

RANDOM SEARCH

Table 7.1 Comparison of guided and random searches

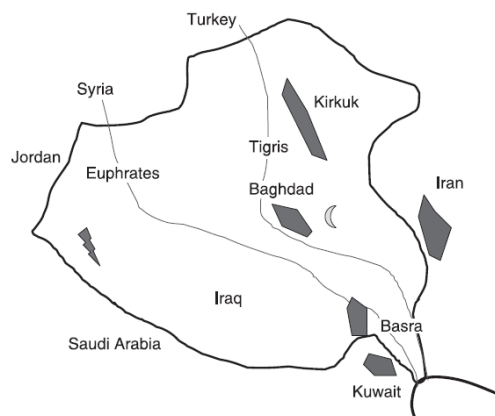
<i>Guided search (e.g., freon)</i>	<i>Random search (e.g., taxol)</i>
Depends on a large database and reliable theory	Does not require much database and theory
Requires a few creative experts	Must be carried out by a large enough crew; needs much money, time, and luck
Experts need much education and creativity	Crew does not need very much education and creativity
Concentrates only on a few target areas	Casts a wide net over a large territory
More quick and sure of results, when you know what you are doing and where you are going	Less certain of results, and may be very costly in time and resources
Strong guidance can work as blinders to prevent discoveries of new territories, especially when theory is wrong or not comprehensive enough	Can stumble upon unexpected findings and open brand new territories not related to previous experience or theory

Starting Point and Promising Directions

Starting point → Lead compound that has some desired properties

Explores around the lead compound using small amount of additives, blending with other material, changing processing condition and temperature, changing structure of chemical reaction.

Convergent or Cluster Strategy



Exploration of new oil wells → 1 successful well for 10 wells drilled
Incremental drill and wildcat drill

Drug Search

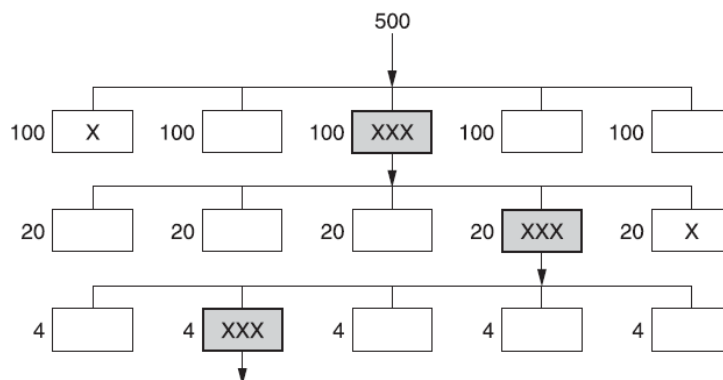
Starting point → existing product or new discovery that has some of desired properties but deficient in other critical properties.

Starting point → Lead Compound
Subsequent search around it → Lead optimization

Closely related molecular structures → closely clustered properties

Cluster Strategy

→ Convergent search



Divergent or Wildcat Strategy

→ When the province around the lead compound has been exhaustively explored

Pioneer → virgin territory approach

Example:

1940, drug search around morphine → had no promising

Methadone → many properties of morphine → totally different and unrelated structure

Combinatorial Chemistry

→ Drug discovery and high performance chemistry

Bruce Merrifield (1963) → Solid phase peptide synthesizer machine → Nobel prize in chemistry 1984

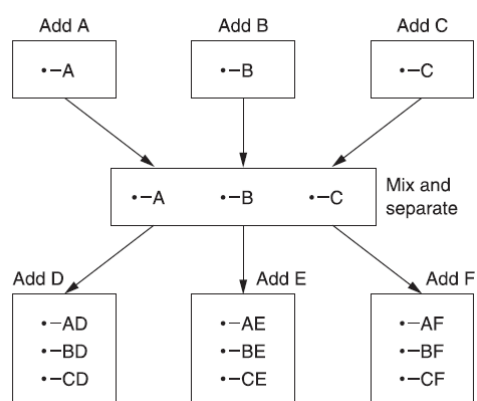
Combinatorial chemistry

→ Parallel synthesis: Simultaneous synthesis of numerous product

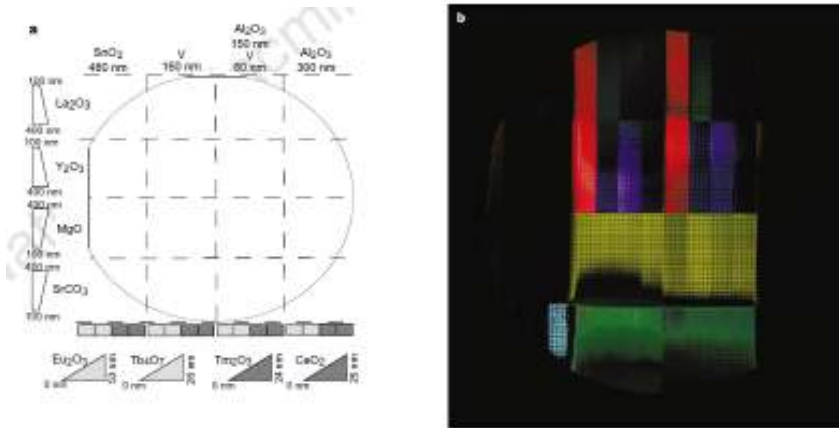
→ Combinatorial synthesis: Numerous reaction within one single reaction vessel followed by separation

Mix and Split Method

Pioneered by Furka in 1988



Case Study: A combinatorial approach to the discovery and optimization of luminescent materials NATURE | VOL 389 | 30 OCTOBER 1997



Case Study: DSSC

