovery technologies

Several emerging directions promise to advance the field beyond current limitations. Machine-learning-guided protein and peptide design is accelerating the creation of binders with tailored affinity

and specificity, supported by high-throughput screening and directed evolution [103]. Autonomous biological systems, such as microbes engineered to secrete lanthanophores for simultaneous leaching and capture, offer opportunities for fully integrated biorecovery. Smart biomaterials, including elastin-like polypeptide fusions, enable environmentally benign release triggered by temperature or pH [62]. Finally, engineered living materials and consortia provide a route to self-renewing systems capable of performing leaching, binding, and regeneration within a single resilient platform.

5 Conclusions

Rare earth element recovery is undergoing a transformative shift where conventional hydrometallurgy is being complemented by biology-enabled, molecular-precision strategies. Whereas traditional acid leaching and solvent extraction are limited by high reagent consumption and modest selectivity, synthetic biology now enables the design of programmable recognition motifs, catalytic pathways, and sustainable biomaterials with far lower environmental impact.

Collectively, engineered proteins, peptides, microbial systems, and biomacromolecular devices form a coherent technological framework for next-generation biorefining. These platforms demonstrate capabilities once considered unattainable for biological systems, including sub-picomolar affinity, single-ion discrimination, and continuous operation in both living and immobilized configurations. Their applicability across primary ores, tailings, and diverse waste streams reinforces the potential for building a circular and resilient REE supply chain.

The convergence of synthetic biology, computational protein design, and advanced process engineering is accelerating the development of scalable reactors and integrated hybrid flowsheets. Although challenges in kinetics, chemical stability, and large-scale integration persist, the integration of molecular design with process-level engineering establishes a technically sound and environmentally sustainable pathway for securing the critical metals essential to modern energy and manufacturing systems. Looking forward, the technological framework established for REEs—programmable recognition, engineered biosynthesis, and hybrid device fabrication—offers a blueprint adaptable to other critical metals (e.g., cobalt, gallium, indium). Success will hinge on tailoring the molecular binding sites to the distinct coordination chemistry of each target, yet the core synthetic biology strategies remain powerfully applicable. This broader potential underscores the role of biological engineering in building a more sustainable and circular metabolism for diverse critical materials.

Data availability

All data needed to support the conclusions in the paper are presented in the manuscript. Additional data related to this paper may be requested from the corresponding author upon request.

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Declaration of competing interest

All the contributing authors report no conflict of interests in this work.

Author contribution statement

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Informed consent

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During the preparation of this work, the authors used DeepSeek in order to improve the writing fluency. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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